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

FORM 10-K

(Mark one)

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

For the fiscal year ended December 31, 2021 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 001-33876

Athersys, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**20-4864095**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
3201 Carnegie Avenue, Cleveland, Ohio	**44115-2634**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code (216) 431-9900

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

Title of each class	Trading Symbol	Name of each exchange on which registered
Common Stock, par value $0.001 per share	**ATHX**	**The NASDAQ Stock Market LLC**

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

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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 Securities Exchange Act of 1934. 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 is a shell company (as defined in Rule 12b-2 of the Act). Yes ☐ No ☒

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. ☐

The aggregate market value at June 30, 2021, the last business day of the registrant's most recently completed second fiscal quarter, of shares of the registrant's common stock (based upon the closing price per share of $1.44 of such stock as quoted on the NASDAQ Capital Market on such date) held by non-affiliates of the registrant was approximately $185.1 million.

The registrant had 243,980,180 shares of common stock outstanding on March 9, 2022.

Documents Incorporated By Reference.

Part III of this Annual Report on Form 10-K incorporates by reference certain information from the registrant's definitive proxy statement with respect to the 2022 annual meeting of stockholders.

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ATHERSYS, INC.

Unless otherwise stated or the context otherwise indicates, all references in this Annual Report on Form 10-K to "Athersys," "us," "our," "we" or "the Company" mean Athersys, Inc. and its subsidiaries.

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PART I

ITEM 1. BUSINESS

We are a biotechnology company that is focused primarily in the field of regenerative medicine. We are committed to the discovery and development of best-in-class therapies designed to extend and enhance the quality of human life and have established a portfolio of therapeutic product development programs to address significant unmet medical needs in multiple disease areas. Our MultiStem® (invimestrocel) cell therapy, a patented and proprietary allogeneic stem cell product candidate, is our lead platform product and is currently in late-stage clinical development. Our most advanced therapeutic program is focused on the treatment of ischemic stroke, which is currently being evaluated in a potential registrational trial in Japan and a pivotal Phase 3 clinical trial ongoing in North America under a Special Protocol Assessment, or SPA, Europe and certain other international locations. All of our current clinical development programs are focused on treating critical care and other conditions where current standard of care is limited or inadequate for many patients. These represent major areas of clinical need, as well as substantial commercial opportunities.

We believe our MultiStem cell therapy product candidate represents a potential breakthrough in the field of regenerative medicine and stem cell therapy and could be used to treat a range of disease indications. MultiStem treatment has shown the potential to enhance tissue repair and healing in multiple ways, including reducing inflammatory damage, protecting tissue that is at risk following acute or ischemic injury, and promoting formation of new blood vessels in regions of ischemic injury. These cells appear to be responsive to the environment in which they are administered, by homing to sites of injury and/or organs involved in injury response and providing active disease response. These cells also produce proteins that may provide benefit in both acute and chronic conditions and regulate other cell types. In contrast to traditional pharmaceutical products or biologics that generally act through a single biological mechanism of action, MultiStem cell therapy may enhance healing and tissue repair through several distinct mechanisms acting in parallel, resulting in a more effective therapeutic response.

We believe the therapeutic and commercial potential for MultiStem cell therapy to be very broad, applying to many areas of significant unmet medical need, and we are pursuing opportunities in several potential multi-billion dollar markets. While traditional pharmaceuticals and biologic therapies typically may be used to treat only a single disease or a narrowly defined set of related conditions, MultiStem cell therapy may have far broader potential and could be developed in different formulations and with different delivery approaches to effectively treat a wide range of disease indications.

The MultiStem product candidate under development may be unique among regenerative medicine approaches because it has the potential to be manufactured on a large scale, can be administered in an "off-the-shelf" manner with minimal processing, and has the potential to augment healing by providing biological potency and therapeutic effects that other cell therapy approaches may not be able to achieve. Additionally, MultiStem treatment has consistently demonstrated good tolerability in both preclinical and clinical studies. Like conventional drugs and biologics, the product candidate is cleared from the body over time, which we believe may enhance product safety relative to other types of stem cell therapy. While the product candidate does not permanently engraft in the patient, the therapeutic effects of treatment with MultiStem cells appear to be durable based on both clinical and preclinical results.

We have evaluated the use of MultiStem cell therapy as a potential treatment in several disease areas. Working with an international network of leading investigators and prominent research and clinical institutions, and through our own internal efforts, we have explored the potential for MultiStem cell therapy to be used as a treatment of acute and chronic forms of neurological conditions or injury, inflammatory and immune disorders, certain pulmonary conditions and cardiovascular disease. We have advanced several MultiStem programs into clinical development, targeting areas of significant medical need and major commercial market opportunities, and have three ongoing clinical trials in the critical care area. We have a collaboration with HEALIOS K.K., or Healios, to develop and commercialize MultiStem for the treatment of certain indications in Japan. Among other things, Healios has a license to our technology and is responsible for the development and commercialization of MultiStem for ischemic stroke and acute respiratory distress syndrome, or ARDS, in Japan on an exclusive basis.

Our lead program is our pivotal Phase 3 clinical trial to evaluate the potential for MultiStem treatment of patients who have suffered neurological damage from an ischemic stroke entitled, "*MultiStem Administration for Stroke Treatment and Enhanced Recovery Study-2,*" or MASTERS-2. The results from our completed Phase 2 study demonstrated favorable tolerability for MultiStem, consistent with the results from prior studies. Though the Phase 2 study did not achieve the primary endpoints for the intent-to-treat population, MultiStem treatment was associated with lower rates of mortality and life-threatening adverse events, infections and pulmonary events, and a reduction in hospitalization and time in the intensive care unit, or ICU. In addition, analyses show that patients who received MultiStem treatment earlier in the study's treatment window (24 to 36 hours post-stroke, in accordance with the original study protocol) had better recovery in comparison to placebo. Furthermore, analysis of biomarker data obtained from samples of study subjects indicated that MultiStem treatment reduced post-stroke inflammation compared to placebo, and the results suggest that this effect was more pronounced for subjects who received MultiStem earlier within the treatment window. This effect is consistent with our hypothesis regarding mechanisms of action

and related preclinical data, and with the clinical data suggesting faster and improved recovery for MultiStem-treated patients relative to current standard of care.

The one-year follow-up data from the Phase 2 trial demonstrated that MultiStem-treated subjects on average continued to improve through one year and had a significantly higher rate of "Excellent Outcome," as defined below, compared to placebo subjects at one year when evaluating all of the intent-to-treat subjects enrolled in the study. Achievement of an Excellent Outcome is important because it means that a patient has substantially improved (i.e., receiving an "Excellent" score in each of the three clinical rating scales used to assess patient improvement) and has regained the ability to live and function independently with a high quality of life. The relative improvement in Excellent Outcome was even more pronounced in the study subjects who received MultiStem treatment within 36 hours of the stroke. If the MultiStem cell therapy candidate is proven effective in our ongoing Phase 3 registrational study, and if it receives a marketing authorization from the United States Food and Drug Administration, or FDA, this treatment window and its favorable administration profile would make this therapy available to most ischemic stroke patients in contrast to other therapies (e.g., tissue plasminogen activator, or tPA, or mechanical thrombectomy), which have shorter treatment windows or are limited to certain patients.

Our MASTERS-2 trial treating ischemic stroke patients is ongoing in the United States and certain other international locations. We received agreement from the FDA under a SPA for the design and planned analysis of MASTERS-2, meaning that the trial is adequately designed to support a Biologic License Application, or BLA, submission for registration if it is successful. The FDA also granted us Fast Track designation for our clinical product for the treatment of ischemic stroke. Fast Track is an important designation given to qualified investigational therapies that show promise in providing benefit to patients in areas of significant unmet medical need. Fast Track designation allows for an expedited regulatory review process after the clinical data is submitted to help speed development of promising therapies to the market in order to help patients in areas where current standard of care is limited. Such designation for a new biologic product means that the FDA will take such actions as are appropriate to expedite the development and review of our application to approve the product, and specifically, under Fast Track designation, the program becomes eligible for rolling submission, accelerated approval and priority review of the BLA, facilitating a timely regulatory review. This program subsequently received the Regenerative Medicine Advanced Therapy, or RMAT, designation from the FDA that was established under the 21st Century Cures Legislation. The RMAT designation may be obtained for eligible cell therapy and other regenerative medicine and advanced therapies when the FDA agrees that preliminary clinical evidence indicates that the therapy has demonstrated the potential to effectively address unmet medical needs for a serious or life-threatening disease or condition. The RMAT designation is the equivalent of the non-regenerative medicine product's Breakthrough Therapy designation, and designated products benefit from all Breakthrough Therapy features. The designation enables sponsors to discuss with the FDA multidisciplinary strategic development plans, including expediting manufacturing development plans for commercialization to support priority review and accelerated approval.

The design of MASTERS-2 has also received a Final Scientific Advice positive opinion from the European Medicines Agency, or EMA, representing the EMA's agreement that successful results from the trial could result in registration and marketing approval of the MultiStem cell therapy. This positive opinion provides further alignment among the key regulators regarding potential commercialization of the MultiStem product candidate upon success of this single pivotal trial. We believe these designations could accelerate the development, regulatory review and subsequent commercialization of products, like MultiStem cell therapy for ischemic stroke and ARDS, if future clinical evaluation demonstrates appropriate safety and therapeutic effectiveness.

Enrollment in our MASTERS-2 study is ongoing. In prior periods, we have faced challenges to clinical site initiations, as well as patient screening and enrollment, due to the COVID-19 pandemic and supply interruptions, among other things. As COVID-19 case numbers decline and supply has stabilized, we have undertaken initiatives intended to accelerate new site openings in the U.S. and abroad and increase patient enrollment at sites currently open, including by addressing site-specific operations and inventory management issues. These plans are intended to enable us to finish enrollment of the MASTERS-2 study by the end of 2022 or as soon as possible thereafter; however, completion continues to depend on the impact of the results of Healios' TREASURE study, discussed below, and the possible resurgence of COVID-19. We would expect, for instance, that favorable TREASURE study results would have a positive effect on site initiations and patient accruals as success drives further interest in and focus on the study among investigators and clinical research groups.

We have also worked closely with Healios to support their development efforts in Japan. In 2016, the Pharmaceuticals and Medical Devices Agency in Japan, or the PMDA, authorized the Clinical Trial Notification for Healios' Phase 2/3 trial of MultiStem (referred to in Japan as HLCM051) entitled, "*Treatment Evaluation of Acute Stroke for Using in Regenerative Cell Elements*," or TREASURE. This clinical trial is currently ongoing in Japan and patient enrollment was completed in August 2021. In November 2021, Healios announced that, based on the advice of the PMDA to avoid any potential bias to the 365-day data (and related secondary endpoints) that could result from unblinding and disclosure of 90-day data (primary endpoint), the decision was made that the 90-day unblinding, data analysis and release would take place after the 365-day data is locked. This will follow the last patient's one-year follow-up visit. Healios expects this last patient visit to occur in March of 2022. Japan's regenerative medicine regulatory framework is designed to enable rapid development of qualified regenerative medicine

therapies by providing either conditional or full approval of qualified therapies. Under the framework, Healios' ischemic stroke program has been awarded the Sakigake designation by the PMDA, which is designed to expedite regulatory review and development and is analogous to FAST Track designation from the FDA.

In January 2019 and January 2020, we announced summary results and one-year follow-up results, respectively, from our exploratory clinical study of the intravenous administration of MultiStem cell therapy to treat patients who are suffering from ARDS, which is referred to as the MUST-ARDS study. ARDS is a serious immunological and inflammatory condition characterized by widespread inflammation in the lungs. ARDS can be triggered by COVID-19, pneumonia, sepsis, trauma or other events, and represents a major cause of morbidity and mortality in the critical care setting. It has significant implications, as it prolongs ICU and hospital stays and requires convalescence in the hospital and rehabilitation. According to the World Health Organization and other recent clinical and epidemiological data, ARDS is the leading cause of death among COVID-19 infected patients. Given the limited interventions and drug treatments for ARDS, it is an area of high unmet clinical need. Due to the high treatment costs of ARDS, a successful cell therapy could be expected to generate significant savings for the healthcare system by reducing the number of days on a ventilator and in the ICU and importantly, could reduce mortality and improve quality of life for those suffering from the condition. Our exploratory study results provide further confirmation that the MultiStem treatment was well-tolerated, and lower mortality and a greater number of ventilator-free and ICU-free days were observed in the MultiStem-treated patient group compared to the placebo group. Average quality-of-life outcomes observed were higher in the MultiStem group compared to placebo through one year. Our clinical program evaluating MultiStem cell therapy for the treatment of ARDS received Fast Track designation from the FDA in May 2019 and the RMAT designation in September 2020.

Further, in August 2021, Healios reported top-line data from its ONE-BRIDGE study in Japan for patients with pneumonia-induced and COVID-induced ARDS. Healios continues ongoing consultations with the regulatory authorities to prepare for the potential application for manufacturing and marketing approval. We are working with Healios to prepare the regulatory applications for approval and for potential commercialization in Japan.

We and Healios have conducted thorough analyses of the data from the MUST-ARDS and ONE-BRIDGE studies. The studies had comparable patient populations receiving the same MultiStem dose amount shortly following an ARDS diagnosis. Between the studies, excluding the COVID-ARDS cohort in the ONE-BRIDGE study, 60 ARDS subjects were enrolled in the studies, 40 receiving MultiStem treatment and the remaining 20 receiving placebo or standard of care. On a pooled basis, strong trends were observed in ventilator-free days, or VFD, survival, improved quality-of-life and reduction of key inflammatory biomarkers. For example, MultiStem-treated subjects had, on average, 5.5 more VFD in the first 28 days following diagnosis than non-treated subjects ($p=0.07$) and, on a median basis, 10.5 more VFD.

In 2020, in response to the COVID-19 pandemic, the FDA authorized the initiation of our MACOVIA study to assess the safety and efficacy of MultiStem therapy in subjects with moderate to severe ARDS induced by COVID-19. The MACOVIA study features an open-label lead-in followed by a double-blinded, randomized, placebo-controlled Phase 2 and 3 portions, and the study is presently designed to enroll up to approximately 400 patients. During 2021, we amended the protocol with the FDA to adjust the scope of the MACOVIA study to include subjects with ARDS from causes other than COVID-19. Recently, we received approval from the FDA to use MultiStem product manufactured with our bioreactor-based technology in the study, an important development milestone. The study is being conducted at leading pulmonary critical care centers throughout the United States. However, the scope and timing of our MACOVIA study may be adjusted to reflect rapidly changing standards of care for ARDS patients and depending on regulatory discussions and business considerations. Currently, we are working to complete enrollment of the Phase 2 part of the MACOVIA trial before the end of 2022.

Under our collaboration with Healios to develop and commercialize MultiStem for the treatment of certain indications in Japan, Healios has a license to our technology and is responsible for the development and commercialization of MultiStem for certain indications in Japan on an exclusive basis. Healios' license includes MultiStem cell therapy for ischemic stroke and ARDS in Japan and the use of our technology for Healios' organ bud program targeted to liver disease and other indications, as well as certain other rights, including a license for the use of our MultiStem product to treat certain ophthalmological indications and a license to treat diseases of the liver, kidney, pancreas and intestinal tissue through administration of our products in combination with cells derived from induced pluripotent stem cells, or iPSC-derived cells. We have provided manufacturing services and supplied Healios with clinical product for the licensed indications.

We and Healios are preparing for potential commercialization of the MultiStem product candidate, and we are actively preparing the regulatory documents to support a BLA in the United States, Europe and Japan. We are also investing in process development and commercial manufacturing initiatives intended to enable us to supply product to address the large potential critical care markets. We have been developing a bioreactor-based manufacturing platform for such commercialization. In our clinical studies, we are continuing to use cell factory-based material and plan to use bioreactor manufactured product, for which we now have FDA approval for use in our ARDS and trauma clinical trials in the United States. As we continue to prepare for commercialization, we believe that the cell factory-based approach for production is not well suited for serving, on more than a limited basis, large markets or conditions requiring higher dose treatments due to the limited potential for scale-up, relatively

high costs and the possibility of reliability issues due to the complexity of the cell factory-based manufacturing process. A full transition to bioreactor-based material for the commercial setting will require a demonstration of comparability, which could include the requirement for analytical and *in vitro* data, some non-clinical studies and possibly data from additional clinical studies. Our commercial product supply strategy envisions both third-party contractor and internal manufacturing to provide redundancy and accelerate capacity development. For our internal manufacturing, in January 2021, we entered into a lease for a building that could potentially be developed into a state-of-the-art, commercial-scale manufacturing facility for our cell therapy product. We are evaluating the building out of the facility in stages as we complete our pivotal clinical trials, and assuming success, submit the required regulatory filings for commercialization.

In April 2020, the FDA authorized the initiation of a Phase 2 clinical trial evaluating MultiStem cell therapy for the early treatment of traumatic injuries and the subsequent complications that result following severe trauma, and patient enrollment commenced in December 2020. This first-ever study of a cell therapy for treatment for a variety of traumatic injuries is being conducted by The University of Texas Health Science Center at Houston, or UTHealth, at the Memorial Hermann-Texas Medical Center in Houston, Texas, one of the busiest Level 1 trauma centers in the United States. This study is being supported under a grant awarded to the McGovern Medical School at UTHealth from the Medical Technology Enterprise Consortium, and the Memorial Hermann Foundation is providing additional funding. We are providing the investigational clinical product for the trial, as well as regulatory and operational support.

While development of our clinical programs for human health indications remains our priority, based on our research to date and work performed at our Belgian subsidiary, ReGenesys BV, or ReGenesys, we are also evaluating our cell therapy for use in treating disease and conditions in the animal health segment. We have established research and development collaborations and are pursuing commercial partnership opportunities to further develop this program.

Our development approach has historically involved establishing collaborative relationships with leading research and clinical centers in the United States and internationally. This has enabled us to advance multiple programs in areas of defined unmet medical need in a resource efficient manner. Furthermore, by emphasizing the potential application of our technologies in areas of significant clinical need, we believe we are well positioned to utilize recent regulatory initiatives that are designed to promote the rapid and cost-effective development of innovative new therapies, and actively pursue such initiatives. These include recent programs in the United States and Europe being implemented by the FDA and the EMA involving existing and potentially broadened application of accelerated review and approval pathways, as well as the accelerated Regenerative Medicine regulatory framework in Japan that is designed to enable rapid conditional authorization of qualified regenerative medicine therapies. We believe such initiatives could accelerate the development and commercialization of products like MultiStem cell therapy, if clinical results demonstrate appropriate safety and therapeutic effectiveness. Japan's regenerative medicine regulatory framework, enacted in 2014, has already resulted in the commercial approval of several cell therapy products developed by other companies that we are aware of, along with coverage and reimbursement of those products, and we and Healios intend to utilize this framework.

In August 2021, we entered into a Comprehensive Framework Agreement for Commercial Manufacturing and Ongoing Support, or the Framework Agreement, with Healios, which better aligns the collaboration structure for potential commercial success in Japan. The Framework Agreement provides Healios, among other things, access to our manufacturing technology to enable Healios to manufacture MultiStem products using a qualified manufacturer, clarifies our role in providing support services to Healios necessary for regulatory approval, manufacturing readiness and commercial launch in Japan, provides for the deferral of certain milestones and royalties to enable Healios to invest in certain manufacturing activities, and expands Healios' license in Japan to include two new unspecified additional indications under certain conditions. To increase alignment between the companies and create incentives for accelerated execution and investment, the agreement provides for up to $8.0 million in new milestone payments available to us that are tied to certain Japanese commercial manufacturing activities and the establishment of large-scale manufacturing relevant to Japan, and warrants issued to Healios to purchase up to a total of 10,000,000 shares of our common stock, which we refer to as the 2021 Warrants. One of the 2021 Warrants is for the purchase of up to 3,000,000 shares at an exercise price of $1.80 per share, subject to specified increases, and generally is only exercisable within 60 days of receipt of either conditional or full marketing approval from the PMDA for the intravenous administration of MultiStem to treat patients who are suffering from ARDS. The other 2021 Warrant is for the purchase of up to 7,000,000 shares at an exercise price of $2.40 per share, subject to specified increases, and generally is only exercisable within 60 days of receipt of either conditional or full marketing approval from the PMDA for the intravenous administration of MultiStem to treat patients who are suffering from ischemic stroke. The 2021 Warrants may be terminated by us under certain conditions and have an exercise cap triggered at Healios' ownership of 19.9% of our common stock.

Business Strategy

Our principal business objective is to discover, develop and commercialize novel therapeutic products for disease indications that represent significant areas of clinical need and where we believe there is a substantial commercial opportunity. The key elements of our strategy are outlined below:

- *Advance our Lead Programs through Clinical Development to Registration and Commercialization*. We are focused on the design and execution of clinical studies, e.g., ischemic stroke, ARDS and trauma, intended to enable product registration in major markets. We are also engaged in activities intended to enable effective commercialization, e.g., preparation for scaled commercial manufacturing, product branding, product reimbursement and marketing strategies. We may partner with other companies to complete such development and preparation activities, and to market the product upon regulatory approval.
- *Efficiently Conduct Clinical Development to Establish Clinical Proof-of-Concept and Biological Activity for Other Applications of our Product Candidates.* We conduct our clinical studies with the intent to establish safety and efficacy proof-of-concept and/or evidence of biological activity in a number of important disease areas where our cell therapies are expected to have benefit, such as we have done with ARDS. Our strategy is to conduct well-designed studies beginning early in the clinical development process, thus establishing a robust foundation for later-stage development, partnering activity and expansion into complementary areas. We are committed to a rigorous clinical and regulatory approach, which we believe has helped us to advance our programs efficiently, providing high quality, transparent communications and regulatory submissions. Our discussions with the FDA, EMA and PMDA have resulted in productive interactions and important designations that have helped to advance our programs efficiently.
- *Continue to Refine and Improve our Manufacturing and Related Processes and Deepen our Understanding of Therapeutic Mechanisms of Action.* A key aspect of MultiStem cell therapy is the *ex vivo* expansion capacity of the cells that comprise the product. This enables large-scale production of the clinical product, which is associated with greater consistency, specificity and cost of goods advantages over other cell therapies. We are building on this intrinsic biological advantage by advancing and optimizing our production and process development approaches, through our internal capabilities and efforts, and working with contract manufacturers. We are focused on development and optimization of new and proprietary manufacturing techniques and the pharmacy-to-bedside approach to support late-stage development and potential commercialization of the MultiStem product. Additionally, we will continue to refine our understanding of our products' activities and mechanisms of action to prepare the foundation for product enhancements and next generation opportunities.
- *Enter into Arrangements with Business Partners to Accelerate Development and Create Value.* In addition to our internal development efforts, an important part of our strategy is to work with collaborators and partners to accelerate product development, reduce our development costs and broaden our commercial access. We have entered into licensing and collaborative arrangements with qualified partners to achieve these objectives. We anticipate that this strategy will help us to develop a portfolio of high-quality product development opportunities, enhance our clinical development and commercialization capabilities and increase our ability to generate value from our proprietary technologies. Historically, we have entered into licensing arrangements with companies such as Healios, Chugai Pharmaceutical Co., Ltd., Pfizer Inc., Bristol-Myers Squibb Company, Johnson & Johnson, Wyeth Pharmaceuticals Inc. (now part of Pfizer), RTI Surgical, Inc. and others. Licensing partnerships generate revenue and provide capital that helps enable us to advance our programs further in development.
- *Efficiently Explore New High Potential Therapeutic Applications, Leveraging Third-Party Research Collaborations and our Results from Related Areas.* Our MultiStem cell therapy has shown promise in many disease areas, including in treating neurological conditions, inflammatory and immune disorders, certain pulmonary conditions, cardiovascular disease and other conditions where the current standard of care is limited or inadequate for many patients. We are committed to exploring potential clinical indications where our therapies may achieve best-in-class profile and where we believe we can effectively address significant unmet medical needs. In order to achieve this goal, we established collaborative research relationships with investigators from many leading research and clinical institutions across the United States and Europe, including the Cleveland Clinic, Case Western Reserve University, University of Minnesota, the Medical College of Georgia at Augusta University, the University of Oregon Health Sciences Center, UTHealth, the University of Pittsburgh Medical Center, the Katholieke Universiteit Leuven, University of Regensburg, and other institutions. Through this network of collaborations, we have evaluated MultiStem cell therapy in a range of preclinical models that reflect various types of human disease or injury. These collaborative relationships have enabled us to cost effectively explore where MultiStem cell therapy may have relevance and how it may be utilized to advance treatment over current standard of care. Additionally, we have shown that we can leverage clinical safety data and preclinical results from some programs to support accelerated clinical development efforts in other areas, saving substantial development time and resources compared to traditional drug development where each program is separately developed.

- *Continue to Expand our Intellectual Property Portfolio.* We have a broad intellectual property estate that covers our proprietary products and technologies, as well as methods of production and methods of use. Our intellectual property is important to our business and we take significant steps to protect its value. We have ongoing research and development efforts, both through internal activities and through collaborative research activities with others, which aim to develop new technologies, applications and intellectual property and enable us to file patent applications that cover new applications of our existing technologies or product candidates, including MultiStem cell therapy and other opportunities. We currently have over 435 patents related to our technologies, providing protection in the United States, Europe, Japan and other areas.

Our Current Programs

By applying our proprietary MultiStem cell therapy product, we established therapeutic product development programs treating neurological conditions, inflammatory and immune disorders, certain pulmonary conditions, cardiovascular disease and other conditions where the current standard of care is limited or inadequate for many patients. Our lead programs are focused in the critical care area, with treatment provided in hospitals often in intensive care situations. Our programs in clinical development include the following:

- Ischemic Stroke: We are conducting a pivotal Phase 3 clinical trial of MultiStem cell therapy for the treatment of ischemic stroke, referred to as MASTERS-2. We initiated the study with a limited number of high-enrolling sites and continue to bring on additional sites in line with clinical operations objectives. In prior periods, we have faced challenges to clinical site initiations, as well as patient screening and enrollment, due to the COVID-19 pandemic and supply interruptions, among other things. As COVID-19 case numbers decline and supply has stabilized, we have undertaken initiatives intended to accelerate new site openings in the U.S. and abroad and increase patient enrollment at sites currently open, including by addressing site-specific operations and inventory management issues. These plans are intended to enable us to finish enrollment of the MASTERS-2 study by the end of 2022 or as soon as possible thereafter; however, completion continues to depend on the impact of the results of Healios' TREASURE study, discussed below, and the possible resurgence of COVID-19. We would expect, for instance, that favorable TREASURE study results would have a positive effect on site initiations and patient accruals as success drives further interest in and focus on the study among investigators and clinical research groups.

  The MASTERS-2 study has received several regulatory distinctions including SPA, Fast Track and RMAT designations from the FDA, as well as a Final Scientific Advice positive opinion from the EMA, each described further below. We believe these designations could accelerate the development, regulatory review and subsequent commercialization of products like MultiStem cell therapy for ischemic stroke, if future clinical evaluation demonstrates appropriate safety and therapeutic effectiveness.

  We received agreement from the FDA under a SPA for the design and planned analysis of our MASTERS-2 pivotal Phase 3 trial. The SPA provides agreement from the FDA that the protocol design, clinical endpoints, planned conduct and statistical analyses encompassed in MASTERS-2 are sufficient to meet the objectives in support of a regulatory submission for approval of the MultiStem product for treating ischemic stroke patients if the trial is successful. The FDA has also granted us Fast Track designation for our clinical product for the treatment of ischemic stroke. Such designation for a new biologic product means that the FDA will take such actions as are appropriate to expedite the development and review of our application to approve the product, and specifically, under Fast Track designation, the program becomes eligible for rolling submission, accelerated approval and priority review of the BLA facilitating a timely regulatory review. The design of MASTERS-2 has also received a Final Scientific Advice positive opinion from the EMA, representing the EMA's agreement that successful results from the trial could result in registration and marketing approval of the MultiStem cell therapy. This positive opinion provides further alignment among the key regulators regarding potential commercialization of the MultiStem product upon success of this single pivotal trial. We subsequently received RMAT designation from the FDA, which was established under the 21st Century Cures Act. The RMAT designation may be obtained for eligible cell therapy and other regenerative medicine and advanced therapies when the FDA agrees that preliminary clinical evidence indicates that the therapy has demonstrated the potential to effectively address unmet medical needs for a serious or life-threatening disease or condition. The RMAT designation is the equivalent of the non-regenerative medicine product's Breakthrough Therapy designation, and designated products benefit from all Breakthrough Therapy features. The designation enables sponsors to discuss with the FDA multidisciplinary strategic development plans, including expediting manufacturing development plans for commercialization to support priority review and accelerated approval.

  Our MASTERS-2 clinical trial is a randomized, double-blind, placebo-controlled clinical trial designed to enroll 300 patients in the United States and certain other international locations who have suffered moderate to moderate-severe ischemic stroke. The enrolled subjects are receiving either a single intravenous dose of MultiStem cell therapy or placebo, administered within 18-36 hours of the occurrence of the stroke, in addition to the standard of care. The

primary endpoint will evaluate disability using modified Rankin Scale, or mRS, scores at three months, comparing the distribution, or the "shift," between the MultiStem treatment and placebo groups. The mRS shift analyzes patient improvement across the full disability spectrum, enabling recognition of improvements in disability and differences in mortality and other serious outcomes among strokes of different severities. The study will also assess Excellent Outcome (the achievement of mRS ≤1, NIHSS ≤1, and Barthel Index ≥95) at three months and one year as key secondary endpoints. Additionally, the study will consider other measures of functional recovery, biomarker data and clinical outcomes, including hospitalization, mortality and life-threatening adverse events, and post-stroke complications such as infection.

Healios' TREASURE study in Japan has been conducted at hospitals in Japan that have extensive experience in providing care for stroke victims and the study was planned for 220 patients. Enrolled subjects received either a single dose of MultiStem or placebo, administered within 18-36 hours of the occurrence of the stroke, in addition to standard of care in these patients, randomized, double-blind, placebo-controlled trial. The study is evaluating patient recovery through approximately 90 days and at one year following initial treatment based on Excellent Outcome and other neurological, functional and clinical endpoints. The trial could lead to registration under Japan's regenerative medicine regulatory framework, which is designed to enable rapid development of qualified regenerative medicine therapies by providing either conditional or full approval of qualified therapies. Under the framework, Healios' ischemic stroke program has been awarded the Sakigake designation by the PMDA, which is designed to expedite regulatory review and approval, and is analogous to Fast Track designation from the FDA. Healios has completed enrollment in the TREASURE study. In November 2021, Healios announced that, based on the advice of the PMDA, to avoid any potential bias to the 365-day data (and related secondary endpoints) that could result from unblinding and disclosure of 90-day data (primary endpoint), the decision was made that the 90-day unblinding, data analysis and release would take place after the 365-day data is locked. This will follow the last patient's one-year follow-up visit. Healios expects this last patient visit to occur in March of 2022. We look forward to completing both the MASTERS-2 and TREASURE trials and using the accelerated pathway afforded to us by the regulators in the United States, Europe and Japan.

- ARDS: In January 2020, we announced one-year follow-up results from our exploratory MUST-ARDS study. The study results provide further confirmation that the MultiStem treatment was well-tolerated and importantly, there were lower mortality and a greater number of ventilator-free and ICU-free days in the MultiStem-treated patient group compared to the placebo group. In 2020, the FDA authorized the MACOVIA study. In May 2019, our clinical program evaluating MultiStem cell therapy for the treatment of ARDS received Fast Track designation from the FDA and in September 2020 received RMAT designation. The MACOVIA study features an open-label lead-in followed by a double-blinded, randomized, placebo-controlled Phase 2 and 3 portions, and the study is currently designed to enroll up to approximately 400 patients at leading pulmonary critical care centers throughout the United States. During 2021, the study was amended to expand enrollment to patients with ARDS induced by pathogens other than COVID-19. Recently, we received approval from the FDA to use MultiStem product manufactured with our bioreactor-based technology in the study, an important development milestone. Further adjustments to the study will depend on regulatory discussions and business considerations. Currently, we are working to complete enrollment of the Phase 2 part of the MACOVIA trial before the end of 2022.

  Further, in 2019, Healios initiated the ONE-BRIDGE study in Japan for patients with pneumonia-induced and COVID-induced ARDS and, in August 2021, Healios reported top-line data from the ONE-BRIDGE study. Healios continues ongoing consultations with the regulatory authorities to prepare for the potential application for manufacturing and marketing approval. We are working with Healios to prepare the regulatory applications for approval and for potential commercialization in Japan.

  We and Healios have conducted thorough analyses of the data from the MUST-ARDS and ONE-BRIDGE studies. The studies had comparable patient populations receiving the same MultiStem dose amount shortly following an ARDS diagnosis. Between the studies, excluding the COVID-ARDS cohort in the ONE-BRIDGE study, 60 ARDS subjects were enrolled in the studies, 40 receiving MultiStem treatment and the remaining 20 receiving placebo or standard of care. On a pooled basis, strong trends were observed in VFDs, survival, improved quality-of-life and reduction of key inflammatory biomarkers. For example, MultiStem-treated subjects had, on average, 5.5 more VFD in the first 28 days following diagnosis than non-treated subjects ($p=0.07$) and, on a median basis, 10.5 more VFD.

- Trauma: In April 2020, the FDA authorized the initiation of a Phase 2 clinical trial evaluating MultiStem cell therapy for the early treatment of traumatic injuries and the subsequent complications that result following severe traumatic injury, and patient enrollment commenced in December 2020. This first-ever study of a cell therapy for the treatment of a wide range of traumatic injuries is being conducted by UTHealth at the Memorial Hermann-Texas Medical Center in Houston, Texas, one of the busiest Level 1 trauma centers in the United States. The study is being supported under a grant awarded to the McGovern Medical School at UTHealth from the Medical Technology Enterprise Consortium,

and the Memorial Hermann Foundation is providing additional funding. We are providing the investigational clinical product for the trial, as well as regulatory and operational support. Enrollment is ongoing.

While development of our clinical programs for human health indications remains our priority, based on our research to date and work performed at our wholly-owned subsidiary, ReGenesys, we are also evaluating our cell therapy for use in treating diseases and conditions in the animal health area. We have demonstrated in preclinical animal health models that our cell therapy can promote tissue repair and healing that could provide meaningful benefits to animal patients, including those suffering from conditions with unmet medical need. We have established research and development collaborations and are pursuing commercial partnership opportunities to further develop this program.

While the MultiStem product platform continues to advance, we are engaged in process development initiatives intended to increase manufacturing scale, reduce production costs, and enhance process controls and product quality, among other things. These initiatives are being conducted both internally and outsourced to select contractors, and the related investments are meant to enable us to meet potential commercial demand in the event of eventual regulatory approval. We have been developing a bioreactor-based manufacturing platform for such commercialization. In our clinical studies, we are continuing to use cell factory-based material and plan to use bioreactor manufactured product. In January 2022, we received FDA approval for use of our bioreactor manufactured product in our ARDS and trauma clinical trials in the United States. As we prepare for potential commercialization, we believe that the cell factory-based approach for production is not well suited for serving, on more than a limited basis, large markets or conditions requiring higher dose treatments due to the limited potential for scale-up, relatively high costs and the possibility of reliability issues due to the complexity of the cell factory-based manufacturing process. A full transition to bioreactor-based material for the commercial setting will require a demonstration of comparability, which could include the requirement for analytical and *in vitro* data, some non-clinical studies and possibly data from additional clinical studies. Until such time as we can manufacture products ourselves in accordance with good manufacturing practices, or GMP, we will continue to rely on third-party manufacturers to make our MultiStem product for clinical trials and eventual commercial sales.

We have a collaboration with Healios that licenses MultiStem cell therapy for ischemic stroke and ARDS in Japan and the use of our technology for Healios' organ bud program targeted to liver disease and other indications, as well as certain other rights, including a license for the use of our MultiStem product to treat certain ophthalmological indications and a license to treat diseases of the liver, kidney, pancreas and intestinal tissue through administration of our products in combination with iPSC-derived cells.

We and Healios are preparing for potential commercialization of the MultiStem product candidate, and we are actively preparing the regulatory documents to support a BLA in the United States, Europe and Japan.

MultiStem Therapy — A Novel Therapeutic Modality

We are developing our MultiStem cell therapy, a proprietary non-embryonic, allogeneic stem cell product candidate, that we believe has potential utility for treating a broad range of diseases and could have widespread application in the field of regenerative medicine. Unlike traditional bone marrow transplants or other stem cell therapies, MultiStem cells may be manufactured on a large scale and may be administered without tissue matching or the need for immune suppression, analogous to type O blood. Potential applications of MultiStem cell therapy include the treatment of critical care indications, neurological conditions, inflammatory and immune disorders, certain pulmonary conditions, cardiovascular disease and other conditions where the current standard of care is limited or inadequate for many patients. We believe that MultiStem cell therapy represents a significant advancement in the field of stem cell therapy. We currently have open Investigational New Drug Applications, or INDs, for the study of MultiStem administration in distinct clinical indications, and several clinical trials are ongoing.

MultiStem cell therapy is a patented biologic product that is manufactured from human stem cells obtained from adult bone marrow, although these cells may alternatively be obtained from other tissue sources. The product consists of a special class of human stem cells that have the ability to express a range of therapeutically relevant proteins and other factors, as well as form multiple cell types. Factors expressed by the cells have the potential to deliver a therapeutic benefit in several ways, such as the reduction of inflammation, regulation of immune system function, protection of damaged or injured tissue, the formation of new blood vessels in regions of ischemic injury and augmentation of tissue repair and healing in other ways. Stability studies have demonstrated that these cells may be stored for an extended period of time in frozen form and are straightforward to prepare and administer, resulting in an "off-the-shelf" profile. Following administration, the cells have been shown to express multiple therapeutically relevant proteins, but unlike a traditional transplant, are subsequently cleared from the body over time, analogous to a drug or other biologics.

We believe that MultiStem represents a potential best-in-class stem cell therapy because it exhibits each of the following characteristics based on research and development conducted to date:

- *Broad plasticity and multiple potential mechanisms of action.* MultiStem cells have a demonstrated ability in animal models to deliver therapeutic benefit by producing factors that protect tissues against damage and

inflammation, as well as enhancing or playing a direct role in revascularization or tissue regeneration, and have also shown the capacity to form a range of other cell types.

- *Large-scale production.* Unlike conventional stem cells, such as blood-forming or HSCs, mesenchymal stem cells or other cell types, MultiStem cells have the potential to be produced on a large scale, processed, and cryogenically preserved, and then used clinically in a rapid and efficient manner. Material obtained from a single donor may be used to produce hundreds of thousands, or even millions, of individual doses, representing a yield far greater than we believe other stem cell technologies have been able to achieve.
- *"Off-the-shelf" utility.* Unlike traditional bone marrow or HSC transplants that require extensive genetic matching between donor and recipient, MultiStem administration does not require tissue matching or administration of immune suppressive drugs. The MultiStem product is administered as a cryogenically preserved allogeneic product, meaning that these cells are not genetically matched between donor and recipient. This feature, combined with the ability to establish large MultiStem banks, could make it practical for clinicians to efficiently administer this cell therapy to a large number of patients.
- *Safety.* Certain other stem cell types, such as undifferentiated embryonic stem cells or induced pluripotent stem cells, have shown the capacity to form ectopic tissue or teratomas, which are tumor-like growths. These could pose serious safety risks to patients. In contrast, MultiStem cells have shown a consistent and favorable tolerability profile that has been compiled over many years of preclinical study in a range of animal models by a variety of investigators and that is supported by clinical data from multiple studies to date.

At each step of the MultiStem production process, cells are analyzed according to pre-established criteria to ensure that a consistent, well-characterized product candidate is produced. Cells are harvested from a prequalified, healthy, consenting donor, and these cells are then expanded to form a master cell bank from which we subsequently produce clinical grade material. We have demonstrated the ability to harvest cells that meet our rigorous criteria from healthy donors with a high degree of consistency. Furthermore, in multiple animal models, MultiStem has been shown to be nonimmunogenic and is administered without the genetic matching that is typically required for conventional bone marrow or stem cell transplantation.

The distinctive profile of the MultiStem product allows us to pursue multiple high value commercial opportunities from a single product platform. Based upon work that we and independent collaborators have conducted over the years, we believe that MultiStem cell therapy has the potential to treat a range of distinct disease indications. As a result, we believe we will be able to leverage our foundation of a consistent tolerability profile and efficacy data to add clinical indications efficiently, enabling us to reduce development costs and timelines substantially.

Health care represents a significant part of the global economy. In the United States, in 2020, health care spending reached $4.1 trillion, or $12,530 per person, and as a share of gross domestic product, health spending accounted for approximately 19.7%, according to the National Health Expenditure Accounts. The United States, along with many other nations, is experiencing an unprecedented demographic shift that is resulting in a significantly expanded population of older individuals. According to United States Census Bureau 2017 National Population Projections, 2035 will be a turning point for demographics in the United States, particularly for the elderly population. By the year 2035, people ages 65 and older are projected to outnumber children for the first time in United States history. By 2035, there will be 78.0 million people 65 years and older compared to 76.7 million under the age of 18 in the United States. The aging of the population will create enormous financial and operational pressure on the healthcare system in the United States and other countries around the world, resulting in significant clinical challenges, but also resulting in substantial commercial opportunities.

The Centers for Disease Control and Prevention, or CDC, reports that older adults are more likely to experience multiple chronic diseases such as coronary heart disease, stroke, diabetes, cancer, arthritis and kidney disease. As a consequence, as people age they spend far more on healthcare. Additionally, according to the CDC, in the United States, 90% of the $3.8 trillion in annual health care expenditures are for people with chronic and mental health conditions.

We have worked with independent investigators at many leading institutions to study the impact of MultiStem cell therapy in a range of preclinical models that reflect various types of human disease or injury. To date, we and our collaborators have published research results illustrating the potential benefits of MultiStem cell therapy in a range of indications including ischemic stroke, traumatic brain injury, or TBI, brain damage due to restricted blood flow in newborns, spinal cord injury, myocardial infarction, vascular disease, acute pulmonary distress, bone marrow transplant support/GvHD, wound healing, organ reperfusion and other indications.

Based on preclinical results, we have advanced MultiStem cell therapy to clinical development stage in several clinical indications or disease areas, including treatment of ischemic stroke caused by a blockage of blood flow in the brain, ARDS, complications from trauma, damage caused by myocardial infarction, certain complications associated with traditional bone marrow or HSC transplantation, inflammatory bowel disease, initially focused on patients suffering from severe, treatment

refractory ulcerative colitis and to treat or prevent certain complications associated with solid organ transplant. We highlight priority areas below. We may expand to other clinical indication areas as results warrant and resources permit.

Neurological Injury and Disease — MultiStem for Ischemic Stroke

Another focus of our regenerative medicine program is MultiStem administration for the treatment of neurological injury as a result of acute or chronic conditions. Neurological injury and disease represent an area of significant unmet medical need, a major burden on the healthcare system, and also represents a substantial commercial opportunity.

Many neurological conditions require extensive long-term therapy, and many require extended hospitalization and/or institutional care, creating an enormous quality of life and cost burden. Stroke represents an area where the clinical need is particularly significant, since it represents a leading cause of death and significant long-term disability. We have published research with independent collaborating investigators that demonstrates that MultiStem administration conveys biological benefits in preclinical models of ischemic stroke, as well as other models of neurological damage and injury, including TBI, neonatal hypoxic ischemia (a cause of neurological damage in infants), and spinal cord injury. We also conducted preclinical work in other neurological areas and have been awarded grants from time-to-time in support of this work, including the potential of MultiStem cells to address chronic conditions such as Multiple Sclerosis, or MS, or Parkinson's disease. Our research has shown that MultiStem cells convey benefits through distinct mechanisms, including reducing inflammatory damage, protecting at risk tissue at the site of injury, and through direct neurotrophic effects that stimulate the recovery of damaged neurons. As a result, we believe that MultiStem cell therapy may have relevance to multiple forms of neurological injury and disease.

Our initial clinical focus in the neurological area involves evaluating MultiStem administration to treat ischemic stroke. According to the CDC, every year, more than 795,000 people in the United States have a stroke and approximately 610,000 of these are first or new strokes. Stroke is a leading cause of serious long-term disability. The vast majority of these (approximately 87%) are ischemic strokes, that are caused by a blockage of blood flow in the brain, that cuts off the supply of oxygen and nutrients, and can result in tissue loss and neurological damage, as well as long-term or permanent disability.

Even though ischemic stroke is one of the leading causes of death and disability in the United States, there has been limited progress toward the development of new treatments that improve the prognosis for stroke victims. The only FDA-approved drug currently available for treating ischemic stroke is the anti-clotting factor, tPA. According to current clinical guidelines, tPA must be administered to stroke patients within several hours after the occurrence of the ischemic stroke to dissolve the clot. Administration of tPA beyond the early treatment window is not recommended, since it can cause cerebral bleeding or even death. Recent advancements in the development of mechanical clot retrievers and extraction devices have also shown benefit to patients, but these devices are limited to certain types of strokes and also in a constrained time window. Because of these limitations, only a small percentage of stroke victims are treated successfully with the currently available therapies—most simply receive supportive or "palliative" care. The long-term costs of stroke are substantial, with many patients requiring extended hospitalization, extended physical therapy or rehabilitation for those patients that are capable of entering such programs, and many require long-term institutional or family care.

In preclinical studies, significant functional improvements have been observed in rodents that have undergone an experimentally-induced stroke, or that have incurred significant neurological damage due to similar types of ischemic events or acute injury, such as a result of neonatal hypoxic ischemia, or TBI, and then received MultiStem treatment. Published research has demonstrated that MultiStem administration even one week after a surgically induced stroke results in substantial long-term therapeutic benefit, as evidenced by the improvement of treated animals compared with controls in a battery of tests examining mobility, strength, fine motor skills, and other aspects of neurological functional improvement. We believe MultiStem treatment conveys significant benefits through several mechanisms, including reduction of inflammation and immune system modulation in the ischemic area, and the protection and rescue of damaged or injured cells, including neuronal tissue. Preclinical research results demonstrated that MultiStem administration 24 hours following a stroke reduced inflammatory damage in the brain and resulted in significant functional improvement, and that some of these results were achieved by reducing the inflammatory response emanating from the spleen in animal models. These results confirmed that MultiStem treatment is well tolerated, does not require immunosuppression and results in a robust and durable therapeutic benefit, and these results are consistent with prior results that show MultiStem can provide significant benefits even when administered up to one week after the initial stroke event, although earlier treatment (e.g., within 24 hours post-stroke) provided more substantial benefits in these preclinical studies.

We completed our first clinical study in ischemic stroke, MASTERS-1, which was a randomized, placebo-controlled Phase 2 clinical trial exploring the administration of MultiStem to patients that have suffered an ischemic stroke in the United States and Europe. The results of this study demonstrated favorable tolerability for MultiStem, consistent with prior clinical studies in other indications. While the study did not achieve the primary and component secondary endpoints for the intent-to-treat population, the MultiStem treatment was associated with lower rates of mortality and life-threatening adverse events, infections and pulmonary events, and also a reduction in hospitalization. In addition, analyses show that patients who received MultiStem

treatment earlier in the study's treatment window (i.e., 24 to 36 hours post-stroke, as specified in the original study protocol) had better recovery in comparison to placebo, and this treatment effect appeared to be more pronounced the earlier the MultiStem administration occurred within this timeframe. Analysis of biomarker data obtained from samples of study subjects indicated that MultiStem treatment reduces post-stroke inflammation compared to placebo. Furthermore, it appears that this effect is more pronounced for subjects receiving MultiStem earlier than 36 hours post-stroke. This effect is consistent with our hypothesis regarding mechanisms of action and related preclinical data, and with the clinical data suggesting faster recovery for MultiStem-treated patients. One-year follow-up data demonstrated that MultiStem-treated subjects on average continued to improve through one-year post-treatment and achieved a significantly higher rate of Excellent Outcome compared to placebo subjects in the intent-to-treat population. We have an ongoing pivotal Phase 3 clinical trial, referred to as MASTERS-2, which if successful and if the product is approved for commercialization, could make therapy available to most stroke patients in contrast to other therapies (e.g., tPA), which have substantially shorter treatment windows.

We are also interested in the application of MultiStem for other neurological indications that represent areas of significant unmet medical need, such as TBI, which represents the leading cause of disability among children and young adults, and a leading cause of death. In preclinical studies of TBI, administration of MultiStem dramatically reduced the extent of damage caused by a TBI and promoted accelerated healing of the blood-brain barrier. With grant funding from the National Institutes of Health, we further advanced our MultiStem programs and cell therapy platform, including further development of MultiStem cell therapy for the treatment of TBI and further development of our cell therapy formulations and manufacturing capabilities.

We are also conducting preclinical work exploring the application of MultiStem treatment in other neurological indications and have presented data at leading scientific conferences that demonstrated that intravenous MultiStem administration one day after spinal cord injury, or SCI, results in statistically significant and sustained improvements in gross locomotor function, fine locomotor function and bladder control compared to control treated animals. We have published findings that showed that MultiStem cell therapy was effective in improving the health and recovery of animals following an acute SCI. Intravenous administration of our cells one day after injury prevented loss of spinal cord tissue, resulting in significant improvement of walking function and urinary control. Further, we also published an article that provides further evidence that our cell therapy has the potential to provide benefit following hypoxic ischemia, an injury caused by oxygen deprivation to the brain before or during birth and a leading cause of cerebral palsy. The article also describes the biological mechanisms through which this cell therapy delivers benefit. These findings are consistent with previous findings in related areas, such as ischemic stroke, and add to the scientific foundation supporting MultiStem cell therapy for the treatment of acute neurological injuries.

We have also used grant funding to investigate the potential for MultiStem treatment for chronic progressive MS based on initial results in preclinical models. Our previous work, supported by Fast Forward and the National Multiple Sclerosis Society, demonstrated the potential benefits of MultiStem cell therapy for treating MS. Using several preclinical animal models that mimic the demyelination associated with MS, researchers observed that MultiStem cell administration results in sustained behavioral improvements, arrests the demyelination process and supports remyelination and repair of affected axons. More recently, we have focused on the mechanisms of action underlying the enhanced remyelination *in vivo* and in vitro.

Inflammatory and Immunological Disorders — MultiStem for Acute Respiratory Distress, Trauma Complications, HSC Transplant Support and other indications

Inflammatory and immune disorders represent a significant burden to society. There are over 80 recognized autoimmune disorders, which are conditions caused by an acute or chronic imbalance in the immune system. In these conditions, cells of the immune system begin to attack certain tissues or organs in the body, resulting in tissue damage and loss of function. Some inflammatory and immune conditions are associated with age-related conditions (e.g., rheumatoid arthritis), but some are due to other causes that may be genetic, environmental or a combination of both (e.g., Type 1 diabetes, inflammatory bowel disease). Still other conditions may reflect complications associated with other diseases or trauma or the treatment of other conditions (e.g., GvHD, a frequent complication associated with transplant procedures used to treat leukemia or related blood-borne cancers). Each of these conditions shares certain biological characteristics, in that the immune system imbalance results from the inappropriate activation of certain populations of immune cells that subsequently results in significant tissue damage and destruction. This immune imbalance may result in a complex cascade of inflammation that can result in pain, progressive tissue deterioration and loss of function. While currently available immunomodulatory drugs have proven to be effective for some patients, they have failed to adequately address the needs of many other patients that suffer from inflammatory and immune disorders.

In both preclinical and clinical studies, MultiStem cells have shown potent immunomodulatory properties, including the ability to reduce active inflammation through various modes of action, stimulate tissue repair and restore immune system balance. Accordingly, we believe that MultiStem cell therapy could have broad application in the area of treating immune system disorders, including certain acute inflammatory conditions, autoimmune diseases and other conditions.

In animal models, MultiStem cells have demonstrated an ability to reduce the severity of pulmonary distress, reduce alveolar edema and return lung endothelial permeability to normal. Intravenous MultiStem treatment early following the onset of the

condition may ameliorate the initial hyper-inflammation and reduce the fibrotic activity that follows, thereby speeding the return to and improving the likelihood of more normal lung function and helping patient recovery.

ARDS is a serious immunological and inflammatory condition characterized by widespread inflammation in the lungs. ARDS can be triggered by COVID-19, pneumonia, sepsis, or other trauma and represents a major cause of morbidity and mortality in critical care settings. It has significant implications, as it prolongs ICU and hospital stays, and requires convalescence in the hospital and rehabilitation. There are limited interventions and no effective drug treatments for ARDS, making it an area of high unmet clinical need with high treatment costs. Given the high treatment costs of ARDS, a successful cell therapy could be expected to generate significant savings for the healthcare system by reducing days on a ventilator, days in the intensive care unit and total days in the hospital, and could reduce mortality and morbidity, as well as improve quality of life for those suffering from the condition.

In January 2019 and January 2020, we announced summary results and one-year follow up results, respectively from our exploratory MUST-ARDS clinical study of the intravenous administration of MultiStem cell therapy to treat patients who are suffering from ARDS. The study results provide further confirmation of tolerability associated with MultiStem treatment. Importantly, MultiStem subjects had lower mortality and a greater number of ventilator-free and ICU-free days compared to patients receiving placebo. Furthermore, analysis of initial biomarker data reflects lower levels of inflammatory markers/ cytokines following MultiStem treatment, an expected mechanism of action in this patient population.

Further, in 2019, Healios initiated the ONE-BRIDGE study in Japan for patients with pneumonia-induced and COVID-induced ARDS and, in August 2021, Healios reported top-line data from the ONE-BRIDGE study. Healios continues ongoing consultations with the regulatory authorities to prepare for the potential application for manufacturing and marketing approval. We are working with Healios to prepare the regulatory applications for approval and for potential commercialization in Japan.

We and Healios have conducted thorough analyses of the data from the MUST-ARDS and ONE-BRIDGE studies. The studies had comparable patient populations receiving the same MultiStem dose amount shortly following an ARDS diagnosis. Between the studies, excluding the COVID-ARDS cohort in the ONE-BRIDGE study, 60 ARDS subjects were enrolled in the studies, 40 receiving MultiStem treatment and the remaining 20 receiving placebo or standard of care. On a pooled basis, strong trends were observed in VFDs, survival, improved quality-of-life and reduction of key inflammatory biomarkers. For example, MultiStem-treated subjects had, on average, 5.5 more VFD in the first 28 days following diagnosis than non-treated subjects ($p=0.07$) and, on a median basis, 10.5 more VFD.

Our research and others' research suggest that the activation of an acute hyperinflammatory response involving the peripheral immune system is a conserved biological response that occurs across multiple forms of trauma. For example, a common complication among trauma victims is Systemic Inflammatory Response Syndrome, which can contribute to or play a causative role in impaired organ system function, organ failure, or even multi-organ failure. We believe MultiStem can help address this systemic inflammatory response and its complications, and promote better recovery following trauma. In April 2020, the FDA authorized the initiation of a Phase 2 clinical trial evaluating MultiStem cell therapy for the early treatment of traumatic injuries and the subsequent complications that result following severe trauma. This first-ever study of a cell therapy for treatment for a variety of traumatic injuries is being conducted by UTHealth at the Memorial Hermann-Texas Medical Center in Houston, Texas, one of the busiest Level 1 trauma centers in the United States. This study is being supported under a grant awarded to the McGovern Medical School at UTHealth from the Medical Technology Enterprise Consortium, and the Memorial Hermann Foundation is providing additional funding. The study is a randomized, double-blind, placebo-controlled Phase 2 clinical trial estimated to enroll approximately 150 severely injured trauma patients within hours of hospitalization who have survived initial treatment and are admitted to the ICU. We are providing the investigational clinical product for the trial, as well as regulatory and operational support. Enrollment commenced in December 2020 and is ongoing.

Another area of focus is the use of MultiStem cell therapy as adjunctive treatment for HSC/bone marrow transplant used as therapy in hematologic malignancy. For many types of cancer, such as leukemia or other blood-borne cancers, treatment typically involves radiation therapy or chemotherapy, alone or in combination. Such treatment can substantially deplete the cells of the blood and immune system, by reducing the number of stem cells in the bone marrow from which they arise. The more intense the radiation treatment or chemotherapy, the more severe the resulting depletion is of the bone marrow, blood and immune system. Other tissues may also be affected, such as cells in the digestive tract and in the pulmonary system. The result may be severe anemia, immunodeficiency, substantial reduction in digestive capacity, and other problems that may result in significant disability or death.

One strategy for treating the depletion of bone marrow is to perform a peripheral blood stem cell transplant or a bone marrow transplant. This approach may augment the patient's ability to form new blood and immune cells and provide a significant survival advantage. However, finding a closely matched donor is frequently difficult or even impossible. Even when such a donor is found, in many cases there are immunological complications, such as GvHD, which may result in serious disability or death.

Working with leading experts in the stem cell and bone marrow transplantation field, we studied MultiStem in animal models of radiation therapy and GvHD. In multiple animal models, MultiStem cells have been shown to be non-immunogenic, even when administered without the genetic matching that is typically required for conventional bone marrow or stem cell transplantation. Furthermore, in animal model systems testing immune reactivity of T-cells against unrelated donor tissue, MultiStem has been shown to suppress the T-cell-mediated immune responses that are an important factor in causing GvHD. MultiStem-treated animals also displayed a significant increase in survival relative to controls. As a result, we believe that MultiStem administration in conjunction with or following standard HSC transplantation may have the potential to reduce the incidence or severity of complications and may enhance gastrointestinal function, which is frequently compromised as a result of radiation treatment or chemotherapy.

We completed a Phase 1 clinical trial examining the safety and tolerability of a single dose or repeat dosing of MultiStem cells administered intravenously to patients receiving a bone marrow or HSC transplant as part of their treatment of leukemia or other hematological condition. The trial was an open-label, multicenter trial that involved leading experts in the field of bone marrow transplantation. We observed a consistent favorable tolerability profile in both the single and multiple dose arms of the study, and at all dose levels tested. Although the trial was not specifically designed to demonstrate efficacy, we also observed clinically meaningful improvement in medically important parameters relative to historical clinical experience, including reduced incidence and severity of acute GvHD, improved relapse free survival, no graft failures and enhanced engraftment rates relative to other forms of treatment.

We were granted orphan drug designation by the FDA and the EMA for MultiStem treatment in the prevention of GvHD, and the MultiStem product was granted Fast Track designation by the FDA for prophylaxis therapy against GvHD following HSC transplantation. Subsequently, our registration study design received a positive opinion from the EMA through the Protocol Assessment/Scientific Advice procedure. Furthermore, the proposed registration study received SPA designation from the FDA, meaning that the trial is adequately designed to support a BLA submission for registration if it is successful.

Other Programs

Animal Health Care

While development of our clinical programs for human health indications remains our priority, based on our research to date and work performed at our Belgian subsidiary, ReGenesys, we have demonstrated in preclinical animal health models that MultiStem cell therapy can promote tissue repair and healing that could provide meaningful benefits to animal patients, including those suffering from serious conditions with unmet medical needs. According to Global Market Insights, the global animal healthcare market for the forecast period 2021 to 2027 is expected to grow at a compound annual growth rate of approximately 4.7% during this period and is estimated to be valued at approximately $190.0 billion in 2027. We have established research and development collaborations and are pursuing commercial partnership opportunities to further develop this program.

Collaborations and Partnerships

Healios

We have entered into a series of agreements with Healios, our collaborator in Japan and currently our largest stockholder. Under the collaboration that began in 2016, Healios is responsible for the development and commercialization of the MultiStem product for the licensed fields in the licensed territories, and we provide support and other services to Healios, including preparations for commercial supply in Japan and the transfer of technology to a Japanese contract manufacturer.

In 2016, we entered into a license agreement, or First License Agreement, with Healios to develop and commercialize MultiStem cell therapy for ischemic stroke in Japan and to provide Healios with access to our proprietary Multipotent Adult Progenitor Cell, or MAPC, technology for use in Healios' organ bud program worldwide, initially for transplantation to treat liver disease or dysfunction. Under the First License Agreement, Healios also obtained a right to expand the scope of the collaboration, and Healios exercised this right in 2018 when we entered into the Collaboration Expansion Agreement, or CEA. Through the CEA, Healios (i) expanded its First License Agreement to include ARDS in Japan and expanded the organ bud license to include additional transplantation indications covered under Healios organ bud technology; (ii) obtained a worldwide exclusive license, or the Ophthalmology License Agreement, for use of MultiStem product to treat certain ophthalmological indications; (iii) obtained an exclusive license in Japan, or the Combination Product License Agreement, for use of the MultiStem product to treat diseases of the liver, kidney, pancreas and intestinal tissue through local administration of MultiStem cell therapy in combination with iPSC-derived cells; (iv) obtained an exclusive, time-limited right of first negotiation, or ROFN Period, to enter into an option for a license to develop and commercialize certain MultiStem treatments in China, which expired in June 2019; and (v) certain other rights, including an option for an additional non-therapeutic technology license, which also expired. For all indications, Healios is responsible for the costs of clinical development in its licensed territories, and we provide manufacturing services to Healios.

Each license agreement with Healios has defined economic terms. Under the First License Agreement that related primarily to the license to ischemic stroke in Japan, we received a nonrefundable, up-front cash payment of $15.0 million, and upon the inclusion of the ARDS field in Japan, we received a nonrefundable, up-front cash payment of $10.0 million. For the additional rights granted to Healios under the CEA, including the Ophthalmology License Agreement and the Combination Product License Agreement, Healios paid us an additional nonrefundable, up-front payment of $10.0 million, which was paid in four quarterly installment payments of $2.5 million. Healios may elect to credit up to $10.0 million against milestone payments that may become due under the First License Agreement, as expanded to include ARDS, with limitations on amounts that may be credited to earlier milestone payments versus later milestone payments.

For each of the ischemic stroke indication and the ARDS indication, we may receive aggregate success-based regulatory filing and approval milestones up to $50.0 million and potential sales milestones up to $175.0 million, amounting to $225.0 million for each indication (or $450.0 million in aggregate), subject to potential milestone credits. On August 5, 2021, we entered into the Framework Agreement with Healios that provides for resolution of certain issues under the existing agreements between the parties and improves the collaboration structure to set the stage for productive efforts as Healios moves closer to potential commercialization of MultiStem in Japan. The Framework Agreement provides for the deferral of certain of the milestones payments during the expensive commercial launch period. For each of the ischemic stroke indication and the ARDS indication, we are entitled to receive tiered royalties on product sales, starting in the low double digits and increasing incrementally into the high teens or potentially higher depending on net sales levels and other factors. The Framework Agreement also provides for the deferral of certain of the tiered royalty payments. Under the Framework Agreement, we are entitled to new milestone payments in the amount of $3.0 million by June 2022 and $5.0 million upon completion of certain commercial manufacturing activities.

The Ophthalmology License Agreement granted Healios worldwide, exclusive rights to treat certain ophthalmological diseases, by using either MultiStem cell therapy on a standalone basis or MultiStem in combination with retinal pigment epithelium cells derived from either iPSC or embryonic stem cells. For the standalone products, we will be entitled to receive success-based regulatory filing and approval milestones aggregating up to $48.1 million, potential sales milestones of up to $87.5 million, and tiered royalties on product sales in the single digits depending on net sales levels. For the combination ophthalmology products, we are entitled to receive a low single-digit royalty, but no milestone payments.

The Combination Product License Agreement granted Healios exclusive rights in Japan to treat diseases of the liver, kidney, pancreas and intestinal tissue through local administration of MultiStem cell therapy in combination with iPSC-derived cells through certain delivery methods. We are entitled to receive a low single-digit royalty on net sales of the combination product treatments, but no milestone payments.

For the organ bud product, we are entitled to receive a fractional royalty on net sales of the organ bud products. For all indications covered by the Healios organ bud technology that utilize our technology, we may receive payments for manufactured product supplied to Healios under a manufacturing supply agreement. Additionally, we have a right of first negotiation for commercialization of an organ bud product in North America, with such right expiring on the later of (i) the date five years from the effective date of the First License Agreement and (ii) 30 days after authorization to initiate clinical studies on an organ bud product under the first investigational new drug application or equivalent in Japan, North America or the European Union, or EU.

In 2018, Healios purchased 12,000,000 shares of our common stock and the 2018 Warrant to purchase up to 20,000,000 additional shares of common stock for $21.1 million, or approximately $1.76 per share. Based upon the expiration of the ROFN Period at June 30, 2019, the 2018 Warrant was no longer exercisable for up to 16,000,000 warrant shares. In March 2020, Healios exercised the remaining warrant shares, and we issued 4,000,000 shares of our common stock at an exercise price equal to the reference price of $1.76 as defined in the 2018 Warrant. Proceeds of approximately $7.0 million were received in April 2020 in accordance with the terms of the 2018 Warrant. In connection with the Framework Agreement, we issued two warrants, or the 2021 Warrants, to Healios to purchase up to a total of 10,000,000 shares of our common stock. One of the 2021 Warrants is for the purchase of up to 3,000,000 shares at an exercise price of $1.80 per share, subject to specified increases, and generally is only exercisable within 60 days of receipt of either conditional or full marketing approval from the PMDA for the intravenous administration of MultiStem to treat patients who are suffering from ARDS. The other 2021 Warrant is for the purchase of up to 7,000,000 shares at an exercise price of $2.40 per share, subject to specified increases, and generally is only exercisable within 60 days of receipt of either conditional or full marketing approval from the PMDA for the intravenous administration of MultiStem to treat patients who are suffering from ischemic stroke.

In 2017, we signed a clinical trial supply agreement for delivering the planned manufacturing services for Healios' clinical trial in Japan treating ischemic stroke patients, which was amended in 2018 to also include the clinical trial supply for Healios' clinical trial treating ARDS patients. The agreement includes a cost-sharing arrangement associated with our supply of clinical product for Healios' TREASURE study in Japan, including Healios' right to apply cost-share payments as a credit against certain milestone payments that may become due for the stroke indication under the First License Agreement, and if so applied,

a stroke sales milestone would be increased, as defined. Alternatively, such cost-share payments may be repaid by us at our election. We successfully delivered all product required by Healios to complete the TREASURE and ONE-BRIDGE studies in 2019.

Also in 2017, we entered into a technology transfer services agreement with Healios, in which Healios provides financial support to establish a contract manufacturer in Japan to manufacture product for Healios. At that time, we also amended the First License Agreement to confer to Healios a limited license to manufacture MultiStem in the event that we are acquired by a third-party.

The First License Agreement will expire automatically when there are no remaining intellectual property rights subject to the license. Additionally, Healios may terminate the First License Agreement under certain circumstances, including for material breach and without cause upon advance written notice. We may terminate the First License Agreement if there is an uncured material breach of the agreement by Healios. Following the expiration or termination of the First License Agreement, Healios shall pay reduced royalties for continued use of our trademarks.

Following termination of the First License Agreement, the licenses granted to Healios to develop and commercialize MultiStem in Japan for ischemic stroke and for ARDS will terminate. Healios will transfer ownership to us of its documents related to the product, the field and the Japan territory, such as regulatory filings, correspondence, approvals and documents; investigator brochures clinical data; and information related to the product. Further, the nonexclusive license to intellectual property developed by Healios during the collaboration shall survive termination and become our confidential information.

The Ophthalmology License Agreement and Combination Product License Agreement will expire with respect to each licensed product in each country upon the latest of four events: (i) expiration of our applicable pre-existing patents, (ii) expiration of our applicable patents filed after the effective date, (iii) loss of all data or other regulatory exclusivity, and (iv) 10 years after first commercial sale. Each agreement may expire earlier for products in territories upon certain defined conditions related to the availability of alternative products. Each agreement would terminate in its entirety when all such product terms for each territory have expired. After expiration of a product in a territory, or the agreement as a whole, Healios' licenses remain in effect and Healios remains obligated to pay royalties at a reduced rate, and for a limited time, at which time the exclusive nature of the licenses convert to non-exclusive. Additionally, Healios may terminate the agreements under certain circumstances, including for material breach and without cause upon advance written notice (in which case Healios' licenses do not survive). We may terminate either of these agreements if there is an uncured material breach of an agreement by Healios (in which case Healios' licenses would not survive).

University of Minnesota

In 2003, we acquired the exclusive rights to the MAPC technology originally developed at the University of Minnesota pursuant to a license agreement with the University. We subsequently further developed this technology, including refining and establishing proprietary methods related to the manufacturing of the cells, creating new intellectual property and patents outside of the license. We are obligated to pay the University of Minnesota a royalty based on worldwide commercial sales of licensed products if covered by a valid licensed patent, as well as sublicensing fees and fees related to manufactured product proceeds, as defined. The low single-digit royalty and sublicense fee rate may be reduced if third-party payments for intellectual property rights are necessary or commercially desirable to permit the manufacture or sale of the product. The royalty payment obligation and the term of the license agreement expire upon the last to expire licensed patent. Based on our current patent portfolio, and absent any continuations, renewals or extensions of existing patents, the last licensed patent to expire under this license agreement is currently expected to expire in 2036. The license agreement does not have a specific termination date, but the University of Minnesota can terminate the license agreement for an uncured event of default, as defined, or upon our bankruptcy and we can terminate the license agreement at any time.

Manufacturing

We work with third parties to manufacture our MultiStem product candidates in accordance with GMP, and until such time as we are able to manufacture products ourselves in accordance with GMP, we will rely on such third-party manufacturers to make our MultiStem product for clinical trials and eventual commercial sales. These third parties may not deliver sufficient quantities of our MultiStem product, manufacture MultiStem product in accordance with specifications, or maintain compliance with applicable government regulations. From time to time, such third-party manufacturers, or their material suppliers, may be subject to inspection by the FDA or other regulators, which under certain circumstances could result in production stoppages and interruptions in supply, affecting the initiation, execution and timing of completion of clinical trials and commercial activities. Furthermore, material supply constraints could result in production delays. We attempt to mitigate risk to our product supply by careful planning of our production and raw material requirements with sufficient lead times for ramp-up by third-party manufacturers. Additionally, we work with and qualify other third-party manufacturers to provide alternative manufacturing capacity, if needed, due to delays or interruptions in supply, but such alternative manufacturers may be subject to similar constraints or issues.

We are also investing in process development initiatives intended to increase manufacturing scale, reduce production costs, and enhance process controls and product quality, among other things. These initiatives are being conducted both internally and outsourced to select contractors, and the related investments are meant to enable us to meet potential commercial demand in the event of regulatory approval. We are continuing to develop a bioreactor-based manufacturing platform for such commercialization. In our clinical studies, we are continuing to use cell factory-based material and plan to use bioreactor manufactured product, for which we now have FDA approval for use in our ARDS and trauma clinical trials in the United States. As we continue to prepare for commercialization, we believe that the cell factory-based approach for production is not well suited for serving, on more than a limited basis, large markets or conditions requiring higher dose treatments due to the limited potential for scale-up, relatively high costs and the possibility of reliability issues due to the complexity of the cell factory-based manufacturing process. A full transition to bioreactor-based material for the commercial setting will require a demonstration of comparability, which could include the requirement for analytical and *in vitro* data, some non-clinical studies and possibly data from additional clinical studies. In January 2021, we entered into a lease for a building that could potentially be developed into a state-of-the-art, commercial-scale manufacturing facility for our cell therapy product. We are considering the feasibility of building out the facility in stages as we complete our pivotal clinical trials, and assuming success, submit the required regulatory filings for commercialization. We believe that we have ownership, control and access to the technologies and intellectual properties that would enable us, or our contract manufacturing partners, to manufacture product needed to serve the indications targeted by our therapy.

Competition

We face significant competition with respect to the various dimensions of our business. With regard to our efforts to develop MultiStem as a novel stem cell therapy, currently, there are a number of companies that are actively developing stem cell products, which encompass a range of different cell types, including embryonic stem cells, umbilical cord stem cells, adult-derived stem cells and processed bone marrow derived cells.

Mesoblast Limited, or Mesoblast, is currently engaged in clinical trials evaluating the safety and efficacy of Revascor, an allogeneic stem cell product based on mesenchymal stem cell precursors that are obtained from healthy consenting donors. These cells also appear to display limited expansion potential and biological plasticity. Additionally, Mesoblast is developing Remestemcel-L, a mesenchymal stem cell product candidate.

Other public companies are or may be developing stem-related therapies, including SanBio, Vericel Corporation, Caladrius Biosciences, Inc., Johnson & Johnson, Cryo-Cell International, Inc., Brainstorm Cell Therapeutics, Inc., ReNeuron Group plc, Cynata Therapeutics Limited, Gamida Cell Ltd. and Pluristem Therapeutics, Inc. In addition, private companies, such as Plureon Corporation and others, are also developing cell therapy related products or capabilities. Given the magnitude of the potential opportunity for stem cell therapy, we expect competition in this area to intensify in the coming years. In addition, our other earlier-stage programs may face competition, including from larger pharmaceutical and biotechnology companies.

Many of our competitors may have substantially greater financial, technical, sales, marketing, and human resources than we do. These companies may succeed in obtaining regulatory approval for competitive products more rapidly than we can for our products. In addition, our competitors may develop technologies and products that are cheaper, safer or more effective than those being developed by us or that would render our technology obsolete. Furthermore, some of these companies may feel threatened by our activities and attempt to delay or impede our efforts to develop our products or apply our technologies.

Intellectual Property

We rely on a combination of patent applications, patents, trademarks, and contractual provisions to protect our proprietary rights. We believe that to have a competitive advantage, we must develop and maintain the proprietary aspects of our technologies. Currently, we require our officers, employees, consultants, contractors, manufacturers, outside scientific collaborators and sponsored researchers, and other advisors to execute confidentiality agreements in connection with their employment, consulting, manufacturing or advisory relationships with us, where appropriate. We also require our employees, consultants, and advisors that we expect to work on our products to agree to disclose and assign to us all inventions conceived during the workday, developed using our property, or which relate to our business. We currently have over 435 patents for our technologies.

We have a broad patent estate with claims directed to compositions, methods of production, and methods of use of certain non-embryonic stem cells and related technologies. We developed, acquired and exclusively licensed intellectual property covering our cell therapy product candidates and other applications in the field. Our broad intellectual property portfolio consists of over 410 issued patents and more than 140 global patent applications around our stem cell technology and MultiStem product platform. This includes 38 United States patents and more than 375 international patents that apply to MAPC and related products, such as MultiStem. The current intellectual property estate, which incorporates additional filings and may broaden over time, could provide coverage for our stem cell product candidates, manufacturing processes and methods of use through 2036 and beyond. Furthermore, an extended period of market exclusivity may apply for certain products (e.g., exclusivity periods for orphan drug designation or biologics).

We also have an intellectual property portfolio related to our small molecule product candidates, functional genomics and other technologies, with 24 global patents with claims directed to compositions, methods of making, and methods of using our candidates and technologies, among other claims.

We have been active in the development, improvement and protection of our intellectual property portfolio through our prosecution efforts, collaborative research efforts, and in-licensing, among other things. From time-to-time, we will also engage in adversarial processes, such as interference or litigation, to protect or advance certain patents or applications. These activities represent an important cost of doing business and can result in successes and setbacks due to the nature of the processes. Over time, we expect to be involved in similar proceedings with the objective of developing the portfolio to support and protect development and commercialization of our or our licensees' cell therapy products.

We believe that we have broad freedom to use and commercially develop our technologies and product candidates. However, in the event that we or our collaborators are developing, manufacturing, or selling potential products that are claimed to infringe a third party's intellectual property, a loss in litigation may prevent us from commercializing our products, unless that party grants us rights to use its intellectual property. Further, we may not be able to obtain any licenses required under any patents or proprietary rights of third parties on acceptable terms, or at all. Even if we were able to obtain rights to the third party's intellectual property, these rights may be non-exclusive, thereby giving our competitors access to the same intellectual property. Ultimately, we may be unable to commercialize some of our potential products or may have to cease some of our business operations as a result of patent infringement claims, which could severely harm our business.

Research and Development

Our research and development costs, which consist primarily of costs associated with clinical trials, preclinical research, product manufacturing and process development for manufacturing, salaries and related personnel costs, legal expenses resulting from intellectual property application and maintenance processes, and laboratory supply and reagent costs, were $71.1 million in 2021, $63.0 million in 2020 and $39.0 million in 2019. The increase in research and development costs in 2021 related primarily to the clinical trials underway and increased manufacturing and process development activities.

Government Regulation

Our research and development activities, and any products we may develop, are subject to stringent government regulation in the United States by the FDA and, in many instances, by corresponding foreign and state regulatory agencies. The European Union, or EU, has vested centralized authority in the EMA and Committee for Medicinal Products for Human Use, or CHMP, to standardize review and approval across EU member nations. In Japan, PDMA, a division of the Ministry of Health, Labour and Welfare, or MHLW, regulates the development and commercialization of medical therapies. Recently, Japan's parliament enacted new legislation to promote the safe and accelerated development of treatments using stem cells. The new regenerative medicine law and revised pharmaceutical affairs law define products containing stem cells as regenerative medicine products and allow for the conditional approval of such products if safety has been confirmed in clinical trials, even if their efficacy has not been fully demonstrated. The legislation creates a new, faster pathway for cell therapy product approval, and offers the potential to enable more rapid entry in the Japanese market. The MHLW has been directed to develop and adopt new rules and procedures to implement this legislation.

These regulatory agencies enforce comprehensive statutes, regulations and guidelines governing the drug development process. This process involves several steps. Initially, a company must generate preclinical data to show safety and potential efficacy before human testing may be initiated. In the United States, for example, a drug company must submit an IND application to the FDA prior to securing authorization for human testing. The IND must contain adequate data on product candidate chemistry, manufacturing and control, safety, toxicology, metabolism and, where appropriate, animal research testing to support potential initial effectiveness.

Any of our product candidates will require regulatory approval and compliance with regulations made by United States and foreign government agencies prior to commercialization in such countries. The process of obtaining FDA or foreign regulatory agency approval has historically been extremely costly and time consuming. The FDA and equivalent foreign regulatory authorities (such as EMA or PMDA) regulate, among other things, the development, testing, manufacturing, quality control, safety, efficacy, record keeping, labeling, storage, approval, advertising, promotion, sale and distribution of biologics and drugs.

The standard process required by the FDA before a pharmaceutical agent may be marketed in the United States includes:

- preclinical tests in animals that demonstrate a reasonable likelihood of safety and effectiveness (if possible) in human patients;
- submission to the FDA of an IND, which must be approved before clinical trials in humans can commence. If Phase 1 clinical trials are to be conducted initially outside the United States, a different regulatory filing such as a clinical trial application is required, depending on the location of the trial;

- adequate and well controlled human clinical trials to establish the safety and efficacy of the drug or biologic product for the intended disease indication;
- for drugs (including biologics), submission of a New Drug Application, or NDA, for new small molecules, and of a BLA, for biologics, with the FDA; and
- FDA approval of the NDA or BLA before any commercial sale or shipment of the drug.

Preclinical studies can take several years to complete, and there is no guarantee that an IND based on those studies will become effective to permit clinical trials to begin. The clinical development phase generally takes ten to fifteen years, or longer, to complete (i.e., from the initiation of Phase 1 through completion of Phase 3 studies), and such sequential studies may overlap or be combined. After successful completion of clinical trials for a new drug or biologic product, FDA approval of the NDA or BLA must be obtained. This process requires substantial time and effort and there is no assurance that the FDA will accept the NDA or BLA for filing and, even if filed, that the FDA will grant approval. In the past, the FDA's approval of an NDA or BLA has taken, on average, one to two years, but in some instances may take substantially longer. If questions regarding safety or efficacy arise, additional studies may be required, followed by a resubmission of the NDA or BLA. Review and approval of an NDA or BLA can take up to several years. The FDA and other regulatory agencies such as the EMA and the PMDA have regulations that allow for faster or expedited approval paths and review cycles that may reduce clinical development phase completion to between five and seven years to commercialization. Such regulations include but are not limited to special expedited paths and designations such as Fast Track (FDA), Break Through (FDA), RMAT (FDA), Prime (EMA), Accelerated (FDA)/Conditional (EMA), Sakigake (PMDA), which provide approval paths and review cycles of between six to ten months. However, there are specific criteria that must be met to qualify for these paths, such as the indication being a serious condition, with limited or no treatment options, and a high unmet medical need, or in addition is an orphan indication (FDA/EMA/PMDA), or qualified under, exceptional circumstances (EMA) or Sakigake designation (Japan).

In addition to obtaining FDA approval for each product being sold in the United States, each drug manufacturing facility must be inspected and approved by the FDA. All manufacturing establishments are subject to inspections by the FDA and by other federal, state, and local agencies, and must comply with GMP requirements. We do not currently have any GMP manufacturing capabilities and rely on contract manufacturers to produce material for any clinical trials that we conduct.

We must also obtain regulatory approval in other countries in which we intend to market any drug. The requirements governing conduct of clinical trials, product licensing, pricing, and reimbursement vary widely from country to country. FDA approval does not ensure regulatory approval in other countries. The current approval process varies from country to country, and the time spent in gaining approval varies from that required for FDA approval. In some countries, the sale price of the drug must also be approved. The pricing review period often begins after market approval is granted. Even if a foreign regulatory authority approves a drug product, it may not approve satisfactory prices for the product.

In addition to regulations enforced by the FDA and international regulatory agencies, we are also subject to regulation under the Occupational Safety and Health Act, the Environmental Protection Act, the Toxic Substances Control Act, the Resource Conservation and Recovery Act, and other present and potential future federal, state, or local regulations. Our research and development activities involve the controlled use of hazardous materials, chemicals, biological materials, and various radioactive compounds. Although we believe that our safety procedures for handling and disposing of such materials currently comply in all material respects 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, we could be held liable for any damages that result and any such liability could exceed our available resources.

Human Capital Resources

We believe that our success will be based on, among other things, the quality of our clinical programs, our ability to invent and develop superior and innovative technologies and products, and our ability to develop, attract and retain talented employees. We have assembled an exceptional team of individuals in all functional areas and levels of the business with significant experience across a number of industries, including biotechnology and pharmaceutical industries. We welcomed 19 new employees in 2021, several of them in key leadership positions. We hired in the areas of process development, research, manufacturing, operations and supply chain, regulatory affairs and other administrative functions.

As of December 31, 2021, we employed 104 full-time employees, including 16 with Ph.D. degrees. Our workforce is approximately 64% diverse by race, ethnicity or gender. We offer a competitive total reward program which consists of base salary, incentive cash bonus potential, a comprehensive health benefit package, paid time off, 401(k) retirement plan participation and equity compensation for all full-time employees. We also utilize the service and support of outside consultants and advisors. We annually evaluate the consistency and competitiveness of our compensation and benefits programs that serve to attract, retain, motivate and reward employees. We sustain our cultural engagement and performance by actively seeking and responding to employee feedback, measuring performance, recognizing employee achievements and identifying areas of

development and professional growth. None of our employees are represented by a union, and we believe we have positive and engaging relationships with our employees.

Health, Safety and Wellness

We are committed to the health and safety of our employees. We provide our employees and their families with access to a variety of health, wellness and other benefit programs that support physical, mental and financial well-being. We maintain a disciplined safety program and all of our employees must comply with annual safety training.

Response to COVID-19

Our focus has been to ensure a safe work environment for our employees in alignment with government and health authority COVID-19 policies and recommendations. We will continue to monitor the CDC guidance and will adjust our policies and practices as necessary.

Available Information

We use the Investors section of our website, www.athersys.com, as a channel for routine distribution of important information, including news releases, analyst presentations and financial information. We post filings as soon as reasonably practicable after they are electronically filed with, or furnished to, the Securities and Exchange Commission, or SEC, including our annual, quarterly, and current reports on Forms 10-K, 10-Q, and 8-K; our proxy statements; and any amendments to those reports or statements. All such postings and filings are available on the Investors section of our website free of charge. In addition, this website allows investors and other interested persons to sign up to automatically receive e-mail alerts when we post news releases and financial information on our website. The SEC also maintains a website, www.sec.gov, which contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC. The content on any website referred to in this Annual Report on Form 10-K is not incorporated by reference into this Annual Report unless expressly noted.

ITEM 1A. RISK FACTORS

The statements in this section, as well as statements described elsewhere in this Annual Report, or in other SEC filings, describe risks that could materially and adversely affect our business, financial condition and results of operations, which could also cause the trading price of our equity securities to decline. These risks are not the only risks that we face. Our business, financial condition and results of operations could also be affected by additional factors that are not presently known to us or that we currently consider to be immaterial to our operations. Although the risks are organized by headings, and each risk is discussed separately, many are interrelated.

Risks Related to Our Business

There is substantial doubt about our ability to continue as a going concern, which may affect our ability to obtain future financing and may require us to curtail our operations. We will need substantial additional funding to develop our products and for our future operations. If we are unable to obtain the funds necessary to do so, we may be required to delay, scale back or eliminate our product development activities or may be unable to continue our business.

The audited financial statements and accompanying notes presented in this Annual Report on Form 10-K include disclosures and an opinion from our independent registered public accounting firm stating that our recurring losses and negative cash flows from operations raise substantial doubt about our ability to continue as a going concern. Our financial statements as of December 31, 2021 and 2020 were prepared under the assumption that we will continue as a going concern and do not include any adjustments that might result from the outcome of this uncertainty.

The development of our product candidates will require a commitment of substantial funds to conduct the research, which may include preclinical and clinical testing, necessary to obtain regulatory approvals and bring our products to market. Net cash used in our operations was $76.2 million in 2021, $61.8 million in 2020 and $35.3 million in 2019.

At December 31, 2021, we had $37.4 million of cash and cash equivalents. However, we will need substantially more funding to advance our product candidates through development and into commercialization, including to put in place manufacturing capacity to support such commercial activity. Our future capital requirements will depend on many factors, including:

- our ability to raise capital to fund our operations;
- the progress, scope, costs and results of our clinical and preclinical testing of any current or future product candidates;
- the possibility of delays in, adverse events of and excessive costs of the development process;
- the cost of manufacturing our product candidates;
- the cost of prosecuting, defending and enforcing patent claims and other intellectual property rights;
- the time and cost involved in obtaining regulatory approvals;
- expenses related to complying with GMP of therapeutic product candidates;
- costs of financing or acquiring additional capital equipment and development technologies;
- competing technological and market developments;
- our ability to establish and maintain collaborative and other arrangements with third parties to assist in bringing our products to market and the cost of such arrangements;
- the amount and timing of payments or equity investments that we receive from collaborators or changes in or terminations of future or existing collaboration and licensing arrangements and the timing and amount of expenses we incur to support these collaborations and license agreements;
- costs associated with the integration of any new operation, including costs relating to future mergers and acquisitions with companies that have complementary capabilities;
- expenses related to the establishment of sales and marketing capabilities for products awaiting approval or products that have been approved;
- expenses related to establishing manufacturing capabilities;
- the level of our sales and marketing expenses; and
- our ability to introduce and sell new products.

The extent to which we utilize our existing equity purchase arrangement with Aspire Capital Fund LLC, or Aspire Capital, as a source of funding will depend on a number of factors, including the prevailing market price of our common stock, the volume of trading in our common stock and the extent to which we are able to secure funds from other sources. The number of shares that we may sell to Aspire Capital under the purchase agreement on any given day and during the term of the agreement is limited. Additionally, we and Aspire Capital may not affect any sales of shares of our common stock under the purchase agreement during the continuance of an event of default.

We have secured capital historically from grant revenues, collaboration proceeds and debt and equity offerings. We will need to secure substantial additional capital to fund our future operations. We cannot be certain that additional capital will be available on acceptable terms or at all. To the extent we raise additional capital through the sale of equity securities, including to Aspire Capital, the ownership position of our existing stockholders could be substantially diluted. If additional funds are raised through the issuance of preferred stock or debt securities, these securities are likely to have rights, preferences and privileges senior to our common stock. Fluctuating interest rates could also increase the costs of any debt financing we may obtain.

Importantly, we expect that the results of Healios' TREASURE study, followed by the results of our MASTERS-2 clinical trial, will have a significant impact, favorable or unfavorable, on our ability to access capital from potential third-party commercial partners or the equity capital markets. Depending on the nature of these results, we may accelerate or may delay certain programs. In the longer term, we will have to continue to generate additional capital to meet our needs until we would become cash flow positive as a result of the sales of our clinical products, if they are approved for marketing.

Failure to successfully address ongoing liquidity requirements will have a material adverse effect on our business. If we are unable to obtain additional capital on acceptable terms when needed, we may be required to take actions that harm our business and our ability to achieve cash flow in the future, including possibly the surrender of our rights to some technologies or product opportunities, delaying our clinical trials or curtailing or ceasing operations.

We have incurred losses since inception, and we expect to incur significant net losses in the foreseeable future and may never become profitable.

Since our inception in 1995, we incurred significant losses and negative cash flows from operations. We incurred net losses of $87.0 million in 2021, $78.8 million in 2020 and $44.6 million in 2019. As of December 31, 2021, we had an accumulated deficit of $583.3 million, and we will not commence sales of our clinical product candidates until they receive regulatory approval for commercialization. We expect to spend significant resources over the next several years to continue our research and product development programs, including clinical trials of our product candidates and process development and manufacturing projects, and to prepare for possible regulatory approval and commercial activities. We expect to continue to incur substantial losses through at least the next several years and may incur losses in subsequent periods, and our ability to commercialize our product candidates is uncertain. To date, substantially all of our revenue has been derived from corporate collaborations, license agreements and government grants. In order to achieve profitability, we must develop products and technologies that can be commercialized by us or through our existing or future collaborations. Our ability to generate revenues and become profitable will depend on our ability, alone or with potential collaborators, to timely, efficiently and successfully complete the development of our product candidates. We have never earned revenue from selling a product and we may never do so, as none of our product candidates have been approved for sale, since they are currently being tested in human and animal studies. We cannot assure you that we will ever earn sales revenue or that we will ever become profitable. If we sustain losses over an extended period, we may be unable to continue our business.

We are heavily dependent on the successful development and commercialization of MultiStem products, and if we encounter delays or difficulties in the development of these product candidates, our business could be harmed.

Our success is heavily dependent upon the successful development of MultiStem products for certain diseases and conditions involving acute or ischemic injury or immune system dysfunction. Our business could be materially harmed if we encounter difficulties in the development of this product candidate, such as:

- delays in the ability to manufacture the product in quantities or in a form that is suitable for any required preclinical studies or clinical trials;
- an inability to produce the product at an appropriate cost or to scale for commercialization;
- delays in the design, enrollment, implementation or completion of required preclinical studies and clinical trials;
- an inability to follow our current development strategy for obtaining regulatory approval from regulatory authorities because of changes in the regulatory approval process;
- less than desired or complete lack of efficacy or safety in preclinical studies or clinical trials; and
- intellectual property constraints that prevent us from making, using or commercializing the product candidate.

The process of manufacturing the MultiStem product platform is complex and we may encounter difficulties in production, particularly with respect to process development or scaling-up of our manufacturing capabilities.

The process of manufacturing the MultiStem product platform is complex, highly-regulated and subject to multiple risks. The complex processes associated with the manufacture of our product candidates expose us to various manufacturing challenges and risks, which may include delays in manufacturing adequate supply of our product candidates, limits on our ability to increase manufacturing capacity, and the potential for product failure and product variation that may interfere with preclinical and clinical trials, along with additional costs. We also may make changes to our manufacturing process at various points during development, and even after commercialization, for various reasons, such as controlling costs, achieving scale, decreasing processing time, increasing manufacturing success rate, or other reasons. Such changes carry the risk that they will not achieve their intended objectives, and any of these changes could cause our product candidates to perform differently and affect the results of current or future clinical trials, or the performance of the product, once commercialized. In some circumstances, changes in the manufacturing process may require us to perform *ex vivo* comparability studies and to collect additional data from patients prior to undertaking more advanced clinical trials. For instance, changes in our process during the course of clinical development may require us to show the comparability of the product used in earlier clinical trials or at earlier portions of a trial to the product used in later clinical trials or later portions of the trial. We may also make further changes to our manufacturing process before or after commercialization, and such changes may require us to show the comparability of the resulting product to the product used in the clinical trials using earlier processes. We may be required to collect additional clinical data from any modified process prior to obtaining marketing approval for the product candidate produced with such modified process. If clinical data are not ultimately comparable to that seen in the earlier trials in terms of safety or efficacy, we may be required to make further changes to our process and/or undertake additional clinical testing, either of which could significantly delay the clinical development or commercialization of the associated product candidate.

If we are unable to attract and retain key personnel and advisors, it may adversely affect our ability to obtain financing, pursue collaborations or develop our product candidates.

We are highly dependent on our senior executives, such as Daniel Camardo, MBA, Chief Executive Officer, William (B.J.) Lehmann, J.D., MBA., President and Chief Operating Officer, John Harrington, Ph.D., Executive Vice President and Chief Scientific Officer, and Ivor Macleod, MBA, CPA, Chief Financial Officer, as well as other personnel.

These individuals are integral to the development and integration of our technologies and to our present and future scientific collaborations, including managing the complex research processes and the product development and potential commercialization processes. Given their leadership, extensive technical, scientific and financial expertise and management and operational experience, these individuals would be difficult to replace. Consequently, the loss of services of one or more of these named individuals could result in product development delays or the failure of our collaborations with current and future collaborators, which, in turn, may hurt our ability to develop and commercialize products and generate revenues.

Our future success depends on our ability to attract, retain and motivate highly qualified management and scientific, development and commercial personnel and advisors. If we are unable to attract and retain key personnel and advisors, it may negatively affect our ability to successfully develop, test and commercialize our product candidates.

We may encounter difficulties managing our growth, which could adversely affect our business.

At various times, we have experienced periods of rapid growth in our employee numbers as a result of a dramatic increase in activity in technology programs, genomics programs, collaborative research programs, discovery programs, clinical trials and scope of operations. At other times, we had to reduce staff in order to bring our expenses in line with our financial resources. Our success will also depend on the ability of our officers and key employees to continue to improve our operational capabilities and our management information and financial control systems, and to expand, train and manage our work force.

Risks related to the current COVID-19 pandemic and other health epidemics and outbreaks could adversely affect our business.

The global outbreak of COVID-19 continues to impact countries, communities, supply chains and markets. As of the date of this Annual Report on Form 10-K, the COVID-19 pandemic has not had a significant adverse effect on our core business operations. However, the pandemic has adversely impacted operations at certain existing and potential future clinical sites involved in our ongoing clinical studies and affected our ability to enroll patients in our clinical trials. It is possible that the COVID-19 pandemic could continue to impact the timing and enrollment of our planned and ongoing clinical trials, delaying clinical site initiation, regulatory review and the potential receipt of regulatory approvals, payment of milestones under our license agreements and commercialization of one or more of our product candidates, if approved. The COVID-19 pandemic could negatively impact our financial liquidity by impairing our ability to access our primary financing sources, including, but not limited to business collaborations, grant funding and equity financings, on the same or reasonably similar terms as were available to us before the pandemic. The COVID-19 pandemic could also disrupt the production capabilities of our contract manufacturing partners and materially and adversely impact our MultiStem trial supply chain. The COVID-19 pandemic is

fluid and continues to evolve, and therefore, we cannot currently predict the extent to which our business, clinical trials, results of operations, financial condition or liquidity will ultimately be impacted.

To the extent the COVID-19 pandemic adversely affects our business and financial results, it may also heighten many of the other risks described in this section and affect our need for substantial additional funding to develop our products and support our operations, delays or difficulties in developing and commercializing our MultiStem product candidates, and delays in clinical trials, including MASTERS-2, and regulatory approvals relating to our products.

Risks Related to Development, Clinical Testing and Regulatory Approval of Our Product Candidates

Our product candidates are currently in the development stage and we have no therapeutic products approved for sale. If we are unable to develop, obtain regulatory approval or market any of our product candidates, our financial condition will be negatively affected, and we may have to curtail or cease our operations.

Many factors, known and unknown, can adversely affect clinical trials and the ability to evaluate a product's efficacy. During the course of treatment, patients can die or suffer other adverse events for reasons that may or may not be related to the proposed product being tested. Even if unrelated to our product, certain events can nevertheless adversely impact our clinical trials. As a result, our ability to ultimately develop and market the products and obtain revenues would suffer.

Even promising results in preclinical studies and initial clinical trials do not ensure successful results in later clinical trials, which test broader human use of our products. Many companies in our industry have suffered significant setbacks in advanced clinical trials, despite promising results in earlier trials.

We are in the early stage of product development, and we are dependent on the application of our technologies to discover or develop therapeutic product candidates. We currently do not sell any approved therapeutic products and do not expect to have any products commercially available for several years, if at all. You 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. To date, no one to our knowledge has commercialized any therapeutic products using our technologies and we might never commercialize any product using our technologies and strategy. In addition, we may not succeed in developing new product candidates as an alternative to our existing portfolio of product candidates. If our current product candidates are delayed or fail, or we fail to successfully develop and commercialize new product candidates, our financial condition may be negatively affected, and we may have to curtail or cease our operations.

We may experience delays in clinical trials and regulatory approval relating to our products that could adversely affect our financial results and our commercial prospects for our pharmaceutical or stem cell products.

In addition to the regulatory requirements for our pharmaceutical programs, we will also require regulatory approvals for each distinct application of our MultiStem product. In each case, we will be required to conduct clinical trials to demonstrate safety and efficacy of MultiStem, or various products that incorporate or use MultiStem. For product candidates that advance to clinical testing, we cannot be certain that we or a collaborator will successfully complete the clinical trials necessary to receive regulatory product approvals. This process is lengthy and expensive.

We intend to seek approval for our product candidates through the FDA approval process in the United States, and through other regulatory agencies outside the United States. To obtain regulatory approvals, we must, among other requirements, complete clinical trials showing that our products are safe and effective for a particular indication. Under the approval process, we must submit clinical and non-clinical data to demonstrate the product is safe and effective. For example, we must be able to provide data and information, which may include extended pharmacology, toxicology, reproductive toxicology, bioavailability and genotoxicity studies, to establish suitability for late stage clinical trials.

All of our product candidates are in clinical development. As these programs progress through clinical development, or complete additional non-clinical testing, an indication of a lack of safety or lack of efficacy may result in the early termination of an ongoing study, or may cause us or any of our collaborators to forego further development of a particular product candidate or program. The FDA or other regulatory agencies may require extensive clinical trials or other testing prior to granting approval, which could be costly and time consuming to conduct. Any of these developments could hinder, and potentially prohibit, our ability to commercialize our product candidates. We cannot assure you that clinical trials will demonstrate that our products are safe and effective.

Additionally, we may not be able to find acceptable patients or may experience delays in enrolling patients for our currently planned or any future clinical trials. The FDA, international regulatory agencies or we may suspend our clinical trials at any time if it is believed that we are exposing the subjects participating in the trials to unacceptable health risks. The regulatory authorities or institutional review boards and/or institutional biosafety committees at the medical institutions and healthcare

facilities where we seek to sponsor clinical trials may not permit a trial to proceed or may suspend any trial indefinitely if they find deficiencies in the conduct of the trials.

Product development costs to us and our potential collaborators will increase if we have delays in testing or approvals or if we need to perform more or larger clinical trials than planned. We expect to continue to rely on third-party clinical investigators at medical institutions and healthcare facilities to conduct our clinical trials, and, as a result, we may face additional delaying factors outside our control. Significant delays may adversely affect our financial results and the commercial prospects for our product candidates and delay our ability to become profitable.

The results seen in animal testing of our product candidates may not be replicated in humans.

Safety and efficacy seen in preclinical testing of our product candidates in animals may not be seen when our product candidates undergo clinical testing in humans. Preclinical studies and Phase 1 clinical trials are not primarily designed to test the efficacy of a product candidate in humans, but rather to:

- test short-term safety and tolerability;
- study the absorption, distribution, metabolism and elimination of the product candidate;
- study the biochemical and physiological effects of the product candidate and the mechanisms of the drug action and the relationship between drug levels and effect; and
- understand the product candidate's side effects at various doses and schedules.

Success in preclinical studies or completed clinical trials does not ensure that later studies or trials, including continuing non-clinical studies and large-scale clinical trials, will be successful, nor does it necessarily predict future results. The rate of failure in drug development is quite high, and many companies in the biotechnology and pharmaceutical industries have suffered significant setbacks in advanced clinical trials, even after promising results in earlier trials. Product candidates may fail to show desired safety and efficacy in larger and more diverse patient populations in later stage clinical trials, despite having progressed through early stage trials. Negative or inconclusive results from any of our ongoing preclinical studies or clinical trials could result in delays, modifications, or abandonment of ongoing or future clinical trials and the termination of our development of a product candidate. Additionally, even if we are able to successfully complete late stage clinical trials, the regulatory authorities still may not approve our product candidates.

Even if we obtain regulatory approval of any of our product candidates, the approved products may be subject to post-approval studies and will remain subject to ongoing regulatory requirements. If we fail to comply, or if concerns are identified in subsequent studies, our approval could be withdrawn, and our product sales could be suspended.

If we are successful at obtaining regulatory approval for MultiStem or any of our other product candidates, regulatory agencies in the United States and other countries where a product will be sold may require extensive additional clinical trials or post-approval clinical studies that are expensive and time consuming to conduct. In particular, therapeutic products administered for the treatment of persistent or chronic conditions are likely to require extensive follow-up studies and close monitoring of patients after regulatory approval has been granted for any signs of adverse effects that occur over a long period of time. These studies may be expensive and time consuming to conduct and may reveal side effects or other harmful effects in patients that use our therapeutic products after they are on the market, which may result in the limitation or withdrawal of our drugs from the market. Alternatively, we may not be able to conduct such additional trials, which might force us to abandon our efforts to develop or commercialize certain product candidates. Even if post-approval studies are not requested or required, after our products are approved and on the market, there might be safety issues that emerge over time that require a change in product labeling or that require withdrawal of the product from the market, which would cause our revenue to decline.

Additionally, any products that we may successfully develop will be subject to ongoing regulatory requirements after they are approved. These requirements will govern the manufacturing, packaging, marketing, distribution, and use of our products. If we fail to comply with such regulatory requirements, approval for our products may be withdrawn, and product sales may be suspended. We may not be able to regain compliance, or we may only be able to regain compliance after a lengthy delay, significant expense, lost revenues and damage to our reputation.

Risks Related to Commercialization of Our Product Candidates

If we inadvertently violate the guidelines pertaining to promotion and advertising of our clinical candidates or approved products, we may be subject to disciplinary action by the FDA's Division of Drug Marketing, Advertising, and Communications or other regulatory bodies.

The FDA's Division of Drug Marketing, Advertising, and Communications, or DDMAC, is responsible for reviewing prescription drug advertising and promotional labeling to ensure that the information contained in these materials is not false or misleading. There are specific disclosure requirements and the applicable regulations mandate that advertisements cannot be

false or misleading or omit material facts about the product. Prescription drug promotional materials must present a fair balance between the drug's effectiveness and the risks associated with its use. Most warning letters from DDMAC cite inadequate disclosure of risk information.

DDMAC prioritizes its actions based on the degree of risk to the public health, and often focuses on newly introduced drugs and those associated with significant health risks. There are two types of letters that DDMAC typically sends to companies that violate its drug advertising and promotional guidelines: notice of violation letters, or untitled letters, and warning letters. In the case of an untitled letter, DDMAC typically alerts the drug company of the violation and issues a directive to refrain from future violations but does not typically demand other corrective action. A warning letter is typically issued in cases that are more serious or where the company is a repeat offender. Although we have not received any such letters from DDMAC, we may inadvertently violate DDMAC's guidelines in the future and be subject to a DDMAC untitled letter or warning letter, which may have a negative impact on our business. Similarly, we and our collaborators may inadvertently violate the guidelines of the foreign equivalent of the FDA's DDMAC, e.g., in Europe or Japan.

If we do not comply with applicable regulatory requirements in the manufacture and distribution of our product candidates, we may incur penalties that may inhibit our ability to commercialize our products and adversely affect our revenue.

Our failure or the failure of our potential collaborators or third-party manufacturers to comply with applicable FDA or other regulatory requirements including manufacturing, quality control, labeling, safety surveillance, promoting and reporting may result in criminal prosecution, civil penalties, recall or seizure of our products, total or partial suspension of production or an injunction, as well as other regulatory action against our product candidates or us. Discovery of previously unknown problems with a product, supplier, manufacturer or facility may result in restrictions on the sale of our products, including a withdrawal of such products from the market. The occurrence of any of these events would negatively impact our business and results of operations.

If we are unable to create and maintain sales, marketing and distribution capabilities or enter into agreements with third parties to perform those functions, we will not be able to commercialize our product candidates.

We currently have no sales, marketing or distribution capabilities. Therefore, to commercialize our product candidates, if and when such products have been approved and are ready for marketing, we expect to collaborate with third parties to perform these functions. If we establish any such relationships, we will be dependent upon the capabilities of our collaborators or contract service providers to effectively market, sell, and distribute our product. We will either need to share the value generated from the sale of any products and/or pay a fee to the contract sales organization. If they are ineffective at selling and distributing our product, or if they choose to emphasize other products over ours, we may not achieve our expected level of product sales revenues. If conflicts arise, we may not be able to resolve them easily or effectively, and we may suffer financially as a result. If we cannot rely on the sales, marketing and distribution capabilities of our collaborators or of contract service providers, we may be forced to establish our own capabilities. We have no experience in developing, training or managing a sales force and will incur substantial additional expenses if we decide to market any of our future products directly. Developing a marketing and sales force is also time consuming and could delay launch of our future products. In addition, we will compete with many companies that currently have extensive and well-funded marketing and sales operations. Our marketing and sales efforts may be unable to compete successfully against these companies.

To the extent we enter markets outside of the United States, our business will be subject to political, economic, legal and social risks in those markets, which could adversely affect our business.

There are significant regulatory and legal barriers in markets outside the United States that we must overcome to the extent we enter or attempt to enter markets in countries other than the United States. We will be subject to the burden of complying with a wide variety of national and local laws, including multiple and possibly overlapping and conflicting laws. We also may experience difficulties adapting to new cultures, business customs and legal systems. Any sales and operations outside the United States would be subject to political, economic and social uncertainties including, among others:

- changes and limits in import and export controls;
- increases in custom duties and tariffs;
- changes in currency exchange rates;
- economic and political instability;
- changes in government regulations and laws;
- absence in some jurisdictions of effective laws to protect our intellectual property rights; and
- currency transfer and other restrictions and regulations that may limit our ability to sell certain products or repatriate profits to the United States.

Any changes related to these and other factors could adversely affect our business to the extent we enter markets outside the United States.

Foreign governments often impose strict price controls on approved products, which may adversely affect our future profitability in those countries, and the re-importation of drugs to the United States from foreign countries that impose price controls may adversely affect our future profitability.

Frequently, foreign governments impose strict price controls on newly approved therapeutic products. If we obtain regulatory approval to sell products in foreign countries, we may be unable to obtain a price that provides an adequate financial return on our investment. Furthermore, legislation in the United States may permit re-importation of drugs from foreign countries into the United States, including re-importation from foreign countries where the drugs are sold at lower prices than in the United States due to foreign government-mandated price controls. Such a practice, especially if it is conducted on a widespread basis, may significantly reduce our potential United States revenues from any drugs that we are able to develop.

If we elect not to sell our products in foreign countries that impose government mandated price controls because we decide it is uneconomical to do so, a foreign government or patent office may attempt to terminate our intellectual property rights in that country, enabling competitors to make and sell our products.

In some cases, we may choose not to sell a product in a foreign country because it is uneconomical to do so under a system of government-imposed price controls, or because it could severely limit our profitability in the United States or other markets. In such cases, a foreign government or patent office may terminate any intellectual property rights we may obtain with respect to that product. Such a termination could enable competitors to produce and sell our product in that market. Furthermore, such products may be exported into the United States through legislation that authorizes the importation of drugs from outside the United States. In such an event, we may have to reduce our prices, or we may be unable to compete with low-cost providers of our drugs, and we could be financially harmed as a result.

We may be sued for product liability, which could adversely affect our business.

Because our business strategy involves the development and sale by either us or our collaborators of commercial products, we may be sued for product liability. We may be held liable if any product we develop and commercialize, or any product our collaborators commercialize that incorporates any of our technology, causes injury or is found otherwise unsuitable during product testing, manufacturing, marketing, sale or consumer use. In addition, the safety studies we must perform, and the regulatory approvals required to commercialize our pharmaceutical products, will not protect us from any such liability.

We carry product liability insurance that includes coverage for human clinical trials. Currently, we insure a total limit of $15.0 million per occurrence, $15.0 million annual aggregate coverage for both our products liability policy and our clinical trials protection. This limit is comprised of both primary and excess coverage. We also intend to seek product liability insurance for any approved products that we may develop or acquire. However, in the event there are product liability claims against us, our insurance may be insufficient to cover the expense of defending against such claims or may be insufficient to pay or settle such claims. Furthermore, we may be unable to obtain adequate product liability insurance coverage for commercial sales of any of our approved products. If such insurance is insufficient to protect us, our results of operations will suffer. If any product liability claim is made against us, our reputation and future sales will be damaged, even if we have adequate insurance coverage.

Even if we or our collaborators receive regulatory approval for our products, those products may never be commercially successful.

Even if we develop pharmaceuticals or MultiStem-related products that obtain the necessary regulatory approval, and we have access to the necessary manufacturing, sales, marketing and distribution capabilities that we need, our success depends to a significant degree upon the commercial success of those products. If these products fail to achieve or subsequently maintain market acceptance or commercial viability, our business would be significantly harmed because our future royalty revenue or other revenue would be dependent upon sales of these products. Many factors may affect the market acceptance and commercial success of any potential products that we may discover, including:

- health concerns, whether actual or perceived, or unfavorable publicity regarding our stem cell products or those of our competitors;
- the timing of market entry as compared to competitive products;
- the rate of adoption of products by our collaborators and other companies in the industry;
- any product labeling that may be required by the FDA or other United States or foreign regulatory agencies for our products or competing or comparable products;
- convenience and ease of administration;

- pricing;
- perceived efficacy and side effects;
- marketing;
- availability of alternative treatments;
- levels of reimbursement and insurance coverage; and
- activities by our competitors.

Risks Related to our Dependence on Third Parties

We may not successfully maintain our existing collaborative and licensing arrangements, or establish new ones, which could adversely affect our ability to develop and commercialize our product candidates.

A key element of our business strategy is to commercialize some of our product candidates through collaborations with other companies. Our strategy includes establishing collaborations and licensing agreements with one or more pharmaceutical, biotechnology or device companies, preferably after we have advanced product candidates through the initial stages of clinical development. However, we may not be able to establish or maintain such licensing and collaboration arrangements necessary to develop and commercialize our product candidates. Even if we are able to maintain or establish licensing or collaboration arrangements, these arrangements may not be on favorable terms and may contain provisions that will restrict our ability to develop, test and market our product candidates. Any failure to maintain or establish licensing or collaboration arrangements on favorable terms could adversely affect our business prospects, financial condition or ability to develop and commercialize our product candidates.

Our agreements with our collaborators and licensees may have provisions that give rise to disputes regarding the rights and obligations of the parties. These and other possible disagreements could lead to termination of the agreement or delays in collaborative research, development, supply, or commercialization of certain product candidates, or could require or result in litigation or arbitration. Moreover, disagreements could arise with our collaborators over rights to intellectual property or our rights to share in any of the future revenues of products developed by our collaborators. These kinds of disagreements could result in costly and time-consuming litigation. Any such conflicts with our collaborators could reduce our ability to obtain future collaboration agreements and could have a negative impact on our relationship with existing collaborators.

Currently, our material collaboration and licensing arrangement is with Healios, also a significant holder of our outstanding shares of common stock, to develop and commercialize MultiStem cell therapy for the treatment of ischemic stroke and ARDS in Japan, among other things, and we also have license agreements with third parties pursuant to which we in-license certain aspects of our technologies. These arrangements may not have specific termination dates; rather, each arrangement terminates upon the occurrence of certain events.

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

Our success depends on the performance by our collaborators of their responsibilities under our collaboration arrangements. Some potential collaborators may not perform their obligations in a timely fashion or in a manner satisfactory to us. Typically, we cannot control the amount of resources or time our collaborators may devote to our programs or potential products that may be developed in collaboration with us. We are currently involved in multiple research and development collaborations with academic and research institutions. These 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.

Additionally, our current or future corporate collaborators will retain the ability to pursue other research, product development or commercial opportunities that may be directly competitive with our programs. If these 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 or be unwilling to properly fund their share of the development expenses for our programs. Any of these developments could harm our product and technology development efforts, which could seriously harm our business.

We rely on third parties to manufacture our MultiStem product candidate.

Our current business strategy relies on third parties to manufacture our MultiStem product candidates in accordance with GMP established by the FDA or similar regulations in other countries. Reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured MultiStem ourselves. Although we are primarily responsible for regulatory compliance with respect to the manufacture of MultiStem product, we rely on third parties to manufacture the product as cost effectively as possible and to ensure product quality. Additionally, the production of our MultiStem product requires the availability of raw materials that are sourced through a limited number of suppliers. The failure of third-party manufacturers or suppliers to perform adequately or the termination of our arrangements with any of them may adversely affect our business.

These third parties may not deliver sufficient quantities of our MultiStem product, manufacture MultiStem product in accordance with specifications and cost expectations or comply with applicable government regulations. From time to time, such third-party manufacturers, or their material suppliers, may experience production delays, stoppages or interruptions in supply, which may affect the initiation, execution and timing of completion of clinical trials and commercial activities. Furthermore, our third-party manufacturers may have disruptions in their business operations as a result of business or strategic decisions or due to economic difficulties facing their businesses, cybersecurity incidents, terrorist activity, public health crises (such as COVID-19), fires or other natural disasters and could cease operations entirely. The number of third-party manufacturers with the necessary manufacturing and regulatory expertise and facilities is limited, and it could be expensive and take a significant amount of time to arrange for alternative manufacturing arrangements.

If and until we can manufacture our products ourselves, we expect to enter into additional manufacturing agreements for the production of our products. If any manufacturing agreement is terminated or any third-party collaborator fails to meet our product specifications or experiences a significant problem that could result in a delay or interruption in the supply of product materials to us, our clinical trials, business and reputation could be severely impacted. We cannot assure you that manufacturers on whom we will depend will be able to successfully produce our MultiStem product on commercially acceptable terms, or on a timely or cost-effective basis. We cannot assure you that manufacturers will be able to manufacture our products in accordance with our product specifications or will meet regulatory or other requirements. We must have sufficient and acceptable quantities of our product materials to conduct our clinical trials and ultimately to market our products, if and when such products have been approved for marketing. If we are unable to obtain sufficient and acceptable quantities of our product, we may be required to delay the clinical testing and marketing of our products.

Risks Related to Our Intellectual Property Rights

Our ability to compete may decline if we are not successful in adequately protecting our patented and other proprietary technologies.

Our success depends in part on our ability to obtain and maintain intellectual property that protects our technologies and our products. Patent positions may be highly uncertain and may involve complex legal and factual questions, including the ability to establish patentability of compounds and methods for using them for which we seek patent protection. We cannot predict the breadth of claims that will ultimately be allowed in our patent applications, if any, including those we have in-licensed or the extent to which we may enforce these claims against our competitors. We have filed multiple patent applications that seek to protect the composition of matter and method of use related to our programs. In addition, we are prosecuting numerous distinct patent families directed to composition, methods of production and methods of use of MultiStem and related technologies. If we are unsuccessful in obtaining and maintaining these patents related to products and technologies, we may ultimately be unable to commercialize products that we are developing or may elect to develop in the future.

The degree of future protection for our proprietary rights is therefore highly uncertain and we cannot assure you that:

- we were the first to file patent applications or to invent the subject matter claimed in patent applications relating to the technologies or product candidates upon which we rely;
- others will not independently develop similar or alternative technologies or duplicate any of our technologies;
- others did not publicly disclose our claimed technology before we conceived the subject matter included in any of our patent applications;
- any of our pending or future patent applications will result in issued patents;
- any of our patent applications will not result in interferences or disputes with third parties regarding priority of invention;
- any patents that may be issued to us, our collaborators or our licensors will provide a basis for commercially viable products or will provide us with any competitive advantages or will not be challenged by third parties;
- we will develop additional proprietary technologies that are patentable;

- the patents of others will not have an adverse effect on our ability to do business; or
- new proprietary technologies from third parties, including existing licensors, will be available for licensing to us on reasonable commercial terms, if at all.

In addition, patent law outside the United States is uncertain and, in many countries, intellectual property laws are undergoing review and revision. The laws of some countries do not protect intellectual property rights to the same extent as domestic laws. It may be necessary or useful for us to participate in opposition proceedings to determine the validity of our competitors' patents or to defend the validity of any of our or our licensor's future patents, which could result in substantial costs and would divert our efforts and attention from other aspects of our business. With respect to certain of our inventions, we decided not to pursue patent protection outside the United States, both because we do not believe it is cost effective and because of confidentiality concerns. Accordingly, our international competitors could develop and receive foreign patent protection for gene sequences and functions for which we are seeking United States patent protection, enabling them to sell products that we developed.

Technologies licensed to us by others, or in-licensed technologies, are important to our business. The scope of our rights under our licenses may be subject to dispute by our licensors or third parties. Our rights to use these technologies and to practice the inventions claimed in the licensed patents are subject to our licensors abiding by the terms of those licenses and not terminating them. In particular, we depend on certain technologies relating to our MultiStem technology licensed from the University of Minnesota, and the termination of this license could result in our loss of some of the rights that enable us to utilize this technology, and our ability to develop products based on MultiStem could be seriously hampered.

In addition, we may in the future acquire rights to additional technologies by licensing such rights from existing licensors or from third parties. Such in-licenses may be costly. Also, we generally do not control the patent prosecution, maintenance or enforcement of in-licensed technologies. Accordingly, we are unable to exercise the same degree of control over this intellectual property as we do over our internally developed technologies. Moreover, some of our academic institution licensors, collaborators and scientific advisors have rights to publish data and information to which we have rights. If we cannot maintain the confidentiality of our technologies and other confidential information in connection with our collaborations, our ability to protect our proprietary information or obtain patent protection in the future may be impaired, which could have a significant adverse effect on our business, financial condition and results of operations.

We may not have adequate protection for our unpatented proprietary information, which could adversely affect our competitive position.

In addition to patents, we will substantially rely on trade secrets, know-how, continuing technological innovations and licensing opportunities to develop and maintain our competitive position. However, others may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose our technology. To protect our trade secrets, we enter into confidentiality agreements with, among others, employees, consultants, contract manufacturers and potential collaborators. However, these agreements may not provide meaningful protection of our trade secrets or adequate remedies in the event of unauthorized use or disclosure of such information. Likewise, our trade secrets or know-how may become known through other means or be independently discovered by our competitors. Any of these events could prevent us from developing or commercializing our product candidates.

Disputes concerning the infringement or misappropriation of our proprietary rights or the proprietary rights of others could be time consuming and extremely costly and could delay our research and development efforts.

Our commercial success, if any, will be significantly harmed if we infringe the patent rights of third parties or if we breach any license or other agreements that we entered into with regard to our technology or business.

We are aware of other companies and academic institutions that have been performing research in the areas of adult-derived stem cells. In particular, other companies and academic institutions have announced that they have identified nonembryonic stem cells isolated from bone marrow or other tissues that have the ability to form a range of cell types or display the property of pluripotency. To the extent any of these companies or academic institutions currently have, or obtain in the future, broad patent claims, such patents could block our ability to use various aspects of our discovery and development process and might prevent us from developing or commercializing newly discovered applications of our MultiStem technology, or otherwise conducting our business. In addition, it is possible that some of the pharmaceutical product candidates we are developing may not be patentable or may be covered by intellectual property of third parties. For example, over the past several years, we were involved in proceedings in the United States and Europe with a third party focused on a technology developed after the MAPC technology. Ultimately, we reached a settlement agreement with and obtained a license from this third party, positioning us advantageously with respect to the achievement of our business objectives. Over time, we expect to be involved in similar proceedings with the objective of developing the portfolio to support and protect development and commercialization of our or our licensees' cell therapy products.

We are not currently a party to any litigation with regard to our patent or trademark positions. However, the life sciences and other technology industries are characterized by extensive litigation regarding patents and other intellectual property rights. Many life sciences and other technology companies have employed intellectual property litigation as a way to gain a competitive advantage. To the extent we are involved in litigation, interference proceedings, oppositions, reexamination, protest or other potentially adverse intellectual property proceedings as a result of alleged infringement by us of the rights of others or as a result of priority of invention disputes with third parties, we might have to spend significant amounts of money, time and effort defending our position and we may not be successful. In addition, any claims relating to the infringement of third-party proprietary rights or proprietary determinations, even if not meritorious, could result in costly litigation, lengthy governmental proceedings, divert management's attention and resources, or require us to enter into royalty or license agreements that are not advantageous to us. If we do not have the financial resources to support such litigation or appeals, we may forfeit or lose certain commercial rights. Even if we have the financial resources to continue such litigation or appeals, we may lose. In the event that we lose, we may be forced to pay very substantial damages; we may have to obtain costly license rights, which may not be available to us on acceptable terms, if at all; or we may be prohibited from selling products that are found to infringe the patent rights of others.

Should any person have filed patent applications or obtained patents that claim inventions also claimed by us, we may have to participate in an interference proceeding declared by the relevant patent regulatory agency to determine priority of invention and, thus, the right to a patent for these inventions in the United States. Such a proceeding could result in substantial cost to us even if the outcome is favorable. Even if successful on priority grounds, an interference action may result in loss of claims based on patentability grounds raised in the interference action. Litigation, interference proceedings or other proceedings could divert management's time and efforts. Even unsuccessful claims could result in significant legal fees and other expenses, diversion of management's time and disruption in our business. Uncertainties resulting from initiation and continuation of any patent proceeding or related litigation could harm our ability to compete and could have a significant adverse effect on our business, financial condition and results of operations.

An adverse ruling arising out of any intellectual property dispute, including an adverse decision as to the priority of our inventions, could undercut or invalidate our intellectual property position. An adverse ruling could also subject us to significant liability for damages, including possible treble damages, prevent us from using technologies or developing products, or require us to negotiate licenses to disputed rights from third parties. Although patent and intellectual property disputes in the technology area are often settled through licensing or similar arrangements, costs associated with these arrangements may be substantial and could include license fees and ongoing royalties. Furthermore, necessary licenses may not be available to us on satisfactory terms, if at all. Failure to obtain a license in such a case could have a significant adverse effect on our business, financial condition and results of operations.

Risks Related to Our Industry

Many potential competitors, including those who have greater resources and experience than we do, may develop products or technologies that make ours obsolete or noncompetitive.

We face significant competition with respect to our product candidates. With regard to our efforts to develop MultiStem as a novel stem cell therapy, currently, there are a number of companies that are actively developing stem cell products, which encompass a range of different cell types, including embryonic stem cells, adult-derived stem cells, and processed bone marrow derived cells. Our future success will depend on our ability to maintain a competitive position with respect to technological advances. Technological developments by others may result in our MultiStem product platform and technologies, as well as our pharmaceutical formulations, becoming obsolete.

We are subject to significant competition from pharmaceutical, biotechnology and diagnostic companies, academic and research institutions, and government or other publicly funded agencies that are pursuing or may pursue the development of therapeutic products and technologies that are substantially similar to our proposed therapeutic products and technologies, or that otherwise address the indications we are pursuing. Our most significant competitors are major pharmaceutical companies and certain other smaller companies, including Caladrius Biosciences, Inc., Cryo-Cell International, Vericel Corporation, Plureon Corporation and Mesoblast Limited. Most of our current and potential competitors have substantially greater research and development capabilities and financial, scientific, regulatory, manufacturing, marketing, sales, human resources and experience than we do. Many of our competitors have several therapeutic products that have already been developed, approved and successfully commercialized, or are in the process of obtaining regulatory approval for their therapeutic products in the United States and internationally.

Universities and public and private research institutions are also potential competitors. While these organizations primarily have educational objectives, they may develop proprietary technologies related to stem cells or secure patent protection that we may need for the development of our technologies and products. We may attempt to license these proprietary technologies, but these licenses may not be available to us on acceptable terms, if at all. Our competitors, either alone or with their collaborative partners, may succeed in developing technologies or products that are more effective, safer, more affordable or more easily

commercialized than ours, and our competitors may obtain intellectual property protection or commercialize products sooner than we do. Developments by others may render our product candidates or our technologies obsolete.

Our current product discovery and development collaborators are not prohibited from entering into research and development collaboration agreements with third parties in any product field. Our failure to compete effectively would have a significant adverse effect on our business, financial condition and results of operations.

The availability, manner, and amount of reimbursement for our product candidates from government and private payers are uncertain, and our inability to obtain adequate reimbursement for any products could severely limit our product sales.

We expect that many of the patients who seek treatment with any of our products that are approved for marketing will be eligible for Medicare benefits. Other patients may be covered by private health plans. If we are unable to obtain or retain adequate levels of reimbursement from Medicare or from private health plans, our ability to sell our products will be severely limited. The application of existing Medicare regulations and interpretive coverage and payment determinations to newly approved products is uncertain and those regulations and interpretive determinations are subject to change. Medicare may change its reimbursement methodology that reduces the Medicare reimbursement rates for many drugs, which may adversely affect reimbursement for any products we may develop. Medicare regulations and interpretive determinations also may determine who may be reimbursed for certain services and may limit the pool of patients our product candidates are being developed to serve.

Our industry is highly regulated and changes in law may adversely impact our business, operations or financial results. We anticipate continuing debate in the foreseeable future over the research and development, marketing, pricing and reimbursement for health care products and services, including those that would affect our current product candidates. For example, federal, state and foreign governments continue to propose legislation designed to contain or reduce health care costs. Legislation and regulations affecting the pricing of products like our potential products may change further or be adopted before any of our potential products are approved for marketing. Cost control initiatives by governments or third-party payers could decrease the price that we receive for any one or all of our potential products or increase patient coinsurance to a level that make our products under development become unaffordable. In addition, government and private health plans persistently challenge the price and cost-effectiveness of therapeutic products. Accordingly, these third parties may ultimately not consider any or all of our products under development to be cost effective, which could result in products not being covered under their health plans or covered only at a lower price. Any of these initiatives or developments could prevent us from successfully marketing and selling any of our products that are approved for commercialization.

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

Our success will depend in part upon our ability to develop therapeutic products incorporating or discovered through our adult-derived stem cell technology. For social, ethical, or other reasons, governmental authorities in the United States and other countries may call for limits on, or regulation of the use of, adult-derived stem cell technologies. Although we do not use the more controversial stem cells derived from embryos or fetuses, claims that adult-derived stem cell technologies are ineffective, unethical or pose a danger to the environment may influence public attitudes. The subject of stem cell technologies in general has received negative publicity and aroused public debate in the United States and some other countries. Ethical and other concerns about our adult-derived stem cell technology could materially hurt the market acceptance of our therapeutic products and technologies, resulting in diminished sales and use of any products we are able to develop using adult-derived stem cells.

Risks Related to Our Common Stock

If we do not continue to meet the listing standards established by The NASDAQ Capital Market, the common stock may not remain listed for trading.

The NASDAQ Capital Market has established certain quantitative criteria and qualitative standards that companies must meet in order to remain listed for trading on these markets. We cannot guarantee that we will be able to maintain all necessary requirements for listing; therefore, we cannot guarantee that our common stock will remain listed for trading on The NASDAQ Capital Market or other similar markets.

General Risk Factors

We will use hazardous and biological materials in our business. Any claims relating to improper handling, storage or disposal of these materials could be time consuming and costly.

Our products and processes will involve the controlled storage, use and disposal of certain hazardous and biological materials and waste products. We and our suppliers and other collaborators are subject to federal, state and local regulations governing the use, manufacture, storage, handling and disposal of materials and waste products. Even if we and these suppliers and

collaborators comply with the standards prescribed by law and regulation, the risk of accidental contamination or injury from hazardous materials cannot be completely eliminated. In the event of an accident, we could be held liable for any damages that result, and any liability could exceed the limits or fall outside the coverage of any insurance we may obtain and exceed our financial resources. We may not be able to maintain insurance on acceptable terms, or at all. We may incur significant costs to comply with current or future environmental laws and regulations.

If we acquire products, technologies or other businesses, we will incur a variety of costs, may have integration difficulties and may experience numerous other risks that could adversely affect our business.

To remain competitive, we may decide to acquire additional businesses, products and technologies. We currently have no commitments or agreements with respect to, and are not actively seeking, any material acquisitions. We have limited experience in identifying acquisition targets, successfully acquiring them and integrating them into our current infrastructure. We may not be able to successfully integrate any businesses, products, technologies or personnel that we might acquire in the future without a significant expenditure of operating, financial and management resources, if at all. In addition, future acquisitions could require significant capital infusions and could involve many risks, including, but not limited to the following:

- we may have to issue convertible debt or equity securities to complete an acquisition, which would dilute our stockholders and could adversely affect the market price of our common stock;
- an acquisition may negatively impact our results of operations because it may require us to incur large one-time charges to earnings, amortize or write down amounts related to goodwill and other intangible assets, or incur or assume substantial debt or liabilities, or it may cause adverse tax consequences, substantial depreciation or deferred compensation charges;
- we may encounter difficulties in assimilating and integrating the business, technologies, products, personnel or operations of companies that we acquire;
- certain acquisitions may disrupt our relationship with existing collaborators who are competitive to the acquired business;
- acquisitions may require significant capital infusions and the acquired businesses, products or technologies may not generate sufficient revenue to offset acquisition costs;
- an acquisition may disrupt our ongoing business, divert resources, increase our expenses and distract our management;
- acquisitions may involve the entry into a geographic or business market in which we have little or no prior experience; and
- key personnel of an acquired company may decide not to work for us.

Any of the foregoing risks could have a significant adverse effect on our business, financial condition and results of operations.

Increased information technology security threats and more sophisticated and targeted computer crime could pose a risk to our systems, networks, and products.

Increased global information technology security threats and more sophisticated and targeted computer crime pose a risk to the security of our information technology systems and networks and the confidentiality, availability and integrity of our data and communications, as well as those of our current and future vendors, contractors and consultants with whom we share data or information. As the cyber-threat landscape evolves, these attacks are becoming increasingly difficult to detect. Such attacks could include the use of harmful and virulent malware, including ransomware or other denials of service, that can be deployed through various means, including the software supply chain, e-mail, malicious websites and/or the use of social engineering. While we attempt to mitigate these risks by employing a number of measures, including employee refreshers, monitoring of our networks and systems, and maintenance of backup and protective systems, our systems and networks remain potentially vulnerable to cybersecurity incidents by various threat actors, including but not limited to nation states, organized crime, other criminal enterprises, individual actors and/or advanced persistent threat groups. Moreover, the recovery and business continuity plans we have in place currently may prove inadequate in the event of a serious computer security event. Cybersecurity liability insurance is difficult to obtain and may not cover any damages we would sustain based on any breach of our computer security protocols or other cybersecurity attack. Depending on their nature and scope, such threats could potentially lead to the compromising of confidential information (including trade secrets and other proprietary information) and communications, improper use of our systems and networks, manipulation and destruction of data, defective products, production downtimes and operational disruptions, which in turn could adversely affect our reputation, competitiveness and results of operations. For example, the loss of clinical trial data from one or more ongoing or completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. As many of our employees are working remotely, we have relied more on our and third-party information technology systems, which may increase the risk

of a cyberattack. Furthermore, we are subject to an increasing number of data privacy and data protection laws in both the United States and abroad, including the federal Health Insurance Portability and Accountability Act of 1996, the EU's General Data Protection Regulation, and the California Consumer Privacy Act. Failure to comply with these regulations could result in fines, penalties or significant legal liability.

As part of its risk oversight, our Audit Committee is responsible for monitoring risks related to information security and technology, including cybersecurity. The Audit Committee receives annual reports from the Company's Vice President, Information Technologies and Communications, on the Company's cybersecurity risk profile and cybersecurity program.

We may not be able to utilize a significant portion of our net operating loss or research tax credit carryforwards or other tax attributes, which could harm our profitability.

At December 31, 2021, we had U.S. federal net operating loss and research and development tax credit carryforwards of approximately $326.3 million and $20.6 million, respectively. Included in our federal net operating loss as of December 31, 2021 are federal net operating loss carryforwards generated after 2017 of $189.7 million that have an indefinite life, but with usage limited to 80% of taxable income in any given year. The remaining federal net operating losses and tax credits will expire at various dates between 2032 and 2041. We also had foreign net operating loss carryforwards of approximately $31.7 million. Such foreign net operating loss carryforwards do not expire. We also had state and city net operating loss carryforwards aggregating approximately $118.7 million. Such state and city net operating loss carryforwards may be used to reduce future taxable income and tax liabilities and will expire at various dates between 2022 and 2041. Certain state net operating losses do not expire.

Our ability to utilize our U.S. federal net operating loss and tax credit carryforwards generated prior to October 2012, or the Section 382 Limited Attributes, is substantially limited under Section 382 of the Internal Revenue Code of 1986, as amended, or the Code, as a result of our equity offering that occurred in October 2012. Similar limitations may apply for state and local tax purposes. We generated U.S. federal net operating loss carryforwards of $289.6 million, research and development tax credits of $20.6 million, and state and local net operating loss carryforwards of $118.5 million since 2012 through December 31, 2021.

Our ability to utilize tax attributes, including those that are not part of the Section 382 Limited Attributes, may also be limited if we experience an "ownership change," for purposes of Section 382 of the Code. A Section 382 "ownership change" generally occurs if one or more stockholders or groups of stockholders who own at least 5% of our stock increase their ownership by more than 50 percentage points over their lowest ownership percentage within a rolling three-year period. Similar rules may apply under state tax laws. Sales of our common stock to Healios, Aspire Capital pursuant to our equity purchase arrangement, in combination with other issuances or sales of our common stock (including any sales of common stock by Aspire Capital and certain transactions involving our common stock that are outside of our control) could cause an "ownership change." If an "ownership change" occurs, Section 382 of the Code would impose an annual limit on the amount of pre-ownership change net operating loss carryforwards and other tax attributes we can use to reduce our taxable income, potentially increasing and accelerating our liability for income taxes, and also potentially causing those tax attributes to expire unused. It is possible that such an ownership change could materially reduce our ability to use our net operating loss carryforwards or other tax attributes to offset taxable income, which could harm our profitability. We will update our analysis under Section 382 of the Code prior to using our tax attributes.

ITEM 1B. UNRESOLVED STAFF COMMENTS

Not applicable.

ITEM 2. PROPERTIES

Our principal offices are located at 3201 Carnegie Avenue in Cleveland, Ohio. We currently lease approximately 45,000 square feet of space for our corporate offices and laboratories, with state-of-the-art laboratory space. The lease began in 2000 and currently expires in March 2023, with an option for a one-year extension through March 31, 2024. Our rent is approximately $0.3 million per year and our rental rate has not changed since the lease inception in 2000. Also, we currently lease office and laboratory space for our Belgian subsidiary. The lease currently expires in July 2023. The annual rent in Belgium is approximately $0.2 million and is subject to adjustments based on an inflationary index. In January 2021, we entered into an agreement to lease approximately 214,000 square feet of space in Stow, Ohio to potentially support our future manufacturing needs. The lease term is approximately 10 years with the option to renew for five additional terms of five years each. The rent for the first year of the lease term was approximately $1.3 million and rent increases annually at 2% throughout the term of the lease.

ITEM 3. LEGAL PROCEEDINGS

From time to time, we may become subject to various legal proceedings that are incidental to the ordinary conduct of our business. Currently, there are no such proceedings.

ITEM 3A. INFORMATION ABOUT OUR EXECUTIVE OFFICERS

The information under this Item is furnished pursuant to the instructions to Item 401 of Regulation S-K.

The following sets forth the name, age, current position and principal occupation and employment during the past five years of our executive officers.

Daniel A. Camardo, MBA
Age: 53

Mr. Camardo joined Athersys in February 2022 as our Chief Executive Officer. Previously, Mr. Camardo served as the President, U.S., and the Executive Vice President of Horizon Therapeutics plc, a global biotechnology company, overseeing the Rare Disease and Inflammation Business Units from August 2020 to February 2022, and served as Group Vice President from September 2015 to August 2020. Before joining Horizon Therapeutics, Mr. Camardo was Vice President of Sales and Operations at Clarus Therapeutics, a start-up company focused on men's health, from July 2014 to September 2015. Prior to joining Clarus Therapeutics, Mr. Camardo held various commercial leadership roles, including Senior Director, U.S. Commercial Operations and Senior Director, Market Intelligence and Analytics from 2003 to 2014 at Astellas Pharma US, an affiliate of Astellas Pharma Inc., a Japanese global pharmaceutical company. Mr. Camardo became an Adjunct Lecturer in Healthcare at Kellogg School of Management (HCAK), in February 2022 and serves on the Board of CommunityHealth, the largest volunteer-based health center in the nation providing health care at no charge to low income, uninsured adults, in Chicago. Mr. Camardo holds a Bachelor of Arts degree in Economics and Mathematics from the University of Rochester and a Masters of Business Administration from Kellogg School of Management.

William (B.J.) Lehmann, Jr., J.D., MBA
Age: 56

Mr. Lehmann joined Athersys in September 2001 and has served as our President and Chief Operating Officer since June 2006. He also served as our Interim Chief Executive Officer from February 2021 to February 2022. He has been involved in all aspects of the Company's operations since joining Athersys, including business development, partnership management, finance, clinical development, regulatory, legal and intellectual property management. He has helped develop, negotiate and build most of the Company's major business relationships, including research and development collaborations and manufacturing. Prior to that time, Mr. Lehmann was our Executive Vice President of Corporate Development and Finance from August 2002 until June 2006. From 1994 to 2001, Mr. Lehmann was with McKinsey & Company, Inc., or McKinsey, an international management consulting firm, where he worked extensively with new technology and service-based businesses in the firm's Business Building practice. Prior to joining McKinsey, he worked at Wilson, Sonsini, Goodrich & Rosati, a Silicon Valley law firm, and worked with First Chicago Corporation, a financial institution. Mr. Lehmann received his J.D. from Stanford University, his M.B.A. from the University of Chicago, and his B.A. from the University of Notre Dame.

John J. Harrington, Ph.D.
Age: 54

Dr. Harrington co-founded Athersys in 1995 and has served as our Executive Vice President, Chief Scientific Officer and Director since our founding. Dr. Harrington led the development of the RAGE technology, as well as its application for gene discovery, drug discovery and commercial protein production applications. He is a listed inventor on over 20 issued or pending United States patents, has authored numerous scientific publications, and has received numerous awards for his work, including being named one of the top international young scientists by MIT Technology Review in 2002. Dr. Harrington has overseen the therapeutic product development programs at Athersys since its inception and is also focused on the clinical development and manufacturing of MultiStem. During his career, he has also held positions at Amgen, an American multinational biopharmaceutical company, and Scripps Clinic, a health system in San Diego, California. He received his B.A. in Biochemistry and Cell Biology from the University of California at San Diego and his Ph.D. in Cancer Biology from Stanford University.

Ivor Macleod, CPA, MBA
Age: 60

Mr. Macleod joined Athersys in January 2020 as our Chief Financial Officer. Previously he served as the Chief Financial Officer and Chief Compliance Officer of Eisai Inc., the U.S. pharmaceutical subsidiary of Eisai Co., Ltd., a research-based human health care company that discovers, develops and markets products globally, from 2015 to 2018. Prior to joining Eisai, Mr. Macleod served as Vice President Finance - Merck Research Labs at Merck & Co., Inc., a global health care company that delivers innovative health solutions through its prescription medicines, vaccines, biologic therapies and animal health productions, from 2012 to 2015. Before joining Merck, Mr. Macleod served from 1998 to 2012 at F. Hoffmann-La Roche, Inc., a multinational health care company, in various roles, including as North American Chief Financial Officer from 2000 to 2011 and General Manager from 2010 to 2011. Mr. Macleod received his B.S. from St. Andrews University in Scotland and his M.B.A. from the University of Arizona. Mr. Macleod is a Certified Public Accountant licensed in Virginia.

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

Our common stock is traded on The NASDAQ Capital Market under the symbol "ATHX."

Holders

As of March 9, 2022, there were approximately 454 holders of record of our common stock. Additionally, shares of common stock are held by financial institutions as nominees for beneficial owners that are deposited into participant accounts at the Depository Trust Company, which are held of record by Cede & Co. and are included in the holders of record as one stockholder.

Unregistered Sales

Since 2011, we have had in place equity purchase agreements with Aspire Capital, which provide us the ability to sell shares of our common stock to Aspire Capital from time-to-time. During the quarter ended December 31, 2021, we sold an aggregate of 7,481,000 shares of common stock to Aspire Capital under our equity purchase agreement, generating aggregate proceeds of $7.3 million. Each issuance of these unregistered shares qualifies as an exempt transaction pursuant to Section 4(a)(2) of the Securities Act of 1933. Each issuance qualified for exemption under Section 4(a)(2) of the Securities Act of 1933 because none involved a public offering. Each offering was not a public offering due to the number of persons involved, the manner of the issuance and the number of securities issued. In addition, in each case Aspire Capital had the necessary investment intent.

ITEM 6. [RESERVED]

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis in conjunction with "Item 8. Financial Statements and Supplementary Data" included below in this Annual Report on Form 10-K.

Overview

We are a biotechnology company that is focused primarily in the field of regenerative medicine. Our MultiStem® (invimestrocel) cell therapy, a patented and proprietary allogeneic stem cell product, is our lead platform product and is currently in clinical development in several therapeutic and geographic areas. Our most advanced program is an ongoing Phase 3 clinical trial for the treatment of ischemic stroke. Our current clinical development programs are focused on treating neurological conditions, inflammatory and immune disorders, certain pulmonary conditions, cardiovascular disease and other conditions where the current standard of care is limited or inadequate for many patients, particularly in the critical care segment.

Current Programs

Our MultiStem cell therapy product development programs in the clinical development stage include the following:

- **Ischemic Stroke:** We are conducting a pivotal Phase 3 clinical trial of MultiStem cell therapy for the treatment of ischemic stroke, referred to as MASTERS-2. Our MASTERS-2 clinical trial is a randomized, double-blind, placebo-controlled clinical trial designed to enroll 300 patients in the United States and certain other international locations, who have suffered moderate to moderate-severe ischemic stroke. We initiated the study with a limited number of high-enrolling sites and have been bringing on additional sites over time in line with clinical product supply and clinical operations objectives. In prior periods, we have faced challenges to clinical site initiations, as well as patient screening and enrollment, due to the COVID-19 pandemic and supply interruptions, among other things. As COVID-19 case numbers decline and supply has stabilized, we have undertaken initiatives intended to accelerate new site openings in the U.S. and abroad and increase patient enrollment at sites currently open, including by addressing site-specific operations and inventory management issues. These plans are intended to enable us to finish enrollment of the MASTERS-2 study by the end of 2022 or as soon as possible thereafter; however, completion continues to depend on the impact of the results of the TREASURE study being conducted by HEALIOS K.K., or Healios, discussed below, and the possible resurgence of COVID-19. We would expect, for instance, that favorable TREASURE study results would have a positive effect on site initiations and patient accruals as success drives further interest in and focus on the study among investigators and clinical research groups.

  The MASTERS-2 study has received several regulatory distinctions including Special Protocol Assessment, or SPA, designation, Fast Track designation and Regenerative Medicine Advanced Therapy, or RMAT, designation from the United States Food and Drug Administration, or FDA, as well as a Final Scientific Advice positive opinion from the European Medicines Agency, or EMA.

  In addition, Healios, our collaborator in Japan, has an ongoing clinical trial, TREASURE, evaluating the safety and efficacy of administration of MultiStem cell therapy for the treatment of ischemic stroke in Japan. TREASURE will be evaluated under the progressive regulatory framework for regenerative medicine therapies in Japan. Under the new framework, Healios' ischemic stroke program has been awarded the Sakigake designation by the Pharmaceuticals and Medical Devices Agency in Japan, or PMDA, which is designed to expedite regulatory review and approval and is analogous to Fast Track designation from the FDA. In August 2021, Healios reported that it completed patient enrollment in its TREASURE study. In November 2021, Healios announced that, based on the advice of the PMDA, to avoid any potential bias to the 365-day data (and related secondary endpoints) that could result from unblinding and disclosure of 90-day data (primary endpoint), the decision was made that the 90-day unblinding, data analysis and release would take place after the 365-day data is locked. This will follow the last patient's one-year follow-up visit. Healios expects this last patient visit to occur in March of 2022. We look forward to the completion of both the MASTERS-2 and TREASURE trials and using the accelerated pathways to review and approval afforded to us by the regulators in the United States, Europe and Japan.

- **ARDS:** In January 2019 and January 2020, we announced summary results and one-year follow up results, respectively, from our exploratory clinical study of the intravenous administration of MultiStem cell therapy to treat patients who are suffering from acute respiratory distress syndrome, or ARDS, which is referred to as the MUST-ARDS study. The study results continue to demonstrate a predictable and favorable tolerability profile. Importantly, there were lower mortality and a greater number of ventilator-free and ICU-free days in the MultiStem-treated patient group compared to the placebo group. Average quality-of-life outcomes were higher in the MultiStem group compared

to placebo through one year. In April 2020, in response to the COVID-19 pandemic, the FDA authorized the initiation of a Phase 2/3 pivotal study to assess the safety and efficacy of MultiStem therapy in subjects with moderate to severe ARDS, or the MACOVIA study. In September 2020, the MultiStem cell therapy received RMAT designation for the ARDS program. The MACOVIA study features an open-label lead-in followed by a double-blinded, randomized, placebo-controlled Phase 2 and 3 portions, and the study is presently designed to enroll up to approximately 400 patients at leading pulmonary critical care centers throughout the United States. During 2021, we amended the protocol with the FDA to adjust the scope of the MACOVIA study to include subject with ARDS induced by pathogens other than COVID-19. Recently, we received approval from the FDA to use MultiStem product manufactured with our bioreactor-based technology in the study, an important development milestone. The scope and timing of our MACOVIA study may be adjusted to reflect rapidly changing standards of care for ARDS patients and depending on regulatory discussions and business considerations. Currently, we are working to complete enrollment of the Phase 2 part of the MACOVIA trial before the end of 2022.

Further, in 2019, Healios initiated the ONE-BRIDGE study in Japan for patients with pneumonia-induced and COVID-induced ARDS and, in August 2021, Healios reported top-line data from the ONE-BRIDGE study. We and Healios have conducted thorough analyses of the data from the MUST-ARDS and ONE-BRIDGE studies. The studies had comparable patient populations receiving the same MultiStem dose amount shortly following an ARDS diagnosis. Between the studies, excluding the COVID-ARDS cohort in the ONE-BRIDGE study, 60 ARDS subjects were enrolled in the studies, 40 receiving MultiStem treatment and the remaining 20 receiving placebo or standard of care. On a pooled basis, strong trends were observed in ventilator-free days, or VFD, survival, improved quality-of-life and reduction of key inflammatory biomarkers. For example, MultiStem-treated subjects had, on average, 5.5 more VFD in the first 28 days following diagnosis than non-treated subjects ($p=0.07$) and, on a median basis, 10.5 more VFD. Healios continues ongoing consultations with the regulatory authorities to prepare for the potential application for manufacturing and marketing approval.

- **Trauma:** In April 2020, the FDA authorized the initiation of a Phase 2 clinical trial evaluating MultiStem cell therapy for the early treatment of traumatic injuries and the subsequent complications that result following severe trauma. The trial is being conducted by The University of Texas Health Science Center at Houston, or UTHealth, at the Memorial Hermann-Texas Medical Center in Houston, Texas, one of the busiest Level 1 trauma centers in the United States. This study is being supported under a grant awarded to the McGovern Medical School at UTHealth from the Medical Technology Enterprise Consortium, and the Memorial Hermann Foundation is providing additional funding. We are providing the investigational clinical product for the trial as well as regulatory and operational support.

We are engaged in preclinical development and evaluation of MultiStem cell therapy in other indications for human health, as well as certain indications in the animal health field, and we conduct such work both through our own internal research efforts and through a broad global network of collaborators. We also engage in discussions with third parties about collaborating in the development of MultiStem cell therapy for various programs and/or various geographic territories and may enter into one or more business partnerships to advance these programs over time. We may also elect to develop certain programs independently.

While the MultiStem product platform continues to advance, we are engaged in process development initiatives intended to increase manufacturing scale, reduce production costs and enhance process controls and product quality, among other things. These initiatives are being conducted both internally and outsourced to select contractors, and the related investments are meant to enable us to meet potential commercial demand in the event of eventual regulatory approval. We have been developing a bioreactor-based manufacturing platform for such commercialization, for which we now have FDA approval for use in our ARDS and trauma clinical trials in the United States. Until such time as we are able to manufacture products ourselves in accordance with good manufacturing practices, we will continue to rely on third-party manufacturers to make our MultiStem product for clinical trials and eventual commercial sales. These third parties may not deliver sufficient quantities of our MultiStem product, manufacture MultiStem product in accordance with specifications, or comply with applicable government regulations. From time to time, such third-party manufacturers, or their material suppliers, may experience production delays, stoppages or interruptions in supply, which may affect the initiation, execution and timing of completion of our and our partners' clinical trials or commercial activities.

In addition to our manufacturing efforts, in other areas we are stepping up our planning and preparations for the potential commercialization of our MultiStem product candidate. We are advancing our strategies for market access and reimbursement, working with third-party experts to plan and undertake initiatives to position the product appropriately and effectively communicate to payors its value to them and patients. We are developing our go-to-market strategies, which could include third-party marketing partners in certain areas and the creation of a commercial sales force in other areas. We are also working with outside experts to develop proprietary solutions to the unique requirements related to the cell therapy supply chain and clinical site logistics. For example, working with an outside partner, we have been developing a proprietary cryogenic system designed to securely store and dispense our product in hospital pharmacies or other suitable clinical locations. Our intention is

to be prepared to enable commercialization as soon as reasonably possible following potential successful completion of pivotal studies, application and approval by regulators.

We have a collaboration with Healios that covers MultiStem cell therapy for ischemic stroke and ARDS in Japan. The collaboration also includes the use of our technology for Healios' organ bud program targeted to liver disease and other indications, as well as certain other rights, including a license for the use of our MultiStem product to treat certain ophthalmological indications and a license to treat diseases of the liver, kidney, pancreas and intestinal tissue through administration of our products in combination with induced pluripotent stem cells, or iPSC-derived cells. Under the terms of our various agreements with Healios, we provide manufacturing support services to Healios.

Financial

We have entered into a series of agreements with Healios, our collaborator in Japan and currently our largest stockholder. Under the collaboration that began in 2016, Healios is responsible for the development and commercialization of the MultiStem product for the licensed fields in the licensed territories, and we provide services to Healios for which we are compensated. Each license agreement with Healios has defined economic terms, and we may receive success-based milestone payments, some of which may be subject to credits. In August 2021, we entered into a Comprehensive Framework Agreement for Commercial Manufacturing and Ongoing Support, or the Framework Agreement, with Healios, which provides for resolution of certain issues under the existing agreements between the parties and reframes our collaboration to set the stage for productive efforts as Healios and our collaboration move towards commercialization of MultiStem in Japan. It also provides Healios with deferral of certain milestone payments during the expensive initial commercial launch period. We will be entitled to new milestone payments in the amount of $3.0 million by June 2022 and $5.0 million upon successful completion of certain commercial manufacturing activities. Also, we are entitled to receive tiered royalties on net product sales, as defined in the license agreements.

In connection with an equity investment in us made by Healios in 2018, Healios had a warrant, or the 2018 Warrant, to purchase up to 4,000,000 shares of our common stock at an exercise price equal to a reference price, as defined, but no less than $1.76 per share. In March 2020, Healios exercised the 2018 Warrant in full at $1.76 per share and in April 2020 we received proceeds of approximately $7.0 million in accordance with the terms of the 2018 Warrant. In August 2021, we issued two warrants, or the 2021 Warrants, to Healios in connection with the Framework Agreement, to purchase up to a total of 10,000,000 shares of our common stock. One of the 2021 Warrants is for the purchase of up to 3,000,000 shares at an exercise price of $1.80 per share, subject to specified increases, and generally is only exercisable within 60 days of receipt of either conditional or full marketing approval from the PMDA for the intravenous administration of MultiStem to treat patients who are suffering from ARDS. The other 2021 Warrant is for the purchase of up to 7,000,000 shares at an exercise price of $2.40 per share, subject to specified increases, and generally is only exercisable within 60 days of receipt of either conditional or full marketing approval from the PMDA for the intravenous administration of MultiStem to treat patients who are suffering from ischemic stroke.

We have had equity purchase agreements in place since 2011 with Aspire Capital Fund LLC, or Aspire Capital, that provide us the ability to sell shares to Aspire Capital from time-to-time. Currently, we have an agreement with Aspire Capital that was entered into in June 2021, or the 2021 Equity Facility, and includes Aspire Capital's commitment to purchase up to an aggregate of $100.0 million of shares of our common stock over a defined timeframe. Our prior $100.0 million equity facility that was entered into in 2019, or the 2019 Equity Facility, was fully utilized and terminated during the third quarter of 2021. The terms of the 2021 Equity Facility are similar to the previous equity facilities with Aspire Capital, and we filed a registration statement for the resale of 40,000,000 shares of our common stock.

During the years ended December 31, 2021, 2020 and 2019, we sold 40,031,000, 11,425,000 and 14,475,000 shares, respectively, to Aspire Capital at average prices of $1.61, $1.67 and $1.41 per share, respectively.

Results of Operations

Since our inception, our revenues have consisted of license fees, contract revenues, royalties and milestone payments from our collaborators, and grant proceeds. We have not derived revenue from our commercial sale of therapeutic products to date since we are in clinical development. Research and development expenses consist primarily of external clinical and preclinical study fees, manufacturing and process development costs, salaries and related personnel costs, legal expenses resulting from intellectual property prosecution processes, facility costs, and laboratory supply and reagent costs. We expense research and development costs as they are incurred. We expect to continue to make significant investments in research and development to enhance our technologies, advance clinical trials of our product candidates, expand our regulatory affairs and product development capabilities, conduct preclinical studies of our product, manufacture our product candidates, improve our manufacturing and process development and prepare for potential commercialization of our MultiStem cell therapy product. General and administrative expenses consist primarily of salaries and related personnel costs, professional fees and other corporate expenses. We expect to continue to incur substantial losses through at least the next several years.

Year Ended December 31, 2021 Compared to Year Ended December 31, 2020

Revenues. Revenues increased to $5.5 million for the year ended December 31, 2021 from $1.4 million in 2020. The increase is primarily related to an increase in contract revenues from our collaboration with Healios, which increased $4.1 million period-over-period. Our collaboration revenues fluctuate from period-to-period based on new licenses conferred and the delivery of goods and services under our arrangement with Healios. We expect our collaboration revenues to vary over time as we contract with Healios to perform manufacturing services and as we potentially enter into new collaborations.

Research and Development Expenses. Research and development expenses increased to $71.1 million for the year ended December 31, 2021 from $63.0 million for the year ended December 31, 2020. The increase in research and development expenses year-over-year of $8.1 million related primarily to increased clinical trial, manufacturing and process development costs of $5.3 million and personnel costs of $3.2 million, including stock-based compensation expense and expense of $0.9 million related to cash retention agreements payable in May 2022. These increases were partially offset by decreases in other research and development costs of $0.4 million. Based on our current clinical development, manufacturing, process development and regulatory affairs plans, we expect our 2022 annual research and development expenses to be higher compared to 2021, and such costs will vary over time based on clinical manufacturing campaigns, the timing and stage of clinical trials underway, manufacturing process development projects and regulatory initiatives. These variations in activity level may also impact our accounts payable, accrued expenses and prepaid expenses balances from period-to-period. Other than external expenses for our clinical and preclinical programs, we do not track our research expenses by project; rather, we track such expenses by the type of cost incurred.

General and Administrative Expenses. General and administrative expenses increased to $20.1 million in 2021 from $15.9 million in 2020. The $4.2 million increase was due primarily to increases in legal expenses incurred in connection with the complaint filed by Dr. Hardy TS Kagimoto against the Company and its settlement, the expenses associated with Dr. Gil Van Bokkelen's resignation and his separation letter agreement, including $2.4 million of non-cash stock compensation expense and expense of $0.5 million related to cash retention agreements payable in May 2022.

Depreciation. Depreciation expense increased to $1.4 million in 2021 from $0.9 million in 2020 due to additional equipment being placed in service and accelerated depreciation related to certain equipment assets for which the remaining useful life was modified.

Other Income (Expense), net. Other income, net, for the year ended December 31, 2021 was $0.1 million, and other expense, net, was $0.4 million for 2020, and is comprised of interest income and expense and foreign currency gains and losses.

Comparison of the years ended December 31, 2020 and 2019

See the Management Discussion and Analysis section of our Annual Report on Form 10-K for the year ended December 31, 2020 for a discussion of our results of operations for the year ended December 31, 2020 compared to the year ended December 31, 2019.

Liquidity and Capital Resources

Our sources of liquidity include our cash balances and equity purchase agreement with Aspire Capital. At December 31, 2021, we had $37.4 million in cash and cash equivalents. We have primarily financed our operations through business collaborations, grant funding and equity financings, including through our equity facility. We conduct all of our operations through our subsidiary, ABT Holding Company. Consequently, our ability to fund our operations depends on ABT Holding Company's financial condition and its ability to make dividend payments or other cash distributions to us. There are no restrictions such as government regulations or material contractual arrangements that restrict the ability of ABT Holding Company to make dividend and other payments to us.

We have prepared our consolidated financial statements on a going concern basis, which assumes that we will realize our assets and satisfy our liabilities in the normal course of business. However, we have incurred losses since inception of operations in 1995, have negative operating cash flows, including in each of the last three years, and had an accumulated deficit of $583.3 million at December 31, 2021. Our losses have resulted principally from costs incurred in research and development, clinical and preclinical product development, manufacturing and process development, acquisition and licensing costs, and general and administrative costs associated with our operations. These circumstances raise substantial doubt about our ability to continue as a going concern. The accompanying financial statements do not include any adjustments to reflect the possible future effect on the recoverability and classification of assets or the amounts and classifications of liabilities that may result from the outcome of the uncertainty concerning our ability to continue as a going concern.

We plan to raise additional capital through the use of our equity purchase agreement with Aspire Capital and, depending on market conditions, through equity offerings. We are also entitled to receive potential milestones payments, subject to certain credits, and royalties from Healios under our licensed programs. Under the Framework Agreement, we are entitled to a new milestone payment in the amount of $3.0 million by June 2022. We receive payments from Healios for certain manufacturing support services. Certain proceeds from Healios may be used by Healios to offset milestone payments that may become due in the future. Additionally, we have the ability to defer certain spending and potentially defer and delay certain non-core programs. While we believe this plan to generate additional funds will alleviate the conditions that raise substantial doubt, these plans are not entirely within our control and cannot be assessed as being probable of occurring. For the foreseeable future, our ability to continue our operations is dependent upon our ability to obtain additional capital.

We have had equity purchase agreements in place with Aspire Capital since 2011 that provide us the ability to sell shares to Aspire Capital from time to time. Currently, we are party to the 2021 Equity Facility, which includes Aspire Capital's commitment to purchase up to an aggregate of $100.0 million of shares of our common stock over a defined timeframe. The terms of the 2021 Equity Facility are similar to the previous equity purchase agreements, and we filed a registration statement for the resale of 40,000,000 shares of our common stock. The 2019 Equity Facility was fully utilized and terminated during the third quarter of 2021, and, during the third and fourth quarter of 2021, we have sold shares to Aspire Capital under the 2021 Equity Facility.

As previously disclosed, under the terms of the 2021 Equity Facility, on any business day on which the closing sale price of our common stock equals or exceeds $1.00 per share, or the Floor Price, we have the right, in our sole discretion, to present Aspire Capital with a purchase notice, directing Aspire Capital to purchase up to 200,000 shares of our common stock per trading day, provided that the aggregate price of such purchase shall not exceed $500,000 per trading day, up to $100.0 million of our common stock in the aggregate. As our stock price recently has been below the Floor Price and to afford us some flexibility in accessing the 2021 Equity Facility, Aspire has agreed to lower the Floor Price to $0.50, which was the floor price under the 2019 Equity Facility.

During the years ended December 31, 2021 and 2020, we sold 40,031,000 and 11,425,000 shares, respectively, to Aspire Capital at average prices of $1.61 and $1.67 per share, respectively.

We will require substantial additional funding in order to continue our research and product development programs, including clinical trials of our product candidates and process development and manufacturing projects, and to prepare for possible regulatory approval and commercial activities. We have agreements with several contract manufacturing organizations for the manufacture of our MultiStem product candidate to supply our planned and ongoing clinical trials. These agreements represent significant financial commitments, including deposits prior to commencement of manufacturing and progress payments through the course of the manufacturing process.

We intend to meet our short-term liquidity needs with available cash, including available proceeds from our existing equity facility, potential delays in certain non-core programs, and our ability to defer certain spending. Furthermore, we are actively pursuing new collaborative opportunities and other potential sources of funding, which could reduce the current level of usage of our equity facility and potentially accelerate certain costs. If sufficient capital is available, we would plan to accelerate our clinical activity and preparation for regulatory application, approval and commercialization, including commercial manufacturing.

Importantly, we expect that the results of Healios' TREASURE study, followed by the results of our MASTERS-2 clinical trial, will have a significant impact, favorable or unfavorable, on our ability to access capital from potential third-party commercial partners or the equity capital markets. Depending on the nature of these results, we may accelerate or may delay certain programs. In the longer term, we will have to continue to generate additional capital to meet our needs until we would become cash flow positive as a result of the sales of our clinical products, if they are approved for marketing. Such capital would come from new and existing collaborations and the related license fees, milestones and potential royalties, the sale of equity securities from time to time including through our equity facility, grant-funding opportunities, deferral of certain discretionary costs and the staging of certain development costs, as needed.

Additionally, we may raise capital from time to time through our equity purchase arrangement with Aspire, subject to its volume and price limitations and equity offerings. We also manage our cash by deferring certain discretionary costs and staging certain development costs to extend our operational runway, as needed. Over time, we may consider borrowing from financing institutions or royalty financing arrangements.

Our capital requirements over time depend on a number of factors, including progress in our clinical development programs, preparing for potential commercialization of our product candidates, potential product launch, our clinical and preclinical pipeline of additional opportunities and their stage of development, additional external costs such as payments to contract research organizations and contract manufacturing organizations, additional personnel costs and the costs in filing and prosecuting patent applications and enforcing patent claims. Furthermore, delays in product supply for our clinical trials may impact the timing and cost of such studies, and delays in product supply following Healios' potential product launch may impact the timing of royalties that we may receive. The availability of funds impacts our ability to advance multiple clinical programs concurrently, and any shortfall in funding could result in our having to delay or curtail research and development efforts. Further, these requirements may change at any time due to technological advances, business development activity or competition from other companies. We cannot assure you that adequate funding will be available to us or, if available, that it will be available on acceptable terms.

We expect to continue to incur substantial losses through at least the next several years and may incur losses in subsequent periods, and our ability to commercialize our product candidates is uncertain. The amount and timing of our future losses are highly uncertain. Our ability to achieve and thereafter sustain profitability will be dependent upon, among other things, successfully developing, commercializing and obtaining regulatory approval or clearances for our technologies and products resulting from these technologies.

Cash Flow Analysis

Net cash used in operating activities was $76.2 million, $61.8 million and $35.3 million in 2021, 2020 and 2019, respectively, and represented the use of cash to fund operations, clinical trials, preclinical research and process development activities; net of receipts from collaborative arrangements such as Healios. Net cash used in operating activities may fluctuate significantly period-to-period, as it has over the past several years, primarily due to the receipt of collaboration fees and payment of specific clinical trial costs, such as clinical manufacturing campaigns, contract research organization costs and manufacturing process development projects. These variations in activity level may also impact our accounts payable, accrued expenses and prepaid expenses balances from period-to-period.

Net cash used in investing activities was $1.4 million, $1.2 million and $0.6 million in 2021, 2020 and 2019, respectively, related to the purchase of equipment for our manufacturing and process development activities. We expect that our capital equipment expenditures will increase in 2022 compared to 2021 primarily to support our manufacturing and manufacturing process development needs.

Financing activities provided net cash of $63.4 million in 2021, $79.5 million in 2020, and $19.9 million in 2019. In April 2020, we completed an underwritten public offering of our common stock, generating net proceeds of approximately $53.7 million, and Healios exercised its 2018 Warrant for which we received proceeds of $7.0 million. In May 2020, we also received $0.5 million from Healios from the issuance of our common stock related to its participation right under the terms of our investor rights agreement with Healios, which was entered into in March 2018 and governs certain of our and Healios' rights relating to its ownership of our common stock. Financing activities in 2021, 2020 and 2019 also include our equity sales to Aspire Capital and net of shares of common stock retained in exchange for withholding tax payments on share-based awards.

Critical Accounting Policies and Management Estimates

The SEC defines critical accounting policies as those that are in management's view, important to the portrayal of our financial condition and results of operation and demanding of management's judgement. Our discussion and analysis of financial condition and results of operations are based on our consolidated financial statements, which have been prepared in accordance with United States generally accepted accounting principles. The preparation of these financial statements requires us to make estimates on experience and on various assumptions that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. The following accounting estimates are deemed to be critical to us.

Stock-Based Compensation

We determine the estimated fair value of each stock option on the date of grant using the Black-Scholes option-pricing model. The expected term of stock options granted represent the period of time that stock option grants are expected to be outstanding and subsequent to June 2020, is determined based on our historical experience and patterns. Prior to June 2020, we used the "simplified" method to calculate the expected term of option grants. The risk-free interest rate is based on the U.S. Treasury yield for a period consistent with the expected term of the stock option at the time of the grant. We determine volatility by using our historical stock volatility. We account for forfeitures as they occur. We have never paid or declared dividends or paid dividends on our common stock and have no plans to do so in the foreseeable future. Changes in these assumptions may lead to variability with respect to the amount of stock compensation expense we recognize related to stock options.

Additionally, stock-based compensation for an award with a performance condition requires the judgement of management. For such awards, stock-based compensation is recognized when the achievement of such performance condition is determined to be probable. If the outcome of such performance condition is not determined to be probable or is not met, no compensation expense is recognized.

Refer to Note C, *Accounting Policies,* for a discussion of our accounting policies and recently issued accounting standards.

CAUTIONARY NOTE ON FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 that involve risks and uncertainties. These forward-looking statements relate to, among other things, the timing of initiation of new clinical sites and patient enrollment in our clinical trials, the expected timetable for development of our product candidates, our growth strategy, and our future financial performance, including our operations, economic performance, financial condition, prospects, and other future events. We have attempted to identify forward-looking statements by using such words as "anticipates," "believes," "can," "continue," "could," "estimates," "expects," "intends," "may," "plans," "potential," "should," "suggest," "will," or other similar expressions. These forward-looking statements are only predictions and are largely based on our current expectations. These forward-looking statements appear in a number of places in this Annual Report.

In addition, a number of known and unknown risks, uncertainties, and other factors could affect the accuracy of these statements. Some of the more significant known risks that we face are the risks and uncertainties inherent in the process of discovering, developing, and commercializing products that are safe and effective for use as therapeutics, including the uncertainty regarding market acceptance of our product candidates and our ability to generate revenues. The following risks and uncertainties may cause our actual results, levels of activity, performance, or achievements to differ materially from any future results, levels of activity, performance, or achievements expressed or implied by these forward-looking statements:

- the possibility of unfavorable results from ongoing and additional clinical trials involving MultiStem;
- the risk that positive results in a clinical trial may not be replicated in subsequent or confirmatory trials or success in an early stage clinical trial may not be predictive of results in later stage or large scale clinical trials;
- our ability to raise capital to fund our operations, including but not limited to, our ability to access our traditional financing sources and to continue as a going concern;
- the timing and nature of results from MultiStem clinical trials, including the MASTERS-2 Phase 3 clinical trial evaluating the administration of MultiStem for the treatment of ischemic stroke, and the Healios TREASURE and ONE-BRIDGE clinical trials in Japan evaluating the treatment in stroke and ARDS patients, respectively, including the timing of the release of data by Healios from its clinical trials, which could be delayed by, among other things, the regulatory process with the PMDA;
- our ability to meet milestones and earn royalties under our collaboration agreements, including the success of our collaboration with Healios;
- the success of our MACOVIA clinical trial evaluating the administration of MultiStem for the treatment of ARDS induced by COVID-19 and other pathogens, and the MATRICS-1 clinical trial being conducted with The University of Texas Health Science Center at Houston evaluating the treatment of patients with serious traumatic injuries;
- the impact of the COVID-19 pandemic on our ability to complete planned or ongoing clinical trials;
- the possibility that the COVID-19 pandemic could continue to delay clinical site initiation, clinical trial enrollment, regulatory review and potential receipt of regulatory approvals, payments of milestones under our license agreements and commercialization of one or more of our product candidates, if approved;
- the availability of product sufficient to meet commercial demand shortly following any approval, such as in the case of accelerated approval for the treatment of COVID-19 induced ARDS;

- the impact on our business, results of operations and financial condition from the ongoing and global COVID-19 pandemic, or any other pandemic, epidemic or outbreak of infectious disease in the United States;
- the possibility of delays in, adverse results of, and excessive costs of the development process;
- our ability to successfully initiate and complete clinical trials of our product candidates;
- the impact of the COVID-19 pandemic on the production capabilities of our contract manufacturing partners and our MultiStem trial supply chain;
- the possibility of delays, work stoppages or interruptions in manufacturing by third parties or us, such as due to material supply constraints, contaminations, operational restrictions due to COVID-19 or other public health emergencies, labor constraints, regulatory issues or other factors that could negatively impact our trials and the trials of our collaborators;
- uncertainty regarding market acceptance of our product candidates and our ability to generate revenues, including MultiStem cell therapy for neurological, inflammatory and immune, cardiovascular and other critical care indications;
- changes in external market factors;
- changes in our industry's overall performance;
- changes in our business strategy;
- our ability to protect and defend our intellectual property and related business operations, including the successful prosecution of our patent applications and enforcement of our patent rights, and operate our business in an environment of rapid technology and intellectual property development;
- our possible inability to realize commercially valuable discoveries in our collaborations with pharmaceutical and other biotechnology companies;
- our collaborators' ability to continue to fulfill their obligations under the terms of our collaboration agreements and generate sales related to our technologies;
- the success of our efforts to enter into new strategic partnerships and advance our programs;
- our possible inability to execute our strategy due to changes in our industry or the economy generally;
- changes in productivity and reliability of suppliers;
- the success of our competitors and the emergence of new competitors; and
- the risks mentioned elsewhere in this Annual Report on Form 10-K under Item 1A, "Risk Factors." and our other filings with the SEC.

Although we currently believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee our future results, levels of activity or performance. We undertake no obligation to publicly update forward-looking statements, whether as a result of new information, future events or otherwise, except as otherwise required by law. You are advised, however, to consult any further disclosures we make on related subjects in our reports on Forms 10-Q, 8-K and 10-K furnished to the SEC. You should understand that it is not possible to predict or identify all risk factors. Consequently, you should not consider any such list to be a complete set of all potential risks or uncertainties.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Interest Rate Risk

Our exposure to interest rate risk is related to our investment portfolio and our borrowings, if any. Fixed rate investments and borrowings may have their fair market value adversely impacted from changes in interest rates. Due in part to these factors, our future investment income may fall short of expectations. Further, we may suffer losses in investment principal if we are forced to sell securities that have declined in market value due to changes in interest rates. When appropriate based on interest rates, we invest our excess cash primarily in debt instruments of the United States government and its agencies and corporate debt securities, and as of December 31, 2021, we had no investments.

We have entered into loan arrangements with financial institutions when needed and when available to us. At December 31, 2021, we had no borrowings outstanding.

ITEM 8. **FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA**

Athersys, Inc.

Consolidated Financial Statements

Years Ended December 31, 2021, 2020 and 2019

Contents

Report of Independent Registered Public Accounting Firm

The Stockholders and Board of Directors of Athersys, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Athersys, Inc. (the Company) as of December 31, 2021 and 2020, the related consolidated statements of operations and comprehensive loss, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2021, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2021 and 2020, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2021, in conformity with U.S. generally accepted accounting principles.

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. As discussed in Note B to the financial statements, the Company has incurred net losses since its inception, has negative operating cash flows and has stated that substantial doubt exists about the Company's ability to continue as a going concern. Management's evaluation of the events and conditions and management's plans regarding these matters are also described in Note B. 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 audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

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

Critical Audit 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 the critical audit matter does not alter in any way our opinion on the consolidated 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.

Revenue Recognition from Collaboration Arrangements

Description of the Matter	As discussed in Note F to the consolidated financial statements, the Company amended its collaboration agreement with HEALIOS K.K. (Healios) to require the Company to provide services to Healios necessary for regulatory approvals, manufacturing readiness, and commercial launch in Japan. The Company is recognizing revenue as the services are being performed. Auditing the Company's revenue recognition for the amendment to the Healios agreement is complex because significant judgment may be required to apply the authoritative accounting guidance to the arrangement, including the estimate of variable consideration and determining the measure of progress of services related to manufacturing readiness for regulatory approvals and commercial launch in Japan.
How we addressed the matter in our audit	Our audit procedures included, among others, evaluating the Company's assessment and application of the authoritative guidance to the Healios arrangement, reading the contract amendment entered into during the period, and evaluating management's interpretation of contract provisions. We evaluated whether the transaction price including management's estimate of variable consideration was properly measured for the identified performance obligation. We also evaluated the Company's key assumptions and tested the completeness and accuracy of the underlying data used to determine the progress of performance at the end of the reporting period. For example, we compared the estimate of total expected costs to amounts specified within the Company's contracts with its vendors. In addition, we compared the estimate of total expected costs to actual incurred costs.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 1998.

Cleveland, Ohio
March 15, 2022

Athersys, Inc.

Consolidated Balance Sheets

(In Thousands, Except Share and Per Share Amounts)

	December 31,	
	2021	**2020**
Assets		
Current assets:		
Cash and cash equivalents	**$ 37,407**	$ 51,546
Accounts receivable from Healios	**1,414**	89
Unbilled accounts receivable from Healios	**3,000**	—
Prepaid expenses and other	**4,206**	2,926
Total current assets	**46,027**	54,561
Operating right-of-use assets, net	**8,960**	648
Property and equipment, net	**3,692**	3,155
Deposits and other	**1,505**	1,350
Total assets	**$ 60,184**	$ 59,714
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	**$ 15,781**	$ 11,337
Accounts payable to Healios	**1,119**	1,705
Operating lease liabilities, current	**1,011**	480
Accrued compensation and related benefits	**4,133**	1,779
Accrued clinical trial related costs	**3,773**	6,870
Accrued expenses and other	**704**	718
Deferred revenue - Healios	**3,340**	65
Total current liabilities	**29,861**	22,954
Operating lease liabilities, non-current	**8,755**	197
Advance from Healios	**5,199**	5,201
Stockholders' equity:		
Preferred stock, at stated value; 10,000,000 shares authorized, and no shares issued and outstanding at December 31, 2021 and 2020	**—**	—
Common stock, $0.001 par value; 600,000,000 shares authorized, and 242,844,180 issued and outstanding at December 31, 2021 and 300,000,000 shares authorized, and 201,973,582 shares issued and outstanding at December 31, 2020	**243**	202
Additional paid-in capital	**599,470**	527,549
Accumulated deficit	**(583,344)**	(496,389)
Total stockholders' equity	**16,369**	31,362
Total liabilities and stockholders' equity	**$ 60,184**	$ 59,714

See accompanying notes.

Athersys, Inc.

Consolidated Statements of Operations and Comprehensive Loss

(In Thousands, Except Per Share Amounts)

	Years Ended December 31,		
	2021	2020	2019
Revenues			
Contract revenue from Healios	**$ 5,514**	$ 1,432	$ 5,517
Grant revenue	**—**	8	116
Total revenues	**5,514**	1,440	5,633
Costs and expenses			
Research and development (including stock compensation expense of $3,642, $3,351 and $2,217 in 2021, 2020 and 2019, respectively)	**71,080**	62,994	39,045
General and administrative (including stock compensation expense of $4,914, $4,028 and $2,634 in 2021, 2020 and 2019, respectively)	**20,065**	15,888	11,378
Depreciation	**1,427**	890	698
Total costs and expenses	**92,572**	79,772	51,121
Loss from operations	**(87,058)**	(78,332)	(45,488)
Other income (expense), net	**103**	(433)	906
Net loss and comprehensive loss	**$ (86,955)**	$ (78,765)	$ (44,582)
Net loss per common share, basic and diluted	**$ (0.39)**	$ (0.42)	$ (0.29)
Weighted average shares outstanding, basic and diluted	**224,274**	187,472	151,696

See accompanying notes.

Athersys, Inc.

Consolidated Statements of Stockholders' Equity

(In Thousands, Except Share Amounts)

	Preferred Stock		Common Stock		Additional Paid-in Capital	Accumulated Deficit	Total Stockholders' Equity
	Number of Shares	Stated Value	Number of Shares	Par Value			
Balance at January 1, 2019	—	$ —	144,292,739	$ 144	$ 416,014	$ (373,042)	$ 43,116
Stock-based compensation	—	—	—	—	4,851	—	4,851
Issuance of common stock, net of issuance costs	—	—	14,825,000	15	20,269	—	20,284
Issuance of common stock under equity compensation plans	—	—	673,846	1	(399)	—	(398)
Net and comprehensive loss	—	—	—	—	—	(44,582)	(44,582)
Balance at December 31, 2019	—	—	159,791,585	160	440,735	(417,624)	23,271
Stock-based compensation	—	—	—	—	7,379	—	7,379
Issuance of common stock, net of issuance costs	—	—	37,012,500	37	72,745	—	72,782
Issuance of common stock to Healios	—	—	4,310,526	4	7,570	—	7,574
Issuance of common stock under equity compensation plans	—	—	858,971	1	(880)	—	(879)
Net and comprehensive loss	—	—	—	—	—	(78,765)	(78,765)
Balance at December 31, 2020	—	—	201,973,582	202	527,549	(496,389)	31,362
Stock-based compensation	**—**	**—**	**—**	**—**	**8,556**	**—**	**8,556**
Issuance of common stock, net of issuance costs	**—**	**—**	**40,031,000**	**40**	**64,223**	**—**	**64,263**
Issuance of common stock under equity compensation plan	**—**	**—**	**839,598**	**1**	**(858)**	**—**	**(857)**
Net and comprehensive loss	—	—	—	—	—	**(86,955)**	**(86,955)**
Balance at December 31, 2021	**—**	**$ —**	**242,844,180**	**$ 243**	**$ 599,470**	**$ (583,344)**	**$ 16,369**

See accompanying notes.

Athersys, Inc.

Consolidated Statements of Cash Flows

(In Thousands)

	Years Ended December 31,		
	2021	**2020**	**2019**
Operating activities			
Net loss	**$ (86,955)**	$ (78,765)	$ (44,582)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation	**1,427**	890	698
Stock-based compensation	**8,556**	7,379	4,851
Operating right-of-use assets, net	**235**	—	—
Changes in operating assets and liabilities:			
Accounts receivable from Healios - billed and unbilled	**(4,325)**	856	3,783
Prepaid expenses, deposits and other	**(1,605)**	(2,126)	1,102
Accounts payable, accrued expenses and other	**3,795**	9,456	(1,836)
Accounts payable to Healios	**(586)**	637	1,068
Deferred revenue - Healios	**3,275**	—	(609)
Advance from Healios	**(2)**	(137)	199
Net cash used in operating activities	**(76,185)**	(61,810)	(35,326)
Investing activities			
Purchases of equipment	**(1,360)**	(1,162)	(579)
Net cash used in investing activities	**(1,360)**	(1,162)	(579)
Financing activities			
Proceeds from issuance of common stock, net	**64,263**	72,782	20,311
Proceeds from issuance of common stock to Healios, net	**—**	7,574	—
Shares retained for withholding tax payments on stock-based awards	**(857)**	(879)	(424)
Net cash provided by financing activities	**63,406**	79,477	19,887
(Decrease) Increase in cash and cash equivalents	**(14,139)**	16,505	(16,018)
Cash and cash equivalents at beginning of year	**51,546**	35,041	51,059
Cash and cash equivalents at end of year	**$ 37,407**	$ 51,546	$ 35,041
Non-cash investing activities:			
Right-of-use assets obtained in exchange for lease liabilities	**9,162**	—	—

See accompanying notes.

A. Background

Athersys, Inc., including its consolidated subsidiaries (collectively, "we," "us," "Athersys," and the "Company") is a biotechnology company focused in the field of regenerative medicine and operates in one business segment. Our operations consist of research, clinical development, manufacturing and manufacturing process development activities, and our most advanced program is in a pivotal Phase 3 clinical trial.

We expect that the the results of the TREASURE study, the clinical trial of our partner in Japan, HEALIOS K.K. ("Healios"), followed by the results of our MASTERS-2 clinical trial, will have a significant impact, favorable or unfavorable, on our ability to access capital from potential third-party commercial partners or the equity capital markets. Depending on the nature of these results, we may accelerate or may delay certain programs. In the longer term, we will have to continue to generate additional capital to meet our needs until we would become cash flow positive as a result of the sales of our clinical products, if they are approved for marketing. Such capital would come from new and existing collaborations and the related license fees, milestones and potential royalties and the sale of equity securities from time to time including through our equity facility and grant-funding opportunities.

Healios Framework Agreement

On August 5, 2021, we expanded our partnership with Healios by entering into the Comprehensive Framework Agreement for Commercial Manufacturing and Ongoing Support (the "Framework Agreement") to optimize and better align the collaboration structure to drive therapeutic reach and commercial success in Japan for the MultiStem product following potential regulatory approval. The Framework Agreement provides for planned investment by Healios in certain manufacturing preparation activities. We have agreed to defer certain milestone payments and potentially adjust royalty payments during the initial commercial launch period. Refer to Note F, *Collaborative Arrangements and Revenue Recognition*, for additional information.

On February 16, 2021, the Company, Healios and Dr. Hardy TS Kagimoto, the Chairman and Chief Executive Officer of Healios and a member of our board of directors (the "Board"), entered into a cooperation agreement (the "Cooperation Agreement"). The Cooperation Agreement provided for the parties' cooperation on certain commercial matters, including a commitment to work in good faith to finalize negotiations on all aspects of their supply, manufacturing, information provision and regulatory support relationship.

The Cooperation Agreement also provided for, among related matters, the dismissal with prejudice of the complaint filed by Dr. Kagimoto against the Company seeking the inspection of the Company's books and records in the Court of Chancery of the State of Delaware on November 21, 2020 (the "Section 220 Litigation"). Pursuant to the Cooperation Agreement, in April 2021, we reimbursed Healios and Dr. Kagimoto for reasonable out-of-pocket fees and expenses, including legal expenses, incurred in connection with the Section 220 Litigation, which were not to exceed $0.5 million in the aggregate.

In connection with the execution of the Framework Agreement, certain issues as contemplated by the Cooperation Agreement were resolved and the Cooperation Agreement was amended to extend certain customary standstill provisions until the conclusion of our 2023 annual meeting of stockholders.

Retention Program

In the first quarter of 2021, we entered into retention letter agreements ("Retention Agreements") with our executive officers and certain other employees in leadership positions. Each Retention Agreement provides for, among other things, a cash retention bonus and a stock option award, each with vesting tied to continued employment. The cash retention bonuses generally represent a percentage of the employee's annual compensation and generally vest in full if employed on May 1, 2022. The stock option awards generally vest one-third on May 1, 2022 with the remainder vesting on May 1, 2023 and include a provision for accelerated vesting upon termination without cause. The total stock compensation expense related to the stock option awards is approximately $2.7 million and is being expensed ratably over the vesting period. In April 2021, we expanded the retention program to all then-current employees of the Company, providing for a cash retention bonus with vesting also tied to continued employment through May 1, 2022. The total cash retention bonus is approximately $2.5 million, which is being expensed ratably over the respective vesting periods.

Chief Executive Officer Separation Letter Agreement

Effective February 15, 2021, Dr. Gil Van Bokkelen resigned from his position as the Company's Chief Executive Officer and Chairman of the Board. In connection with his resignation, the Company and Dr. Van Bokkelen entered into a separation letter agreement (the "Separation Letter") entitling him to severance payments and benefits with an aggregate value of approximately $1.0 million payable in installments over an 18-month period, and providing for a total lump sum payment of approximately

$0.2 million. At December 31, 2021, we recorded a liability in the amount of $0.4 million, which represents the remaining installments payable to Dr. Van Bokkelen. The lump sum payment was made to Dr. Van Bokkelen in March 2021. The related expense is recorded in general and administrative expense on the consolidated statements of operations and comprehensive loss.

The terms of the Separation Letter also provided for the accelerated vesting of Dr. Van Bokkelen's outstanding restricted stock units ("RSUs") and the modification of his stock option awards by providing for accelerated vesting of his unvested stock options and the extension of time during which certain vested stock options can be exercised. In the first quarter of 2021, following the evaluation of the modification, we recorded stock compensation expense of approximately $1.4 million related to the accelerated vesting of Dr. Van Bokkelen's stock options and $0.9 million related to the accelerated vesting of his RSUs.

B. Going Concern

We have prepared our consolidated financial statements on a going concern basis, which assumes that we will realize our assets and satisfy our liabilities in the normal course of business. However, we have incurred net losses since our inception in 1995 and have negative operating cash flows. These factors, among others, raise substantial doubt about our ability to continue as a going concern within one year after the date that these financial statements are issued.

At December 31, 2021, we had cash and cash equivalents of $37.4 million. We will require significant additional capital to continue our research and development programs, including progressing our clinical product candidates to potential commercialization and preparing for commercial-scale manufacturing and sales. The accompanying consolidated financial statements do not include any adjustments to reflect the possible future effect on the recoverability and classification of assets or the amounts and classification of liabilities that may result from the outcome of the uncertainty concerning our ability to continue as a going concern. Management plans to raise additional capital through the use of our equity purchase agreement with Aspire Capital Fund, LLC ("Aspire Capital") and, depending on market conditions, through equity offerings. We are entitled to a new milestone payment from Healios in the amount of $3.0 million by June 2022. Additionally, management has the ability to defer certain spending and potentially defer and delay certain non-core programs. While management believes this plan to generate additional funds will alleviate the conditions that raise substantial doubt, these plans are not entirely within its control and cannot be assessed as being probable of occurring. For the foreseeable future, our ability to continue our operations is dependent upon the ability to obtain additional capital.

C. Accounting Policies

Accounting Standards Adopted

In December 2019, the FASB issued ASU 2019-12, *Income Taxes (Topic 740) - Simplifying the Accounting for Income Taxes*, which simplifies the accounting for income taxes by removing certain exceptions to the general principles in Topic 740. The ASU is effective for fiscal years beginning after December 15, 2020. We adopted this ASU prospectively as of January 1, 2021 and the adoption of this ASU did not have a material impact on our consolidated financial statements and disclosures.

Accounting Standards Not Yet Adopted

In June 2016, the FASB issued ASU 2016-13, *Measurement of Credit Losses on Financial Instruments (Topic 326)*. This ASU replaces the incurred loss impairment methodology in current GAAP with a methodology that reflects expected credit losses and requires consideration of a broader range of reasonable and supportable information to inform credit loss estimates. Subsequent to issuing ASU 2016-13, the FASB issued ASU 2019-10, *Financial Instruments - Credit Losses (Topic 326): Effective Dates*, delaying the effective date for smaller reporting companies until January 2023. We are currently evaluating the potential impact of adoption of this standard on our consolidated financial statements and disclosures, and we do not intend to early adopt.

Principles of Consolidation

The consolidated financial statements include our accounts and results of operations and those of our wholly owned subsidiaries. All intercompany accounts and transactions have been eliminated in consolidation.

Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. Actual results could differ from those estimates.

Reclassification

Certain reclassifications of prior period presentations have been made to conform to the current period presentation.

Revenue Recognition

Our license and collaboration agreements may contain multiple elements, including license and technology access fees, research and development funding, product supply revenue, service revenue, cost-sharing, milestones and royalties. The deliverables under our arrangements are evaluated under FASB Accounting Standards Codification No. 606 ("Topic 606") which requires an entity to recognize revenue in a manner that depicts the transfer of promised goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services.

Milestone Payments

Topic 606 does not contain guidance specific to milestone payments, but rather requires potential milestone payments to be considered in accordance with the overall model of Topic 606. As a result, revenues from contingent milestone payments are recognized based on an assessment of the probability of milestone achievement and the likelihood of a significant reversal of such milestone revenue at each reporting date. This assessment may result in recognizing milestone revenue before the milestone event has been achieved. Since milestone payments in the Healios arrangement are generally related to development and commercial milestone achievement by Healios, we only include milestones that are unconditionally entitled to in the estimated transaction price of the Healios arrangement. Conditional or contingent milestones are constrained to the extent that a significant reversal of revenue could result in future periods. Refer to Note F, *Collaborative Arrangements and Revenue Recognition,* for further information.

Grant Revenue

Grant revenue, which is not within the scope of Topic 606 for our grant arrangements, consists of funding under cost reimbursement programs primarily from federal and non-profit foundation sources for qualified research and development activities performed by us, and as such, are not based on estimates that are susceptible to change. Such amounts are invoiced and recorded as revenue as grant-funded activities are performed, with any advance funding recorded as deferred revenue until the activities are performed.

Royalty Revenue

We generate royalty revenue from the sale of licensed products by our licensees. Royalty revenue is recognized upon the later to occur of (i) achievement of the collaborator's underlying sales and (ii) satisfaction of any performance obligation(s) related to these sales, in each case assuming the license to our intellectual property is deemed to be the predominant item to which the sales-based royalties relate.

Contractual Right to Consideration and Deferred Revenue

Amounts included in deferred revenue or contract assets are determined at the contract level, and for our Healios arrangement, such amounts are included in a contract asset or liability depending on the overall status of the arrangement. Amounts received from customers or collaborators in advance of our performance of services or other deliverables are included in deferred revenue, while amounts for performance of services or other deliverables in excess of the customer payment received are included in contract assets, with those accounts that are unconditional and billed being included in accounts receivable separate from contract assets. Grant proceeds received in advance of our performance under the grant is included in deferred revenue.

Cash and Cash Equivalents

We consider all highly liquid investments with a maturity of three months or less when purchased to be cash equivalents. Cash equivalents are primarily invested in money market funds. The carrying amount of our cash equivalents approximates fair value due to the short maturity of the investments.

Research and Development

Research and development expenditures, which consist primarily of costs associated with clinical trials, preclinical research, clinical product manufacturing and process development for manufacturing, personnel, legal fees resulting from intellectual property application and maintenance processes, and laboratory supply and reagent costs, including direct and allocated overhead expenses, are charged to expense as incurred.

Clinical Trial Costs

Clinical trial costs are accrued based on work performed by outside contractors that manage and perform the trials, and those that manufacture the investigational product. We obtain initial estimates of total costs based on enrollment of subjects, trial duration, project management estimates, manufacturing estimates, patient treatment costs and other activities. Actual costs may be charged to us and recognized as the tasks are completed by the contractor or, alternatively, may be invoiced in accordance with agreed-upon payment schedules and recognized based on estimates of work completed to date. Accrued clinical trial costs may be subject to revisions as clinical trials progress, and any revisions are recorded in the period in which the facts that give rise to the revisions become known.

Royalty Payments and Sublicense Fees

We are required to make royalty payments to certain parties based on our product sales under license agreements. No royalties were recorded during the year ended December 31, 2021, since we have not yet generated sales revenue. We are also required to record sublicense fees from time-to-time in connection with license fees from collaborators and clinical and commercial milestone achievement. Sublicenses fees were not significant in 2021 and 2020, and we recorded sublicense fees of $0.1 million in research and development expenses in the consolidated statements of operations and comprehensive loss in the year ended December 31, 2019.

Long-Lived Assets

Property and equipment is stated at acquired cost net of depreciation and amortization. Laboratory and office equipment are depreciated on the straight-line basis over the estimated useful lives (three to ten years). Leasehold improvements are amortized over the shorter of the lease term or estimated useful life. We expense repair and maintenance costs as incurred. We capitalize replacements and improvements that increase the estimated useful life of an asset. We retain fully depreciated assets in property and equipment and the related accumulated depreciation accounts until we remove them from service.

Long-lived assets are evaluated for impairment when events or changes in circumstances indicate that the carrying amount of the asset or related group of assets may not be recoverable. If the expected future undiscounted cash flows are less than the carrying amount of the asset or related group of assets, an impairment loss is recognized at that time. Measurement of impairment may be based upon appraisal, market value of similar assets or discounted cash flows.

Leasing Arrangements

We lease equipment, buildings and office space under operating lease arrangements. We have various supply agreements with third-party manufacturers, which involve the lease of manufacturing facilities and equipment, as defined in Topic 842. We have elected to separate lease and non-lease components for these arrangements. These manufacturing agreements have variable lease payments, which typically become binding once certain manufacturing milestones are achieved, and as such, are not included in right-of-use ("ROU") assets and lease liabilities until such payments are no longer variable. We do not separate lease and non-lease components for all other currently existing asset classes. We apply the short-term lease exemption to all qualified lease agreements. The short-term lease exemption allows for the non-recognition of ROU assets and lease liabilities for leases with a term of twelve months or less.

We determine if an arrangement is or contains a lease at contract inception and exercise judgment and apply certain assumptions when determining the discount rate, lease term and lease payments. Generally, we do not have knowledge of the discount rate implicit in the lease and, therefore, in most cases we use the incremental borrowing rate to compute the present value of future lease payments. The incremental borrowing rate is determined based on lease term and leased asset, and is adjusted for the impacts of collateral. The lease term includes the non-cancelable period of the lease plus any additional periods covered by an option to extend that we are reasonably certain to exercise, or an option to extend that is controlled by the lessor. Lease expense for lease payments is recognized on a straight-line basis over the lease term. Payments for certain lease agreements are adjusted annually for changes in an index or rate.

We had no finance leases, residual value guarantees, restrictive covenants, subleases or sale leaseback transactions at December 31, 2021 and 2020. All ROU assets are periodically reviewed for impairment losses. Refer to Note K, *Leasing Arrangements*, for further information.

Patent Costs and Rights

Costs of applying for, prosecuting and maintaining patents and patent rights are expensed as incurred. We have filed for broad intellectual property protection on our proprietary technologies and have numerous United States and international patents and patent applications related to our technologies.

Warrants

We account for common stock warrants as either liabilities or as equity instruments depending on the specific terms of the warrant agreements. Generally, warrants are classified as liabilities, as opposed to equity, if the agreement includes the potential for a cash settlement or an adjustment to the exercise price, and warrant liabilities are recorded at their fair values at each balance sheet date. We had no warrant liabilities or warrant equity instruments recorded in the consolidated financial statements at December 31, 2021 and 2020. Refer to Note G, *Capitalization and Warrant Instruments*, for a discussion of common stock warrants issued to Healios in 2021.

Concentration of Credit Risk

Our accounts receivable are generally comprised of amounts due from collaborators and granting authorities and are subject to concentration of credit risk due to the absence of a large number of customers. At December 31, 2021 and 2020, our accounts receivable are due from Healios. We do not typically require collateral from our customers.

Legal Matters

We evaluate the development of legal matters on a regular basis and accrue a liability when we believe a loss is probable and the amounts can be reasonably estimated.

Stock-Based Compensation

Compensation expense related to stock options granted is measured at the grant date based on the estimated fair value of the award and is recognized using the straight-line method over the requisite service period, for awards without performance conditions. We determine the estimated fair value of each stock option on the date of grant using the Black-Scholes option-pricing model. The expected term of stock options granted represent the period of time that stock option grants are expected to be outstanding. The risk-free interest rate is based on the U.S. Treasury yield for a period consistent with the expected term of the stock option at the time of the grant. We determine volatility by using our historical stock volatility. We account for forfeitures as they occur. We have never paid or declared dividends or paid dividends on our common stock and have no plans to do so in the foreseeable future. Changes in these assumptions may lead to variability with respect to the amount of stock compensation expense we recognize related to stock options.

Stock-based compensation for an award with a performance condition is recognized when the achievement of such performance condition is determined to be probable. If the outcome of such performance condition is not determined to be probable or is not met, no compensation expense is recognized.

Prior to June 2020, we used the "simplified" method to calculate the expected term of option grants. In June 2020, we modified our stock option awards for all then-current employees and directors by providing an extension to the period of time during which vested stock options can be exercised. The extension to the period of time during which stock options can be exercised also applies to all stock options granted after June 2020. Subsequent to the modification date, our stock options no longer qualify to use the "simplified" method, and the expected term of our option grants is determined based on the historical experience and patterns, as well as current trends as previously described.

The fair value of our restricted stock units is equal to the closing price of our common stock on the date of grant and is expensed over the vesting period on a straight-line basis. Restricted stock units typically vest over a four-year period. Refer to Note H, *Stock-Based Compensation*, for additional information.

Stock option awards to employees typically vest over a four-year period, have an exercise price equal to the fair market value of a share of common stock on the grant date and have a contractual term of 10 years. The following weighted-average input assumptions were used in determining the fair value of our stock options granted:

	December 31,		
	2021	2020	2019
Volatility	**75.2 %**	72.2 %	71.1 %
Risk-free interest rate	**0.8 %**	0.6 %	2.0 %
Expected life of option	**5.4 years**	5.7 years	6.2 years
Expected dividend yield	**0.0 %**	0.0 %	0.0 %

Income Taxes

Deferred tax liabilities and assets are determined based on the differences between the financial reporting and tax basis of assets and liabilities and are measured using the tax rate and laws currently in effect. We evaluate our deferred income taxes to determine if a valuation allowance should be established against the deferred tax assets or if the valuation allowance should be reduced based on consideration of all available evidence, both positive and negative, using a "more likely than not" standard.

We had no liability for uncertain income tax positions as of December 31, 2021 and 2020. Our policy is to recognize potential accrued interest and penalties related to the liability for uncertain tax benefits, if applicable, in income tax expense. Net operating loss and credit carryforwards since inception remain open to examination by taxing authorities and will for a period post utilization.

Net Loss per Share

Basic and diluted net loss per share have been computed using the weighted-average number of shares of common stock outstanding during the period.

We have outstanding options and restricted stock units and, in 2021 and 2019, had outstanding warrants that were not used in the calculation of diluted net loss per share because to do so would be antidilutive. The following instruments, were excluded from the calculation of diluted net loss per share because their effects would be antidilutive:

	Years ended December 31,		
	2021	2020	2019
Stock options	**23,043,035**	18,150,409	13,975,671
Restricted stock units	**1,985,057**	2,374,006	2,032,180
Warrants	**—**	—	4,000,000
	25,028,092	20,524,415	20,007,851

We issued 10,000,000 common stock warrants to Healios in 2021 which are excluded from the calculation of diluted net loss per share, as the underlying performance condition associated with each warrant has not been satisfied and is not yet considered probable at the end of the reporting period. Refer to Note G. *Capitalization and Warrant Instruments*, for a discussion of the common stock warrants issued to Healios in 2021.

D. Property and Equipment, net

	December 31,	
Property and equipment consists of (in thousands):	**2021**	2020
Laboratory equipment	**$ 9,352**	$ 9,225
Office equipment and leasehold improvements	**4,000**	3,336
Process development equipment not yet in service	**458**	294
	13,810	12,855
Accumulated depreciation and amortization	**(10,118)**	(9,700)
	$ 3,692	$ 3,155

During 2021 and 2020, we disposed of approximately $1.0 million and $0.1 million of obsolete equipment, respectively, all of which were fully depreciated. During the second quarter of 2021, we determined that certain equipment assets would no longer be necessary to support future manufacturing activities due to modifications to our processes, which reduced the estimated useful lives of such equipment. The modifications were decided on during the second quarter of 2021 and we accelerated depreciation, which resulted in an additional $0.5 million in depreciation on the consolidated statements of operations and comprehensive loss.

E. Financial Instruments

Fair Value Measurements

We classify the inputs used to measure fair value into the following hierarchy:

Level 1	Unadjusted quoted prices in active markets for identical assets or liabilities.
Level 2	Unadjusted quoted prices in active markets for similar assets or liabilities, or unadjusted quoted prices for identical or similar assets or liabilities in markets that are not active, or inputs other than quoted prices that are observable for the asset or liability.
Level 3	Unobservable inputs for the asset or liability.

Cash equivalents primarily consist of money market funds with overnight liquidity and no stated maturities. We classified cash equivalents as a Level 1 due to the short-term nature of these instruments and measured the fair value based on quoted prices in active markets for identical assets.

F. Collaborative Arrangements and Revenue Recognition

Healios Collaboration

In 2016, we entered into a license agreement (the "First License Agreement") with Healios to develop and commercialize MultiStem cell therapy for ischemic stroke in Japan and to provide Healios with access to our proprietary MAPC technology for use in Healios' organ bud program, initially for transplantation to treat liver disease or dysfunction. Under the terms of the First License Agreement, Healios also obtained a right to expand the scope of the collaboration to include the exclusive rights to develop and commercialize MultiStem for the treatment of two additional indications in Japan which included acute respiratory distress syndrome ("ARDS") and another indication in the orthopedic area, and all indications for the organ bud program.

Under the collaboration, Healios is responsible for the development and commercialization of the MultiStem product in the licensed territories, and we provide manufacturing services to Healios, comprising the supply of product for its clinical trials, technology transfer services and services related to commercial readiness in Japan.

In 2017, we signed a clinical trial supply agreement for delivering the planned manufacturing services for Healios' clinical trial in Japan, entitled, "*Treatment Evaluation of Acute Stroke for Using in Regenerative Cell Elements*" ("TREASURE"). The clinical trial supply agreement was amended later that year to clarify the operational elements, terms and cost-sharing arrangement associated with our supply of clinical material and certain adjustments to potential milestone payments related to the clinical product supply for TREASURE.

Also in 2017, we entered into a technology transfer services agreement with Healios, in which Healios provides financial support to establish a contract manufacturer in Japan to produce product for Healios' use. Related to the technology transfer services agreement with Healios, at the request of Healios, we entered into a manufacturing services agreement with Nikon CeLL innovation ("NCLi"), a subsidiary of Nikon Corp. and a significant Healios shareholder. At that time, we also amended the First License Agreement to confer to Healios a limited license to manufacture MultiStem if we are acquired by a third-party. The technology transfer services agreement with Healios was complete as of September 2019 and NCLi continued to provide technology transfer services to us. In the fourth quarter of 2019, the Company and Healios entered into a memorandum of understanding (the "Memorandum") to provide additional technology transfer services.

In June 2018, as contemplated by the First License Agreement, Healios exercised its option to expand the collaboration and entered into the Collaboration Expansion Agreement ("CEA") that included new license agreements and rights that further broadened the collaboration. Under the CEA, Healios (i) expanded its First License Agreement to include ARDS in Japan, expanded the organ bud license to include all transplantation indications, and terminated Healios' right to include a designated orthopedic indication per the First License Agreement; (ii) obtained a worldwide exclusive license, or the Ophthalmology License Agreement, for use of MultiStem product to treat certain ophthalmological indications; (iii) obtained an exclusive license in Japan (the "Combination Product License Agreement"), for use of the MultiStem product to treat diseases of the liver, kidney, pancreas and intestinal tissue through local administration of MultiStem in combination with iPSC-derived cells; (iv) obtained an exclusive, time-limited right of first negotiation ("ROFN Period") to enter into an option for a license to develop and commercialize certain MultiStem treatments in China, which has since expired; and (v) an option for an additional non-therapeutic technology license, which has also expired.

For each of the ischemic stroke indication and the ARDS indication, we may receive success-based regulatory filing and approval and sales milestones aggregating up to $225.0 million in aggregate for each indication, subject to potential milestone credits. Milestone payments are non-refundable and non-creditable towards future royalties or any other payment due from Healios. We may also receive tiered royalties on net product sales, starting in the low double digits and increasing incrementally into the high teens depending on net sales levels.

For standalone products sold by Healios under the Ophthalmology License Agreement, we are entitled to receive success-based regulatory filing and approval and sales milestones aggregating up to $135.6 million and tiered royalties on net product sales in the single digits depending on net sales levels. For the combination products under the Ophthalmology License Agreement, we will be entitled to receive a low single-digit royalty, but no milestone payments. Under the Combination Product License Agreement, we are entitled to receive a low single-digit royalty on net sales of the combination product treatments, but no milestone payments. For the organ bud product, we are entitled to receive a fractional royalty percentage on net sales of the organ bud products.

Under the CEA, the ROFN Period with respect to the option for a license in China was extended to June 30, 2019 in exchange for a $2.0 million payment from Healios that we received in December 2018. The extension payment will be applied as a credit against any potential milestone payments under the current licenses, subject to certain limitations. The ROFN Period expired on June 30, 2019. In connection with the entry into the CEA, we amended the terms of the Healios Warrant as addressed in Note G, *Capitalization and Warrant Instruments*.

In August 2021, the Company and Healios entered into the Framework Agreement, which provides for clarification under and modifies the existing agreements between the parties and reframes our collaboration to set the stage for productive efforts as Healios and our collaboration move towards commercialization of MultiStem in Japan. It also provides Healios with deferral of certain milestone payments during the expensive initial commercial launch period. We will be entitled to new milestone payments in the amount of $3.0 million by June 2022 and $5.0 million upon successful completion of certain commercial manufacturing activities. Additionally, accounts payable to Healios have been reduced to $1.1 million and are due on or before December 31, 2022. In connection with the execution of the Framework Agreement, the Cooperation Agreement was amended to extend certain customary standstill provisions until the conclusion of our 2023 annual meeting of stockholders. We also issued two warrants (together, the "2021 Warrants") to Healios in connection with the Framework Agreement to purchase up to a total of 10,000,000 shares of our common stock. The 2021 Warrants are being accounted for as consideration paid or payable to a customer according to Topic 606, *Revenue from Contracts with Customers*, and Topic 718, *Compensation - Stock Compensation,* under which the recognition of such equity instruments is required at the time that the underlying performance conditions become probable or are satisfied. As of December 31, 2021, the 2021 Warrants have not been recorded as the underlying performance conditions have not been satisfied and are not yet considered probable. Refer to Note G *Capitalization and Warrant Instruments,* for further information.

Healios Revenue Recognition

At the inception of the Healios arrangement and again each time that the arrangement has been modified, all material performance obligations were identified, which include (i) licenses to our technology, (ii) product supply services, and (iii) manufacturing services provided on Healios' behalf.

In order to determine the transaction price, in addition to the fixed payments, we estimate the amount of variable consideration utilizing the expected value or most likely amount method, depending on the facts and circumstances relative to the contract, and the estimates for variable consideration are reassessed each reporting period. We constrain, or reduce, the estimates of variable consideration if it is probable that a significant revenue reversal could occur in future periods.

The pricing for certain product supply provided to Healios was driven off the underlying cost per dose over the entire life of the agreement and subject to variability as those costs change. During 2019, the price per dose from our contract manufacturers decreased for the first time under this arrangement. As such, we reduced the expected transaction price to the current estimated value and applied the reduction to the undelivered elements of the overall arrangement at the time this product supply performance obligation originated. Furthermore, the number of doses of clinical product requested by Healios was amended in 2019, and our revenues were further reduced.

At inception and upon each date a modification has resulted under the Healios arrangement, once the estimated transaction price is established, amounts are allocated to each separate performance obligation on a relative standalone selling price basis. These performance obligations include any remaining, undelivered elements at the time of the modification and any new elements from a modification to the Healios arrangement as the conditions are not met for being treated as a separate agreement.

For performance obligations satisfied over time, we apply an appropriate method of measuring progress each reporting period and, if necessary, adjust the estimates of performance and the related revenue recognition. Our services provided on Healios' behalf are satisfied over time, and we recognize revenue in proportion to the contractual services provided, measured by costs incurred compared to total estimated costs. For performance obligations satisfied at a point in time (i.e., product supply), we recognize revenue upon delivery.

Under the Framework Agreement, it was determined there is currently one performance obligation for services necessary for regulatory approvals, manufacturing readiness, and commercial launch in Japan. We determined the transaction price includes estimated payments for reimbursable services to be performed by us for Healios and the $3.0 million milestone payment due no later than June 2022. We allocated the total transaction price to this one performance obligation. We began recognizing revenue in the third quarter of 2021 as the services were being performed, which are now expected to be completed by the end of 2022. During our evaluation of variable consideration in the fourth quarter of 2021, we increased our estimated transaction price due to changes in the estimated cost of the reimbursable services. The remaining transaction price for the performance obligation that was not yet satisfied is $5.6 million at December 31, 2021. We recognized revenue of approximately $0.5 million for the twelve months ended December 31, 2021, and no revenue for the twelve months ended December 31, 2020 from performance obligations partially satisfied in previous periods.

Accounts receivable from Healios

Accounts receivable from Healios are related to our contracts and are recorded when the right to consideration is unconditional at the amount that management expects to collect. Accounts receivable from Healios do not bear interest if paid when contractually due, and payments are generally due within thirty to forty-five days of invoicing.

Unbilled Accounts Receivable from Healios

Unbilled accounts receivable from Healios represent amounts due to us under contractual arrangements and for which we have an unconditional right to the consideration, but which we have not yet invoiced Healios. At December 31, 2021, the unbilled accounts receivable from Healios was $3.0 million, which represents a milestone payment owed to us under the Framework Agreement for which we are entitled to receive payment by June 2022.

Deferred Revenue - Healios

Amounts included in deferred revenue - Healios on the consolidated balance sheets, are considered a contract liability. During the twelve months ended December 31, 2021, revenue recognized from contract liabilities as of the beginning of the respective period was $0.1 million. No revenue was recognized from contract liabilities during the twelve months ended December 31, 2020. At December 31, 2021, the contract liability included in deferred revenue - Healios, is classified as a current liability since the rights to consideration are expected to be satisfied, in all material respects, within one year.

Advance from Healios

In 2017, we amended the clinical trial supply agreement for the manufacturing of clinical product for TREASURE to clarify a cost-sharing arrangement. The proceeds from Healios that relate specifically to the cost-sharing arrangement may either (i) result in a reduction, as defined in the clinical trial supply agreement, in the proceeds we receive from Healios upon the achievement of two potential milestones and an increase to a commercial milestone under the First License Agreement for stroke or (ii) be repaid to Healios at our election, as defined in the clinical trial supply agreement. The cost-sharing proceeds received are recognized on the balance sheet as a non-current advance from customer until the related milestone is achieved, unless such amounts are repaid to Healios at our election, at which time, the culmination of the earnings process will be complete and revenue will be recognized.

Disaggregation of Revenues

We recognize license-related amounts, including upfront payments, exclusivity fees, additional disease indication fees, and development, regulatory and sales-based milestones, at a point in time when earned. Similarly, product supply revenue is recognized at a point in time, while service revenue is recognized when earned over time. The following table presents our contract revenues disaggregated by timing of revenue recognition and excludes royalty revenue (in thousands):

	Twelve Months Ended December 31, 2021		**Twelve Months Ended December 31, 2020**		**Twelve Months Ended December 31, 2019**	
	Point in Time	**Over Time**	**Point in Time**	**Over Time**	**Point in Time**	**Over Time**
Contract revenue from Healios:						
License fee revenue	**$ —**	**$ —**	$ —	**$ —**	$ 1,624	$ —
Product supply revenue	**283**	**—**	1,432	**—**	2,167	—
Service revenue	**—**	**5,231**	—	**—**	—	1,726
Total disaggregated revenues	**$ 283**	**$ 5,231**	$ 1,432	$ —	$ 3,791	$ 1,726

G. Capitalization and Warrant Instruments

Capitalization

In June 2021, our stockholders approved an amendment to our certificate of incorporation to increase the number of shares of the Company's authorized common stock from 300,000,000 shares to 600,000,000 shares. At December 31, 2021 and December 31, 2020, we had 600,000,000 and 300,000,000 shares of common stock, respectively, and 10,000,000 shares of undesignated preferred stock authorized. No shares of preferred stock have been issued as of December 31, 2021 and 2020.

In April 2020, we completed an underwritten public offering of common stock generating net proceeds of approximately $53.7 million through the issuance of 25,587,500 shares of common stock at the offering price of $2.25 per share.

The following shares, in thousands, of common stock were reserved for future issuance:

	December 31,	
	2021	2020
Stock-based compensation	**28,204**	29,591
Healios Warrants to purchase common stock	**10,000**	—
	38,204	29,591

Healios Investor Rights Agreement

In March 2018, we entered into an investor rights agreement (the "Investor Rights Agreement") with Healios that governs certain of our and Healios' rights relating to its ownership of our common stock. Under the Investor Rights Agreement, Healios is permitted to participate in certain equity issuances as a means to maintain its proportionate ownership of our common stock as of the time of such issuance. In May 2020, we entered into a purchase agreement with Healios, providing for Healios to purchase shares of our common stock in connection with certain equity issuances to Aspire Capital. Healios purchased 310,526 shares of our common stock at $1.72 per share for an aggregate purchase price of $0.5 million, in accordance with the terms of the Investor Rights Agreement.

Under the Investor Rights Agreement, we further agreed that during such time as Healios beneficially owns more than 5.0% but less than 15.0% of our outstanding common stock, our Board of Directors (the "Board") will nominate a Healios nominee suitable to us to become a member of the Board, and during such time as Healios beneficially owns 15.0% or more of our outstanding common stock, our Board will nominate two suitable Healios nominees to become members of the Board, at each annual election of directors. Healios nominated an individual to the Board, who was elected at the 2018 annual stockholders' meeting. As a result of Healios' investment, Healios became a related party, and the transactions with Healios are separately identified within these financial statements as related party transactions.

In connection with the Framework Agreement, Healios agreed to terminate its existing right under the Investor Rights Agreement to nominate two nominees for election to the Board, if Healios beneficially owned 15.0% or more of our outstanding shares of common stock. Healios retains the right to appoint one nominee for election to the Board if Healios beneficially owns 5.0% or more of our outstanding shares of common stock.

Healios Warrants

In March 2018, we issued to Healios a warrant to purchase up to 20,000,000 shares of our common stock (the "2018 Warrant"). Based upon the terms of the 2018 Warrant as amended in June 2018, it was no longer exercisable for up to 16,000,000 warrant shares as of June 2019. In March 2020, Healios elected to exercise the 2018 Warrant in full, and we issued 4,000,000 shares of our common stock at an exercise price equal to the reference price of $1.76 per share, as defined in the 2018 Warrant. Proceeds of approximately $7.0 million were received in April 2020 in accordance with the terms of the 2018 Warrant.

In August 2021, we issued the 2021 Warrants to purchase up to an aggregate of 10,000,000 shares of our common stock. One of the 2021 Warrants is for the purchase of up to 3,000,000 shares at an exercise price of $1.80 per share, subject to specified increases, and generally is only exercisable within 60 days of receipt of either conditional or full marketing approval from the Pharmaceuticals and Medical Devices Agency in Japan (the "PMDA") for the intravenous administration of MultiStem to treat patients who are suffering from acute respiratory distress syndrome. The other 2021 Warrant is for the purchase of up to 7,000,000 shares at an exercise price of $2.40 per share, subject to specified increases, and generally is only exercisable within 60 days of receipt of either conditional or full marketing approval from the PMDA for the intravenous administration of MultiStem to treat patients who are suffering from ischemic stroke. The 2021 Warrants may be terminated by us under certain conditions and have an exercise cap triggered at Healios' ownership of 19.9% of our common stock.

Equity Purchase Agreement

We have had equity purchase agreements in place since 2011 with Aspire Capital that provide us the ability to sell shares to Aspire Capital from time to time. Currently, we have an agreement with Aspire Capital that was entered into in June 2021 (the "2021 Equity Facility") and includes Aspire Capital's commitment to purchase up to an aggregate of $100.0 million of shares of our common stock over a defined timeframe. The terms of the 2021 Equity Facility are similar to the previous equity facilities with Aspire Capital, and we filed a registration statement for the resale of 40,000,000 shares of our common stock in connection with the 2021 Equity Facility. Our prior equity facility that was entered into in 2019 (the "2019 Equity Facility") was fully utilized and terminated during the third quarter of 2021.

During the years ended December 31, 2021, 2020 and 2019, we sold 40,031,000, 11,425,000 and 14,475,000 shares, respectively, to Aspire Capital at average prices of $1.61, $1.67 and $1.41 per share, respectively.

H. Stock-Based Compensation

Our 2019 Equity and Incentive Compensation Plan (the "EICP") authorized at inception an aggregate of approximately 19,000,000 shares of common stock for awards to employees, directors and consultants. The EICP was approved in June 2019 and replaced our prior long-term incentive plans. The EICP authorizes the issuance of stock-based compensation in the form of stock options, stock appreciation rights, restricted stock, restricted stock units, performance shares and units, and other stock-based awards. As of December 31, 2021, a total of 8,933,420 shares (including 282,365 shares related to an expired incentive plan) of common stock have been issued under our equity incentive plans.

In June 2020, we modified option awards granted under the EICP and our prior equity plans for all then-current employees and directors by providing an extension to the period of time during which vested stock options can be exercised, subject to certain tenure-related conditions being met. The modification was applied to all then-outstanding nonqualified stock option awards outstanding on the modification date and to those incentive stock options held by individuals who accepted the modification. Following evaluation of the modification of the stock option awards, we recorded stock compensation expense of $1.2 million for the incremental value of stock option awards vested prior to the modification date. The remaining incremental value of $0.5 million determined at the modification date associated with the unvested stock option awards is being recognized over the remaining vesting period of these modified stock option awards.

As of December 31, 2021, a total of 3,176,331 shares were available for issuance under our EICP, and stock-based awards representing 24,028,092 shares (including 820,478 shares related to an expired incentive plan) of common stock were outstanding. Additionally, inducement stock options granted outside of our equity incentive plans to purchase 1,000,000 shares of common stock were outstanding at December 31, 2021. We recognized $8.6 million, $7.4 million and $4.9 million of stock-based compensation expense in 2021, 2020 and 2019, respectively.

Stock Options

The weighted average fair value of options granted in 2021, 2020 and 2019 was $1.13, $1.50 and $1.00 per share, respectively. The total fair value of options vested during 2021, 2020 and 2019 was $4.8 million, $3.5 million and $3.0 million, respectively. The total intrinsic value of options exercised was not significant during the years ended December 31, 2021 and 2019, respectively, and $0.7 million during the year ended December 31, 2020. At December 31, 2021, total unrecognized estimated compensation cost related to unvested stock options was approximately $8.6 million, which is expected to be recognized by the end of 2025 using the straight-line method. The weighted average contractual life of unvested options at December 31, 2021 was 9.0 years. The aggregate intrinsic value of fully vested and exercisable option shares and option shares expected to vest as of December 31, 2021 not significant.

A summary of our stock option activity and related information is as follows:

	Number of Options	Weighted Average Exercise Price
Outstanding January 1, 2019	10,955,508	$ 1.87
Granted	3,402,608	1.55
Exercised	(48,152)	1.40
Forfeited / Expired	(334,293)	2.71
Outstanding December 31, 2019	13,975,671	1.77
Granted	5,213,168	2.44
Exercised	(362,351)	1.70
Forfeited / Expired	(676,079)	2.32
Outstanding December 31, 2020	18,150,409	1.95
Granted	**6,240,204**	**1.81**
Exercised	**(89,041)**	**1.77**
Forfeited / Expired	**(1,258,537)**	**2.21**
Outstanding December 31, 2021	**23,043,035**	**$ 1.91**
Vested during 2021	**3,824,722**	**$ 1.99**
Vested and exercisable at December 31, 2021	**14,808,108**	**$ 1.88**

	December 31, 2021					
	Options Outstanding			Options Vested and Exercisable		
Exercise Price	Number of Options	Weighted Average Remaining Contractual Life	Weighted Average Exercise Price	Number of Options	Weighted Average Remaining Contractual Life	Weighted Average Exercise Price
$1.00 - $1.55	8,005,583	5.4 years	$ 1.49	6,072,826	4.1 years	$ 1.45
$1.56 - $2.17	8,196,562	6.7 years	$ 1.82	3,260,020	2.9 years	$ 1.74
$2.19 - $3.57	6,840,890	4.4 years	$ 2.51	5,475,262	3.4 years	$ 2.43
	23,043,035			**14,808,108**		

Restricted Stock Units

A summary of our restricted stock unit activity and related information is as follows:

	Number of Restricted Stock Units	Weighted Average Fair Value
Unvested January 1, 2019	1,656,688	$ 1.93
Granted	1,350,150	1.55
Vested-common stock issued	(938,311)	1.87
Forfeited	(36,347)	1.69
Unvested December 31, 2019	2,032,180	1.71
Granted	1,553,671	2.76
Vested-common stock issued	(1,087,718)	1.98
Forfeited	(124,127)	1.95
Unvested December 31, 2020	2,374,006	2.26
Granted	**1,254,399**	**1.63**
Vested-common stock issued	**(1,287,383)**	**2.10**
Forfeited	**(355,965)**	**2.31**
Unvested December 31, 2021	**1,985,057**	**$ 1.97**
Vested/Issued cumulative at December 31, 2021	**7,883,277**	**$ 1.84**

The total fair value of restricted stock units vested during 2021, 2020 and 2019 was $2.7 million, $2.2 million and $1.8 million, respectively. At December 31, 2021, total unrecognized estimated compensation cost related to unvested restricted stock units was approximately $3.8 million, which is expected to be recognized by the end of 2025 using the straight-line method.

I. Income Taxes

At December 31, 2021, we had U.S. federal net operating loss and research and development tax credit carryforwards of approximately $326.3 million and $20.6 million, respectively. Included in our federal net operating loss as of December 31, 2021 are federal net operating loss carryforwards generated after 2017 of $189.7 million that have an indefinite life, but with usage limited to 80% of taxable income in any given year. The remaining federal net operating losses and tax credits will expire at various dates between 2032 and 2041. We also had foreign net operating loss carryforwards of approximately $31.7 million. Such foreign net operating loss carryforwards do not expire. We also had state and city net operating loss carryforwards aggregating approximately $118.7 million. Such state and city net operating loss carryforwards may be used to reduce future taxable income and tax liabilities and will expire at various dates between 2022 and 2041. Certain state net operating losses do not expire.

The utilization of net operating loss and tax credit carryforwards generated prior to October 2012 (the “Section 382 Limited Attributes”) is substantially limited under Section 382 of the Internal Revenue Code of 1986, as amended, (the “IRC”). We generated U.S. federal net operating loss carryforwards of $289.6 million, research and development tax credits of $20.6 million, and state and local net operating loss carryforwards of $118.5 million since 2012. We will update our analysis under Section 382 prior to using these attributes.

A reconciliation of the federal statutory income tax rate to our effective tax rate is as follows:

	Percent of Income before Income Taxes	
	2021	2020
Statutory federal income tax rate	**21.0 %**	21.0 %
State income taxes - net of federal tax benefit	**1.0 %**	0.9 %
Other permanent differences	**(2.1)%**	(1.4)%
Valuation allowances	**(24.8)%**	(25.5)%
Research and development - U.S.	**4.9 %**	5.0 %
Effective tax rate for the year	**— %**	— %

Significant components of our deferred tax assets and liabilities are as follows (in thousands):

	December 31,	
	2021	2020
Deferred tax assets:		
Net operating loss carryforwards	**$ 79,473**	$ 61,670
Research and development credit carryforwards	**20,587**	16,308
Operating lease liabilities	**1,918**	146
Compensation expense	**3,336**	2,752
Other	**2,618**	3,534
Total deferred tax assets before valuation allowance	**107,932**	84,410
Valuation allowance for deferred tax assets	**(106,186)**	(84,255)
Net deferred tax assets after valuation allowance	**1,746**	155
Deferred tax liabilities:		
Right-of-use asset	**(1,746)**	(155)
Total deferred tax liabilities	**(1,746)**	(155)
Net deferred tax assets	**$ —**	$ —

Because of our cumulative losses, substantially all the deferred tax assets have been fully offset by a valuation allowance. We have not paid income taxes for the three-year period ended December 31, 2021.

We file income tax returns with the Internal Revenue Service ("IRS") and certain other taxing jurisdictions. We are subject to income tax examinations by the IRS and by state tax authorities until the net operating losses are settled.

J. Profit Sharing and 401(k) Plan

We have a profit sharing and 401(k) plan that covers substantially all employees and allows for discretionary contributions by us. We make employer contributions to this plan, and the expense was approximately $0.6 million, $0.5 million and $0.4 million in 2021, 2020 and 2019, respectively.

K. Leasing Arrangements

As of December 31, 2021, ROU assets were $9.0 million and lease liabilities were $9.8 million. As of December 31, 2020 and 2019, ROU assets were $0.6 million and $0.7 million, and lease liabilities were $0.7 million and $0.7 million, respectively. The weighted-average remaining term for lease contracts was 8.9 years at December 31, 2021, 1.5 years at December 31, 2020 and 1.6 years at December 31, 2019. As of December 31, 2021, maturities ranged from 15 months to 114 months. The weighted-average discount rate was 8.8% at December 31, 2021, 5.0% at December 31, 2020, and 5.3% at December 31, 2019. We paid $1.3 million, $0.5 million and $0.5 million for operating leases included in the measurement of lease liabilities during the year ended December 31, 2021, 2020 and 2019, respectively.

Warehouse Lease Agreement

In January 2021, we entered into an operating lease agreement to lease approximately 214,000 square feet of warehouse and office space. The initial lease term is approximately ten years and includes five renewal options with terms of five years each. The lease commenced on May 1, 2021, upon us taking control of the warehouse and office space on that date. Base annual rent

for the first year is approximately $1.3 million with 2.0% annual rent escalators. As of the lease commencement date, the right-of-use asset and corresponding operating lease liability was approximately $9.2 million, which represented the present value of remaining lease payments over the initial lease term, using an incremental borrowing rate of 9.0%. The terms of the lease agreement also include an allowance in the amount of $0.7 million for the cost of construction of office and laboratory space, some of which was completed as of December 31, 2021. We are also obligated to pay certain variable expenses separately from the base rent, including utilities, real estate taxes and common area maintenance. Such costs and have been excluded from the calculation of the right-of-use asset and corresponding operating lease liability and are being expensed in the period they are incurred.

Lease Costs

The table below presents certain information related to the lease costs (in thousands) for operating leases as of December 31, 2021, 2020 and 2019:

	Twelve months ended December 31,		
	2021	**2020**	**2019**
Operating lease cost	$ 1,458	$ 516	$ 487
Short-term lease cost	134	111	61
Variable lease cost [(1)]	7,113	1,321	205
Total lease cost	**$ 8,705**	**$ 1,948**	**$ 753**

[(1)] Includes lease components from our third-party manufacturing agreements.

Undiscounted Cash Flows

The following table summarizes future maturities (in thousands) for operating lease liabilities as of December 31, 2021:

2022	$ 1,927
2023	1,566
2024	1,390
2025	1,404
2026	1,432
2027 and beyond	6,803
Total minimum lease payments	14,522
Less: amount of lease payments representing interest	4,756
Present value of operating lease liabilities	**$ 9,766**

L. Quarterly Financial Data (unaudited)

The following table presents quarterly data for the years ended December 31, 2021 and 2020, in thousands, except per share data:

	2021				
	First Quarter	Second Quarter	Third Quarter	Fourth Quarter	Full Year
Revenues	**$ —**	**$ —**	**$ 4,792**	**$ 722**	**$ 5,514**
Loss from operations	**(26,589)**	**(22,572)**	**(16,222)**	**(21,675)**	**(87,058)**
Net loss	**(26,468)**	**(22,599)**	**(16,177)**	**(21,711)**	**(86,955)**
Basic and diluted net loss per common share (1)	**$ (0.13)**	**$ (0.10)**	**$ (0.07)**	**$ (0.09)**	**$ (0.39)**

	2020				
	First Quarter	Second Quarter	Third Quarter	Fourth Quarter	Full Year
Revenues	$ —	$ 84	$ 86	$ 1,270	$ 1,440
Loss from operations	(15,759)	(18,337)	(22,318)	(21,918)	(78,332)
Net loss	(15,644)	(18,372)	(22,543)	(22,206)	(78,765)
Basic and diluted net loss per common share (1)	$ (0.10)	$ (0.10)	$ (0.11)	$ (0.11)	$ (0.42)

(1) Due to the effect of quarterly changes to outstanding shares of common stock and weightings, the annual loss per share will not necessarily equal the sum of the respective quarters.

M. Subsequent Events

On January 20, 2022, we announced that the Board appointed Daniel A. Camardo to the Board and also named Mr. Camardo as the Company's Chief Executive Officer, each effective as of February 14, 2022. In connection with Mr. Camardo's appointment to Chief Executive Officer, the Company and Mr. Camardo entered into an employment agreement ("the Employment Agreement"). The Employment Agreement provides for an initial annual base salary of $0.6 million, a cash signing bonus of $0.3 million and annual cash incentive compensation with a target opportunity equal to 60% of Mr. Camardo's annual base salary subject to Company performance, as well as participation in our equity award program, severance and other standard employment benefits. As an inducement to Mr. Camardo's acceptance of employment with us, Mr. Camardo was granted an initial equity award that is intended to be an inducement award ("the Inducement Award") of a stock option award to purchase 10,000,000 shares of our common stock at a per share exercise price of $0.86. With regard to 4,000,000 shares, vesting of the Inducement Award will occur over a four-year period, with 25% of such portion of the award generally vesting on the first anniversary of the grant date and the remainder generally vesting monthly in substantially equal installments over the remaining 36 months. With regard to 6,000,000 shares, vesting of the Inducement Award will generally occur upon achievement of certain Company milestones, including FDA manufacturing process and marketing approvals, cumulative product sales, and business development and fundraising activities, as and when reasonably evaluated and determined by the Board in its sole discretion. The Inducement Award has up to a 10-year term.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

Not applicable.

ITEM 9A. CONTROLS AND PROCEDURES

Evaluation of disclosure controls and procedures: An evaluation was carried out under the supervision and with the participation of our management, including our principal executive officer and our principal financial officer, of the effectiveness of our disclosure controls and procedures as of the end of the period covered by this Annual Report on Form 10-K. Based on that evaluation, these officers have concluded that as of December 31, 2021, our disclosure controls and procedures are effective.

Management's report on internal control over financial reporting: Management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Exchange Act Rule 13a-15(f). Under the supervision and with the participation of management, including our principal executive officer and principal financial officer, we conducted an evaluation of the effectiveness of internal control over financial reporting based on the 2013 framework in Internal Control — Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on this evaluation under the 2013 framework in Internal Control — Integrated Framework, management concluded that our internal control over financial reporting was effective as of December 31, 2021.

Changes in internal control: During the fourth quarter of 2021, there has been no change in our internal control over financial reporting that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

On March 5, 2022, the Board of Directors of the Company, based upon the recommendation of the Compensation Committee of the Board of Directors of the Company, approved a cash bonus incentive plan (the "Plan") for the year ending December 31, 2022 for the named executive officers of the Company. The Plan provides that each participant is eligible to earn a bonus during the award term of January 1, 2022 through December 31, 2022. The Plan provides for the following target bonus percentages of the named executive officer's salary during the award term, payout being solely based on the achievement of specified corporate goals. The corporate goals include advancing the Company's clinical programs for MultiStem and manufacturing process development initiatives, executing against the established operating plan and capital acquisition objectives. There is no formally adopted plan document for the Plan.

Title	Target Bonus
Chief Executive Officer	60 %
President & Chief Operating Officer	45 %
Executive Vice President & Chief Scientific Officer	45 %
Chief Financial Officer	40 %

A summary of the plan is attached to this Annual Report on Form 10-K as Exhibit 10.27 and is hereby incorporated herein by reference thereto.

ITEM 9C. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS

Not applicable.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The information required by this item is incorporated by reference to the Proxy Statement with respect to the 2022 Annual Meeting of Stockholders.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this item is incorporated by reference to the Proxy Statement with respect to the 2022 Annual Meeting of Stockholders.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED SHAREHOLDER MATTERS

EQUITY COMPENSATION PLAN INFORMATION

The following table sets forth certain information regarding the Company's equity compensation plans as of December 31, 2021, unless otherwise indicated.

Plan Category	Number of securities to be issued upon exercise of outstanding awards	Weighted-average exercise price of outstanding awards	Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a))
	(a) (1)	(b) (2)	(c) (1)
Equity compensation plan approved by security holders	23,207,614	$ 1.77	3,176,331
Equity compensation plan not approved by security holders (3)	820,478	$ 1.49	—
Total	24,028,092		3,176,331

(1) Included in column (a) and (c) are both stock option and RSU awards under our equity compensation plans.

(2) Reflects the weighted-average exercise price of outstanding stock options only, as opposed to RSUs that do not have an exercise price. The weighted average exercise price of all outstanding stock option awards under our plans is $1.94 and the weighted average remaining term is 5.47 years.

(3) The shares of common stock included in this plan category are issuable pursuant to outstanding awards under the Athersys, Inc. Equity Incentive Compensation Plan. This plan expired on June 8, 2017; therefore, no new awards can be issued under this plan.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

The information required by this item is incorporated by reference to the Proxy Statement with respect to the 2022 Annual Meeting of Stockholders.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

The information required by this item is incorporated by reference to the Proxy Statement with respect to the 2022 Annual Meeting of Stockholders.

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

(a)(1) Financial Statements:

The following consolidated financial statements of Athersys, Inc. are included in Item 8:

Report of Independent Registered Public Accounting Firm

Consolidated Balance Sheets as of December 31, 2021 and 2020

Consolidated Statements of Operations and Comprehensive Loss for each of the years ended December 31, 2021, 2020 and 2019

Consolidated Statements of Stockholders' Equity for each of the years ended December 31, 2021, 2020 and 2019

Consolidated Statements of Cash Flow for each of the years ended December 31, 2021, 2020 and 2019

Notes to Consolidated Financial Statements

(a)(2) Financial Statement Schedules:

All schedules are not required under the related instructions or are not applicable and, therefore, omitted.

(a)(3) Exhibits.

Exhibit No.	Exhibit Description
3.1	Certificate of Incorporation of Athersys, Inc., as amended as of June 20, 2013 (incorporated herein by reference to Exhibit 3.1 to the registrant's Quarterly Report on Form 10-Q (Commission No. 001-33876) filed with the Commission on May 8, 2019)
3.2	Certificate of Amendment to Certificate of Incorporation of Athersys, Inc., as amended as of June 7, 2017 (incorporated herein by reference to Exhibit 3.1 to the registrant's Quarterly Report on Form 10-Q (Commission No. 001-33876) filed with the Commission on August 9, 2017)
3.3	Bylaws of Athersys, Inc., as amended and restated as of March 13, 2019 (incorporated herein by reference to Exhibit 3.1 to the registrant's Current Report on Form 8-K (Commission No. 001-33876) filed with the Commission on March 14, 2019)
3.4	Certificate of Amendment to Certificate of Incorporation of Athersys, Inc., as amended, effective as of June 16, 2021 (incorporated herein by reference to Exhibit 3.3 to the registrant's Registration Statement on Form S-3 (Commission No. 333-257409) filed with the Commission on June 25, 2021).
4.1	Description of the Registrant's Securities Registered Pursuant to Section 12 of the Securities Exchange Act of 1934 (incorporated herein by reference to Exhibit 4.3 to the registrant's Annual Report on Form 10-K (Commission No. 001-33876) filed with the Commission on March 16, 2020)
4.2	Common Stock Purchase Warrant (ARDS) issued to HEALIOS K.K. by Athersys, Inc. dated August 5, 2021 (incorporated herein by reference to Exhibit 4.1 to the registrant's Quarterly Report on Form 10-Q (Commission No. 001-33876) filed with the Commission on November 15, 2021)
4.3	Common Stock Purchase Warrant (Ischemic Stroke) issued to HEALIOS K.K. by Athersys, Inc. dated August 5, 2021 (incorporated herein by reference to Exhibit 4.2 to the registrant's Quarterly Report on Form 10-Q (Commission No. 001-33876) filed with the Commission on November 15, 2021)
10.1*	Research Collaboration and License Agreement, dated as of December 8, 2000, by and between Athersys, Inc. and Bristol-Myers Squibb Company (incorporated herein by reference to Exhibit 10.1 to the registrant's Current Report on Form 8-K (Commission No. 000-52108) filed with the Commission on June 14, 2007)
10.2*	Cell Line Collaboration and License Agreement, dated as of July 1, 2002, by and between Athersys, Inc. and Bristol-Myers Squibb Company (incorporated herein by reference to Exhibit 10.2 to the registrant's Current Report on Form 8-K/A (Commission No. 000-52108) filed with the Commission on September 27, 2007)
10.3	Amendment No. 1 to Cell Line Collaboration and License Agreement, dated as of January 1, 2006, by and between Athersys, Inc. and Bristol-Myers Squibb Company (incorporated herein by reference to Exhibit 10.36 to the registrant's Current Report on Form 8-K (Commission No. 000-52108) filed with the Commission on June 14, 2007)
10.4*	Extended Collaboration and License Agreement, dated as of January 1, 2006, by and between Athersys, Inc. and Bristol-Myers Squibb Company (incorporated herein by reference to Exhibit 10.3 to the registrant's Current Report on Form 8-K/A (Commission No. 000-52108) filed with the Commission on September 27, 2007)
10.5	Amendment dated as of March 31, 2009 to the Extended Collaboration and License Agreement, by and between Athersys, Inc. and Bristol-Myers Squibb Company effective January 1, 2006 (incorporated herein by reference to Exhibit 10.1 to the registrant's Current Report on Form 8-K (Commission No. 001-33876) filed with the Commission on April 9, 2009)
10.6	Amendment No. 3 to Extended Collaboration and License Agreement, dated January 31, 2012, by and between ABT Holding Company and Bristol-Myers Squibb Company (incorporated by reference to Exhibit 10.3 to the registrant's Quarterly Report on Form 10-Q (Commission No. 001-33876) filed with the Commission on May 14, 2012)
10.7†	Athersys, Inc. Equity Incentive Compensation Plan (incorporated herein by reference to Exhibit 10.11 to the registrant's Current Report on Form 8-K (Commission No. 000-52108) filed with the Commission on June 14, 2007)
10.8†	Form Incentive Agreement by and between Advanced Biotherapeutics, Inc. and named executive officers, and acknowledged by Athersys, Inc. and ReGenesys, LLC (incorporated herein by reference to Exhibit 10.31 to the registrant's Current Report on Form 8-K (Commission No. 000-52108) filed with the Commission on June 14, 2007)

10.9†	Form Amendment No. 1 to Incentive Agreement by and between Advanced Biotherapeutics, Inc. and named executive officers, and acknowledged by Athersys, Inc. and ReGenesys, LLC (incorporated herein by reference to Exhibit 10.32 to the registrant's Current Report on Form 8-K (Commission No. 000-52108) filed with the Commission on June 14, 2007)
10.10†	Form Amendment No. 2 to Incentive Agreement by and between Advanced Biotherapeutics, Inc. and named executive officers, and acknowledged by Athersys, Inc. and ReGenesys, LLC (incorporated herein by reference to Exhibit 10.1 to the registrant's Current Report on Form 8-K (Commission No. 001-33876) filed with the Commission on June 20, 2013)
10.11*	Exclusive License Agreement, dated as of May 17, 2002, by and between Regents of the University of Minnesota and MCL LLC, assumed by ReGenesys, LLC through operation of merger on November 4, 2003 (incorporated herein by reference to Exhibit 10.34 to the registrant's Current Report on Form 8-K (Commission No. 000-52108) filed with the Commission on June 14, 2007)
10.12	Form Indemnification Agreement for Directors, Officers and Directors and Officers (incorporated herein by reference to Exhibit 10.1 to the registrant's Current Report on Form 8-K (Commission No. 000-52108) filed with the Commission on August 6, 2007)
10.13†	Form of Incentive Stock Option Agreement (incorporated herein by reference to Exhibit 10.47 to the registrant's Annual Report on Form 10-K for the year ended December 31, 2010 (Commission No. 001-33876) filed with the Commission on March 25, 2011)
10.14†	Form of Nonqualified Stock Option Agreement for Non-Employee Directors (incorporated herein by reference to Exhibit 10.48 to the registrant's Annual Report on Form 10-K for the year ended December 31, 2010 (Commission No. 001-33876) filed with the Commission on March 25, 2011)
10.15†	Athersys, Inc. Amended and Restated 2007 Long-Term Incentive Plan (incorporated herein by reference to Exhibit 4.1 to the Company's Registration Statement on Form S-8 (Registration No. 333-212119) filed with the Securities and Exchange Commission on June 20, 2016)
10.16†	Form of Nonqualified Stock Option Agreement for Non-Employee Directors pursuant to the Athersys, Inc. Amended and Restated 2007 Long-Term Incentive Plan (Amended and Restated Effective June 16, 2011) (incorporated herein by reference to Exhibit 10.49 to the registrant's Quarterly Report on Form 10-Q (Commission No. 001-33876) filed with the Commission on May 6, 2011)
10.17†	Form of Restricted Stock Unit Agreement (incorporated herein by reference to Exhibit 10.2 to the registrant's Quarterly Report on Form 10-Q (Commission No. 001-33876) filed with the Commission on August 10, 2011)
10.18†	Form of Restricted Stock Unit Agreement (incorporated herein by reference to Exhibit 10.2 to the registrant's Current Report on Form 8-K (Commission No. 001-33876) filed with the Commission on June 20, 2013)
10.19	License Agreement by and between ABT Holding Company and HEALIOS K.K., dated as of January 8, 2016 (incorporated herein by reference to Exhibit 10.1 to the registrant's Quarterly Report on Form 10-Q (Commission No. 001-33876) filed with the Commission on May 5, 2016)
10.20	First Amendment to License Agreement, dated as of July 21, 2017, by and between ABT Holding Company and HEALIOS K.K. (incorporated herein by reference to Exhibit 10.1 to the registrant's Quarterly Report on Form 10-Q (Commission No. 001-33876) filed with the Commission on November 8, 2017)
10.21	Second Amendment to License Agreement, dated as of September 19, 2017, by and between ABT Holding Company and HEALIOS K.K. (incorporated herein by reference to Exhibit 10.2 to the registrant's Quarterly Report on Form 10-Q (Commission No. 001-33876) filed with the Commission on November 8, 2017)
10.22	Investor Rights Agreement, by and between Athersys, Inc. and HEALIOS K.K., dated as of March 13, 2018 (incorporated herein by reference to Exhibit 10.2 to the registrant's Quarterly Report on Form 10-Q (Commission No. 001-33876) filed with the Commission on May 10, 2018)
10.23 *	Collaboration Expansion Agreement, by and between Athersys, Inc. and HEALIOS K.K., dated as of June 6, 2018 (incorporated herein by reference to Exhibit 10.1 to the registrant's Quarterly Report on Form 10-Q (Commission No. 001-33876) filed with the Commission on August 9, 2018)
10.24	Amendment No. 1 to Collaboration Expansion Agreement, by and between Athersys, Inc. and HEALIOS K.K., dated as of August 31, 2018 (incorporated herein by reference to Exhibit 10.1 to the registrant's Quarterly Report on Form 10-Q (Commission No. 001-33876) filed with the Commission on November 6, 2018)
10.25	Amendment No. 2 to Collaboration Expansion Agreement, by and between Athersys, Inc. and HEALIOS K.K., dated as of December 6, 2018 (incorporated herein by reference to Exhibit 10.44 to the registrant's Annual Report on Form 10-K (Commission No. 001-33876) filed with the Commission on March 15, 2019)

10.26	Amendment No. 3 to Collaboration Expansion Agreement, by and between Athersys, Inc. and HEALIOS K.K., dated as of December 14, 2018 (incorporated herein by reference to Exhibit 10.45 to the registrant's Annual Report on Form 10-K (Commission No. 001-33876) filed with the Commission on March 15, 2019)
10.27†	Summary of Athersys, Inc. 2022 Cash Bonus Incentive Plan
10.28†	Athersys, Inc. 2019 Equity and Incentive Compensation Plan (incorporated herein by reference to Exhibit 4.4 to the registrant's Registration Statement on Form S-8 (Registration No. 333-232075) filed with the Commission on June 12, 2019)
10.29†	Form of Incentive Stock Option Agreement pursuant to the Athersys, Inc. 2019 Equity and Incentive Compensation Plan (incorporated herein by reference to Exhibit 10.2 to the registrant's Quarterly Report on Form 10-Q (Commission No. 001-33876) filed with the Commission on August 7, 2019)
10.30†	Form of Non-Qualified Stock Option Agreement pursuant to the Athersys, Inc. 2019 Equity and Incentive Compensation Plan (incorporated herein by reference to Exhibit 10.3 to the registrant's Quarterly Report on Form 10-Q (Commission No. 001-33876) filed with the Commission on August 7, 2019)
10.31†	Form of Non-Qualified Stock Option Agreement (Directors) pursuant to the Athersys, Inc. 2019 Equity and Incentive Compensation Plan (incorporated herein by reference to Exhibit 10.4 to the registrant's Quarterly Report on Form 10-Q (Commission No. 001-33876) filed with the Commission on August 7, 2019)
10.32†	Form of Restricted Stock Unit Agreement (Executives) pursuant to the Athersys, Inc. 2019 Equity and Incentive Compensation Plan (incorporated herein by reference to Exhibit 10.5 to the registrant's Quarterly Report on Form 10-Q (Commission No. 001-33876) filed with the Commission on August 7, 2019)
10.33†	Form of Restricted Stock Unit Agreement (Non-Executive) pursuant to the Athersys, Inc. 2019 Equity and Incentive Compensation Plan (incorporated herein by reference to Exhibit 10.6 to the registrant's Quarterly Report on Form 10-Q (Commission No. 001-33876) filed with the Commission on August 7, 2019)
10.34†	Offer Letter Agreement, dated as of January 9, 2020, by and between Athersys, Inc. and Ivor Macleod (incorporated herein by reference to Exhibit 10.1 to the registrant's Quarterly Report on Form 10-Q (Commission No. 001-33876) filed with the Commission on May 7, 2020).
10.35†	Employment Agreement, dated as of January 31, 2020, by and between Athersys, Inc. and Ivor Macleod (incorporated herein by reference to Exhibit 10.2 to the registrant's Quarterly Report on Form 10-Q (Commission No. 001-33876) filed with the Commission on May 7, 2020).
10.36†	Inducement Award Agreement, dated as of January 31, 2020, by and between Athersys, Inc. and Ivor Macleod (incorporated herein by reference to Exhibit 10.3 to the registrant's Quarterly Report on Form 10-Q (Commission No. 001-33876) filed with the Commission on May 7, 2020).
10.37†	Form of Incentive Stock Option Agreement pursuant to the Athersys, Inc. 2019 Equity and Incentive Compensation Plan for grants beginning in 2020 (incorporated herein by reference to Exhibit 10.1 to the registrant's Quarterly Report on Form 10-Q (Commission No. 001-33876) filed with the Commission on August 10, 2020).
10.38†	Form of Non-Qualified Stock Option Agreement pursuant to the Athersys, Inc. 2019 Equity and Incentive Compensation Plan for grants beginning in 2020 (incorporated herein by reference to Exhibit 10.2 to the registrant's Quarterly Report on Form 10-Q (Commission No. 001-33876) filed with the Commission on August 10, 2020).
10.39†	Form of Non-Qualified Stock Option Agreement (Directors) pursuant to the Athersys, Inc. 2019 Equity and Incentive Compensation Plan for grants beginning in 2020 (incorporated herein by reference to Exhibit 10.3 to the registrant's Quarterly Report on Form 10-Q (Commission No. 001-33876) filed with the Commission on August 10, 2020).
10.40†	Form of Notice of Amendment to Option Rights for Employees (incorporated herein by reference to Exhibit 10.4 to the registrant's Quarterly Report on Form 10-Q (Commission No. 001-33876) filed with the Commission on August 10, 2020).
10.41†	Form of Notice of Amendment to Option Rights for Directors (incorporated herein by reference to Exhibit 10.5 to the registrant's Quarterly Report on Form 10-Q (Commission No. 001-33876) filed with the Commission on August 10, 2020).
10.42	Cooperation Agreement, dated as of February 16, 2021, by and among Athersys, Inc. and HEALIOS K.K. and Dr. Tadahisa Kagimoto (incorporated herein by reference to Exhibit 10.1 to the registrant's Current Report on Form 8-K (Commission No. 001-33876) filed with the Commission on February 16, 2021).
10.43†	Separation Letter, dated as of February 15, 2021, by and between Athersys, Inc. and Dr. Gil Van Bokkelen (incorporated herein by reference to Exhibit 10.2 to the registrant's Current Report on Form 8-K (Commission No. 001-33876) filed with the Commission on February 16, 2021).

10.44†^	Employment Agreement, dated as of December 3, 2021, by and between Athersys, Inc. and William Lehmann.
10.45†^	Employment Agreement, dated as of December 3, 2021, by and between Athersys, Inc. and Dr. John Harrington.
10.46†^	Employment Agreement, dated as of December 3, 2021, by and between Athersys, Inc. and Ivor Macleod.
10.47†	Retention Letter, dated as of February 26, 2021 between Athersys, Inc. and Mr. William Lehmann, Jr. (incorporated herein by reference to Exhibit 10.1 to the registrant's Current Report on Form 8-K (Commission No. 001-33876) filed with the Commission on March 2, 2021)
10.48†	Retention Letter, dated as of February 26, 2021 between Athersys, Inc. and Dr. John Harrington (incorporated herein by reference to Exhibit 10.2 to the registrant's Current Report on Form 8-K (Commission No. 001-33876) filed with the Commission on March 2, 2021)
10.49†	Retention Letter, dated as of February 26, 2021 between Athersys, Inc. and Mr. Ivor Macleod (incorporated herein by reference to Exhibit 10.3 to the registrant's Current Report on Form 8-K (Commission No. 001-33876) filed with the Commission on March 2, 2021)
10.50^	Common Stock Purchase Agreement, dated as of June 24, 2021, by and between Athersys, Inc. and Aspire Capital Fund, LLC (incorporated herein by reference to Exhibit 10.1 to the registrant's Current Report on Form 8-K (Commission No. 001-33876) filed with the Commission on June 25, 2021)
10.51^	Registration Rights Agreement, dated as of June 24, 2021, by and between Athersys, Inc. and Aspire Capital Fund, LLC (incorporated herein by reference to Exhibit 10.2 to the registrant's Current Report on Form 8-K (Commission No. 001-33876) filed with the Commission on June 25, 2021).
10.52#	Comprehensive Framework Agreement for Commercial Manufacturing and Ongoing Support, by and between Athersys, Inc. and HEALIOS K.K., dated as of August 5, 2021 (incorporated herein by reference to Exhibit 10.1 to the registrant's Quarterly Report on Form 10-Q (Commission No. 001-33876) filed with the Commission on November 15, 2021)
10.53	Amendment to Cooperation Agreement, dated as of August 5, 2021, by and among Athersys, Inc. and HEALIOS K.K. and Dr. Tadahisa Kagimoto (incorporated herein by reference to Exhibit 10.2 to the registrant's Quarterly Report on Form 10-Q (Commission No. 001-33876) filed with the Commission on November 15, 2021)
10.54	Amendment to Investor Rights Agreement, by and between Athersys, Inc. and HEALIOS K.K., dated as of August 5, 2021 (incorporated herein by reference to Exhibit 10.3 to the registrant's Quarterly Report on Form 10-Q (Commission No. 001-33876) filed with the Commission on November 15, 2021)
21.1	List of Subsidiaries
23.1	Consent of Ernst & Young LLP, Independent Registered Public Accounting Firm
24.1	Power of Attorney
31.1	Certification of Daniel A. Camardo, Chief Executive Officer and Director, pursuant to SEC Rules 13a-14(a) and 15d-14(a) adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2	Certification of Ivor Macleod, Chief Financial Officer, pursuant to SEC Rules 13a-14(a) and 15d-14(a) adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1	Certification of Daniel A. Camardo, Chief Executive Officer and Director, and Ivor Macleod, Chief Financial Officer, pursuant to 18 U.S.C. Section 1350, adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101	The following materials from Athersys' Annual Report on Form 10-K for the period ended December 31, 2021, formatted in Inline XBRL (eXtensible Business Reporting Language): (i) the Condensed Consolidated Balance Sheet (ii) the Condensed Consolidated Statements of Operations and Comprehensive Loss (iii) the Condensed Consolidated Statement of Shareholders'Equity (iv) the Condensed Consolidated Statement of Cash Flows (v) Notes to Condensed Consolidated Financial Statements and (vi) document and entity information.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document and contained in Exhibit 101).

* Confidential treatment requested as to certain portions, which portions have been filed separately with the SEC.

† Indicates management contract or compensatory plan, contract or arrangement in which one or more directors or executive officers of the registrant may be participants.

Exhibits marked with an (#) exclude certain portions of the exhibit pursuant to Item 601(b)(10)(iv) of Regulation S-K. A copy of the omitted portions will be furnished to the Securities and Exchange Commission upon request.

^ Schedules and exhibits have been omitted pursuant to Item 601(a)(5) of Regulation S-K. The Company hereby undertakes to furnish on a supplemental basis a copy of any omitted schedule or exhibit upon request by the Securities and Exchange Commission.

ITEM 16. FORM 10-K SUMMARY

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized, in the city of Cleveland, State of Ohio, on March 15, 2022.

ATHERSYS, INC.

By: /s/ Daniel A. Camardo
Daniel A. Camardo

Title: Chief Executive Officer and Director

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 date indicated.

Signature	Title	Date
/s/ Daniel A. Camardo Daniel A. Camardo	Chief Executive Officer and Director (Principal Executive Officer)	March 15, 2022
/s/ Ivor Macleod Ivor Macleod	Chief Financial Officer (Principal Financial and Accounting Officer)	March 15, 2022
* John J. Harrington	Executive Vice President, Chief Scientific Officer and Director	March 15, 2022
* Hardy TS Kagimoto	Director	March 15, 2022
* Lorin J. Randall	Director	March 15, 2022
* Jack L. Wyszomierski	Director	March 15, 2022
* Ismail Kola	Chairman of the Board and Director	March 15, 2022
* Jane Wasman	Director	March 15, 2022
* Baiju R. Shah	Director	March 15, 2022
* Katherine Kalin	Director	March 15, 2022
* Kenneth Traub	Director	March 15, 2022

* Daniel A. Camardo, by signing his name hereto, does hereby sign this Form 10-K on behalf of each of the above named and designated directors of the Company pursuant to Powers of Attorney executed by such persons and filed with the Securities and Exchange Commission.

By: /s/ Daniel A. Camardo
Daniel A. Camardo
Attorney-in-fact

EXHIBIT 31.1

CERTIFICATIONS

I, Daniel A. Camardo, certify that:

1. I have reviewed this annual report on Form 10-K of Athersys, 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.

March 15, 2022

/s/ Daniel A. Camardo

Daniel A. Camardo

Chief Executive Officer and Director

EXHIBIT 31.2

CERTIFICATIONS

I, Ivor Macleod, certify that:

1. I have reviewed this annual report on Form 10-K of Athersys, 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.

March 15, 2022

/s/ Ivor Macleod

Ivor Macleod

Chief Financial Officer

EXHIBIT 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of Athersys, Inc. (the "Company") on Form 10-K for the year ended December 31, 2021, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), each of the undersigned officers of the Company certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to such officer's knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company as of the dates and for the periods expressed in the Report.

Date: March 15, 2022

/s/ Daniel A. Camardo
Name: Daniel A. Camardo
Title: Chief Executive Officer and Director

/s/ Ivor Macleod
Name: Ivor Macleod
Title: Chief Financial Officer

The foregoing certification is being furnished solely pursuant to 18 U.S.C. Section 1350 and is not being filed as part of the Report or as a separate disclosure document.

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