

## Athersys Inc. (NASDAQ/ATHX)

August 26, 2019

### BUY: Extending the Treatment Window for Stroke

Athersys has the potential to change the treatment paradigm for several indications across the neurological, inflammatory, immune and cardiovascular spaces. The company's proprietary stem cell technology, MultiStem, is in two pivotal Phase 3 trials for ischemic stroke with SPA and FDA designations.

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#### Investment Highlights

**Stroke Represents a Substantial Unmet Medical Need.** All presently available treatments for ischemic stroke (tPA & MR) require administration within a few hours of suffering from the stroke. Of those who survive, only about 10% of patients arrive at a hospital in time to receive appropriate treatment. The proprietary MultiStem cell therapy utilizes a unique mechanism of action to allow efficacious delivery up to 36 hours after the stroke, with the potential to ameliorate the resulting damage that results from the primary ischemic insult.

**A Strategic Partnership in Japan with Healios.** Since establishing a partnership in 2016, Healios has been evaluating the safety and efficacy of MultiStem in the treatment of stroke and other indications in the effort to expedite the development and commercialization of regenerative medicine in Japan. Financially, Healios provided an initial up-front cash payment of \$20M for licensing rights to the specified indications. For ischemic stroke and ARDS, Healios has obligations up to \$225M on stroke and \$360M on ARDS and other potential indications. In March 2018, Healios purchased an 8.7% equity stake in Athersys for \$21.1M. If the current Japan trial is successful, it could lead to a rapid approval in Japan where MultiStem has been granted *Sakigake designation* (priority review status).

**Two-Phase 3 Programs – One in Japan, the Other Global.** Athersys is currently enrolling patients in the U.S. pivotal trial – MASTERS-2 (N=300) and partner Healios is enrolling patients in the TREASURE (N=220) study in Japan. *See the details next page.*

**Why Do We Believe MultiStem Works?** We have analyzed the Phase 2 data in some detail. We see an extraordinarily safe therapy that does show compelling data, albeit in a post-hoc-analysis. Key to our understanding is the fact that time is brain. Beyond the 36 hours, the impact of MultiStem is limited. The data suggest that these cells can down-regulate the inflammatory response while upregulating healing. In doing so, they appear to limit the damage to the initial ischemic insult. The data is very consistent with our understanding of the mechanism of action.

**Valuation.** Our therapeutic models for MultiStem assume a probability of success (PoS) factor across the various indications. In addition to this, we also apply a 30% risk rate (r) in our Free Cash Flow to the Firm (FCFF), discounted EPS and Some-Of-The-Parts (SOP) models. Our price target is derived from these three models, equally weighting and averaged to the nearest whole number. The result is a one-year price target of \$11.00 per share. We caution ourselves that models can't predict clinical trial outcomes, but we do suggest that upon success the company is undervalued.

Current Price **\$1.40**  
 Price Target **\$11.00**

Estimates	F2019E	F2020E	F2021E
<b>Expenses (\$000s)</b>	\$ 55,618	\$ 53,500	\$ 46,615
1Q March	\$ 14,705	\$ 12,305	\$ 10,721
2Q June	\$ 14,163	\$ 12,840	\$ 11,188
3Q September	\$ 13,600	\$ 13,375	\$ 11,654
4Q December	\$ 13,150	\$ 14,980	\$ 13,052
	F2019E	F2020E	F2021E
<b>EPS (diluted)</b>	\$ (0.31)	\$ (0.31)	\$ (0.24)
1Q March	\$ (0.09)	\$ (0.08)	\$ (0.06)
2Q June	\$ (0.06)	\$ (0.08)	\$ (0.06)
3Q September	\$ (0.08)	\$ (0.07)	\$ (0.06)
4Q December	\$ (0.07)	\$ (0.08)	\$ (0.06)

EBITDA/Share (\$0.31) (\$0.31) (\$0.24)

EV/EBITDA (x) 553 553 718

#### Stock Data

52-Week Range \$1.20 - \$2.23

Shares Outstanding (mil.) 152.7

Market Capitalization (mil.) \$214

Enterprise Value (mil.) \$170

Debt to Capital 0%

Book Value/Share \$0.19

Price/Book 4.8

Average Three Months Trading Volume (K) 585

Insider Ownership 10.4%

Institutional Ownership 22.4%

Short interest (mil.) 8.7%

Dividend / Yield \$0.00/0.0%



Initiation - August 26, 2019 - Buy - Price Target \$11.00

**Trial Design Parameters:** The Europe – U.S. and Japan trials hope to prove efficacy by demonstrating a significant p-value around the primary endpoint. The US - European trial's design is almost identical to Japan's except that the primary endpoint in the U.S. trial will be a shift analysis, and the secondary endpoint will be "excellent outcomes" (Japan's trial is the opposite).

- **U.S. Primary endpoint:** A difference (p-value) in the modified Rankin Scale (mRS) shift analysis. This metric considers "disability across the full spectrum, enabling recognition of large and small improvements in disability and differences in mortality and other serious outcomes, among strokes of different severities". It is based on disability using an mRS at three months. Other parameters are consistent between the Japan and the U.S. trials such as the treatment window (18-36 hours). The key secondary endpoint (the primary endpoint in the Japan trial) is excellent outcome score (mRS  $\leq$ 1, NIHSS  $\leq$ 1 and Barthel Index  $\geq$ 95) at three months and one year. Additionally, the study will consider other measures of functional recovery, biomarker data, and clinical outcomes, including hospitalization, mortality life-threatening adverse events and post-stroke complications such as infection.
- **The trial in Japan** is a placebo-controlled, double-blind, Phase 2/3 trial testing the efficacy and safety of MultiStem in N=220 patients with ischemic cortical stroke, randomized 1:1 to either MultiStem or placebo, being conducted by Healios. The study is enrolling patients today and based on current enrollment is estimated to complete (top-line data) in late 2020, with full year results in mid-2021.
- **Two Bites at the Apple, The U.S. study.** This is a placebo-controlled, double-blinded, Phase 3 trial of MultiStem in N=300 acute ischemic cortical stroke patients randomized 1:1 to MultiStem or placebo, being conducted by Athersys. The trial enrollment is expected to complete in late 2020, with top-line results (90-day assessment), available approximately 4-5 months after the last patient is enrolled with a one-year follow-up. Since there are two assessments built in, we see two bites at the apple. A statistically significant result at 90 days sets the stage for approval but even if the result is not significant, if it is at the one-year follow-up (remember improvement between active and control, over-time, is exactly what was seen in the Phase 2 trial), we have an approvable product.
- **There are two study-design aspects that we believe are crucial in determining the probability of success for these trials.** First, the intravenous infusions of MultiStem will be given within 36 hours of the stroke diagnosis. As indicated, "time is brain" for these patients, meaning that the longer the inflammatory cascade is able to destroy cells in the patient's brain, the less likely the patient is to successfully recover from the stroke. Athersys (and Healios) have planned the study protocols to have MultiStem administered within a specific therapeutic window that was not only demonstrated to have clinical efficacy in the Phase 2 trial but is backed by years of clinical research on stroke treatment. The administration window of 18-36 hours of the stroke maximizes the impact by limiting the window to 36 hours. We note that this access window reaches 90%-95% of all stroke patients.

**Beyond Stroke, there is a Robust Pipeline.** The profile of the Multipotent Adult Progenitor cells (MAPCs) suggests applications across a variety of indications in neurological, inflammatory and immune, and cardiovascular areas. The MultiStem cells possess therapeutic benefits by exhibiting "drug-like" capabilities in immune system regulation, cell protection, and tissue repair.

**Competitive Advantage with Scalable Manufacturing.** The distinct cellular structure of the Multipotent Adult Progenitor Cells (MAPC) allows MultiStem to be commercially expanded through a proprietary manufacturing process. Once scaled, the cells can be frozen and conveniently stored in a vial for an extended period.

**Risks to our thesis, include the following:** (1) clinical trial; (2) commercial; (3) employee; (4) financial; (5) intellectual property; (6) partnership; and (7) regulatory. We review these and other risks in the risk section of this report.

**Exhibit 1. Upcoming catalysts.**

Product	Indication	Event	Timeline	Impact
MultiStem	Ischemic Stroke	MASTERS-2 pivotal trial completion	1H21	++
MultiStem	Ischemic Stroke	MASTERS-2 pivotal trial final data readout	2H21	+++
MultiStem	Ischemic Stroke	BLA Filing	2H21	++
MultiStem	Ischemic Stroke	FDA Approval (SPA, Fast Track, RMAT)	4Q21	+++
MultiStem	Ischemic Stroke	Commercial Launch	1Q22	+++
MultiStem	Hemorrhagic Stroke	Initiate a Phase 2 Study	2H20	++
MultiStem	Trauma	Phase 2 trial - receive funding from DOD and UTHealth	1H20	+
MultiStem	Trauma	Phase 2 trial - begin enrollment	1H20	+
MultiStem	AMI	Phase 2 - enrollment completion	2H20	++
MultiStem	AMI	Phase 2 - final data readout	2H20	++
MultiStem	ARDS	Phase 3 - begin enrollment for Fast Track designation	2H19	+
MultiStem	ARDS	Phase 3 - pivotal trial completion	1H21	+++

Stock Significance Scale: + of moderate importance; ++ higher level; +++ very important

Source: Company reports and Dawson James Forecasts.

**Exhibit 2. Athersys pipeline.**



Source: Athersys.

## Company Overview

Athersys is an international regenerative medicine company with headquarters in Cleveland, Ohio, and operations in Belgium and Japan. The company was established in 1995 and began publicly trading in 2007. MultiStem is an allogeneic, multipotent adult progenitor stem cell (MAPC) product harvested and expanded from healthy adult donors. MultiStem is the company's lead product. MAPCs are distinct from mesenchymal stem cells due to their ability to expand (grow) faster and stay viable through more doubling times without genetic instability, which are key factors for manufacturing at scale. During expansion, the extracted cells are grown in a particular cell culture media that drives cell potency. As a result, these cells express proteins and other factors involved in tissue repair, and immune system regulation, which Athersys believes makes them ideal for treating inflammatory and ischemic injuries. The advantage of the allogeneic "off the shelf" model is that through one donor Athersys is able to expand cells creating millions of doses that can be frozen and shipped to various hospitals and clinics, and then used on patients suffering from one of a variety of diseases. Over time the MultiStem cells are safely excreted from the body much like a normal drug.

The lead indication for MultiStem is acute ischemic stroke, where Athersys is looking to extend the therapeutic window to 36 hours from the current three to six hours. In 2015 Athersys announced its Phase 2 stroke trial had just missed its primary endpoint, a statistically negative result. The stock fell sharply, down 68% from its highs versus a gain of 11% for the XBI Biotech Index over the same year. In the retrospective analysis, it was revealed that strong efficacy signals were seen in those patients that were treated in the first 36 hours of the initial ischemic insult.

Athersys entered a partnership agreement in January 2016 with Healios, a leader in regenerative medicine in Japan. Healios recognized the high need for stroke therapy in Japan and Asia. This, combined with the fact that only ten percent or so of patients receive adequate therapy in time, translates into an opportunity in Japan to improve lives in stroke patients. Japan is one of the oldest (age quintiles) populations in the world. Through conversations with the FDA and PMDA (Japan's version of the FDA), both companies are running parallel international clinical trials for stroke based on the learnings of the prior Phase 2 study from 2015 and 16. We expect initial clinical results from the first pivotal Japanese trial, the "TREASURE" study, to come in 2H20, with full results in early to middle of 2021. The U.S./European pivotal "MASTERS-2" study should follow.

Athersys is also testing MultiStem in a number of additional inflammatory and ischemic conditions, including trauma and traumatic brain injury (TBI), acute myocardial infarction (AMI) and acute respiratory distress syndrome (ARDS). The hypothesis is that the anti-inflammatory nature of MultiStem makes it amenable to treat multiple disease states of an inflammatory origin. Athersys has completed preliminary safety and proof-of-concept studies in multiple indications including AMI, an exploratory study in ARDS as well as a Phase 2 study in Trauma with a planned study for hemorrhagic stroke and possibly traumatic brain injury (TBI) on the horizon. So, catalysts ahead include clinical readouts for these studies. We view early clinical data from Japanese partner Healios in the stroke indication as a read-through for the potential of MultiStem in the Athersys-sponsored MASTERS-2 stroke trial. While in our opinion the market is taking a wait and see approach to these indications given the high traditional failure rate and a lot of general skepticism around stem cell therapy, we see opportunity. With \$44M in cash and confirmed milestone payments from Healios through at least YE2019, we believe Athersys is well-positioned to see itself through multiple clinical catalysts that could translate into a value inflection for investors.

## Senior Management

**Gil Van Bokkelen, Ph.D., Founder, Chairman, CEO.** Dr. Van Bokkelen has served as CEO and Chairman since August 2000. He co-founded Athersys in 1995 and served as President until 2006. Dr. Van Bokkelen is the Chairman of the Board of Governors for the National Center of Regenerative Medicine. He served as Chairman of the Alliance for Regenerative Medicine from 2010 through 2012, a Washington D.C. based consortium of companies, patient advocacy groups, disease foundations, and clinical research institutions that are committed to the advancement of the field of regenerative medicine and served as ex officio from 2013 to 2014. He has served on several other boards, including the Biotechnology Industry Organization's ECS boards of directors (from 2001 to 2004, and from 2008 to present). He received his Ph.D. in Genetics from Stanford University School of Medicine, his B.A. in Economics and B.A. in Molecular Biology from the University of California at Berkeley.

**William (B.J.) Lehmann, JD.** Mr. Lehmann joined Athersys in September 2001 and has served as President and Chief Operating Officer since June 2006. Prior to that time, Mr. Lehmann was Athersys' Executive Vice President of Corporate Development and Finance from August 2002 until June 2006, when he became President and COO. From 1994 to 2001, Mr. Lehmann was with McKinsey & Company, Inc., an international consulting firm where he worked extensively with new technology and service-based business 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 Harrington, Ph.D., EVP, CSO.** Dr. Harrington co-founded Athersys in 1995 and has served as Chief Scientific Officer, Executive Vice President, and Director since its 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. During his career, he has also held positions as Amgen and Scripps Clinic. 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 School of Medicine.

**Laura K. Campbell, CPA, SVP of Finance.** Ms. Campbell joined Athersys in 1998 and has served as Senior Vice President of Finance since March 2016. Prior to joining Athersys, she was at Ernest & Young LLP for eleven years, specializing in the biotechnology sector and participating in several initial public offerings. Ms. Campbell received her B.S.B.A. from the Ohio State University.

## Investment Summary

**Bull Case.** Stroke is an unmet medical need and a multi-billion dollar opportunity. In terms of drug development, it has been a graveyard as the clinical trials are complex. No two patients have exactly the same recovery from the same stroke. The variation means the patient size of the trial must be large enough to zero out this effect to determine the efficacy signal versus the noise. Athersys ran a pretty comprehensive Phase 2 program and picked up tremendous insights into not only how Multi-stem works and effects patients but in how to run a stroke trial. We found the post-hoc analysis very compelling and certainly providing a strong basis for both the MASTERS (U.S.) and TREASURE (Japan) trials. We also know that “stem-cell” therapy is uniquely safe. Many of the prior failures in this space have been on safety, which for us is not a concern. So, the real question is, is there an efficacy benefit that can be statistically validated? We believe the answer is yes. The MASTERS-2, Phase 3 U.S. pivotal stroke trial has received a special protocol assessment (SPA), Fast Track and RMAT designations and in Japan, and with partner Healios it has received the *Sakigake designation*, which could support rapid approval. We view Healios as an ideal partner for Athersys in Japan. Successful commercialization of MultiStem in Japan provides milestones to Athersys up to \$685 million. We see MultiStem as a platform therapeutic, so success in stroke opens up multiple indications to the company. These include other inflammatory disorders such as trauma and traumatic brain injury (TBI), cardiovascular (acute myocardial infarctions or AMI- heart attacks), acute respiratory distress syndrome (ARDS) and even more over time. Given the market size and the unmet medical need of most of these indications (blockbusters), Athersys has the potential to become a very big company.

**Bear Case.** The development and commercialization of stem cell therapies have historically been regarded with a level of skepticism. Despite the unique profile of multipotent adult progenitor cells (MAPC), bears will argue that Athersys is still susceptible to the inexact science of stem cells and the variabilities associated with stroke and stroke trial outcomes. The company is largely dependent on the success of MultiStem in the stroke indication. The MASTERS-2 and TREASURE studies can be expected to continue enrollment until at least mid. 2020 for TREASURE and late 2020 for the MASTERS-2 study. Bears will argue that other catalysts are not significant, i.e., nothing else matters until these trials read-out. Bears will also argue that the basis of these trials is post-hoc analysis, which can mislead the best clinical intentions. This may explain why the company trades at what we consider to be a distressed valuation.

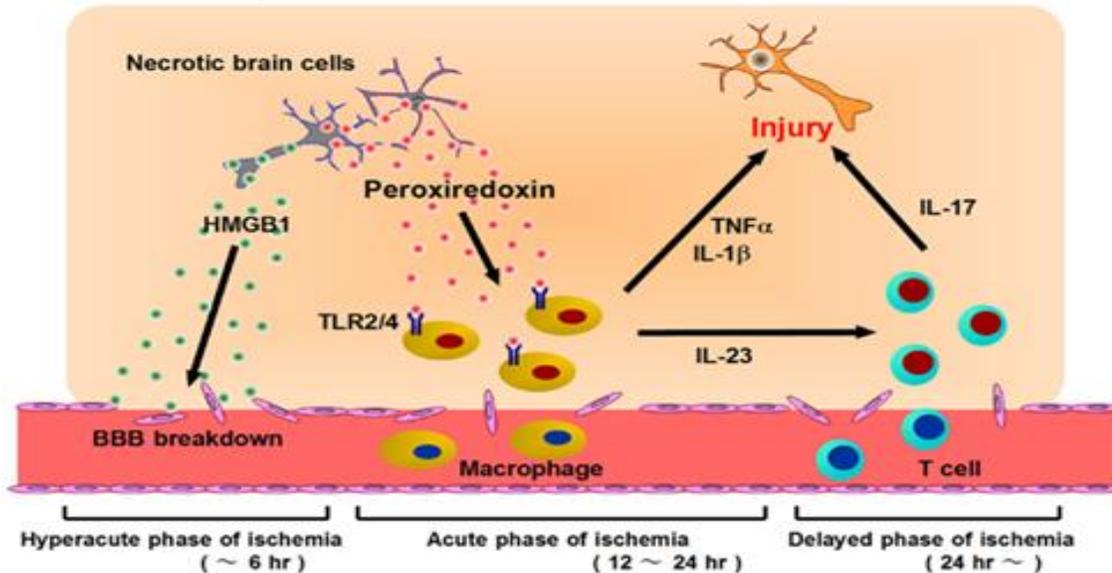
**Our Take.** Look at the data. We have done a very detailed analysis of the Phase 2 stroke trial and find the data compelling, albeit it is in the post-hoc setting. Mechanistically the data is consistent with our thinking about how MultiStem works. Time is brain. There likely is a “sweet spot” where the administration of Multi-stem has a maximum impact of preserving brain and limiting damage. Too early, and the effect may be lost in the initial inflammatory cascade. Too late, and the damage is done. It's likely that in the post-ischemic insult period, 12-36 hours when the body is reacting the insult, that MultiStem can have its maximal effect. This is precisely what the Phase 2 data has demonstrated.

We view the value of Athersys as distressed and not reflective of the current stage of MultiStem as a pivotal therapeutic with an excellent safety profile in a blockbuster market that represents a global unmet medical need. Athersys has two ongoing pivotal Phase 3 clinical trials for MultiStem in the stroke indication; we anticipate the U.S. market alone to be a multi-billion-dollar opportunity. Other indications for MultiStem, including trauma, AMI, and ARDS, could add additional blockbuster revenues to Athersys. Given the distressed valuation, we see the only significant risk as dilution. In our model, and for the sake of conservatism, we assume the company is likely to raise additional capital prior to results of the MASTERS-2 and TREASURE studies, however, the reality is that it is equally likely that Athersys will secure additional regional partnerships around its critical care portfolio in China, Europe and around the globe. At the end of 2Q19 Athersys reported \$44M in cash and depending on how the “runway” is stretched, we anticipate a year of operating capital.

**MultiStem for the treatment of stroke.** Athersys is developing MultiStem for the treatment of ischemic cortical stroke. Along with partner Healios, Athersys has two global Phase 3 trials ongoing (the TREASURE trial in Japan and MASTERS-2 trial in the U.S. and Europe). Both trials are similar in design, size and power and incorporate key lessons learned in the Phase 2 MASTERS-1 study.

**Stroke background.** A stroke occurs when blood flow to portions of the brain is blocked, due to either a blockage or hemorrhage of a vessel. The resulting ischemic cascade leads to significant inflammation and cell death. The resulting neurological deficits, which present classically as the unilateral paralysis of one side of the body, are a result of ischemia and cell death occurring in isolated portions of the brain affecting that portion of the body. In recent years it has been observed that while blood loss to the portion of the brain results in significant morbidity issues, the resulting inflammatory cascade is actually what causes the cell death and irreversible symptoms of a stroke. This is what has led to the phrase "time is brain," meaning the sooner a doctor is able to safely treat a patient, the more likely they are to produce a favorable outcome. Patients, who have been re-perfused, meaning the blockage has been removed and the brain is once again receiving oxygenated blood, often still develop significant symptoms as the newly opened vessel brings in an overabundance of immune cells, which permanently destroy damaged and healthy tissue.

**Exhibit 3. Inflammatory Cascade After Ischemic Stroke.**



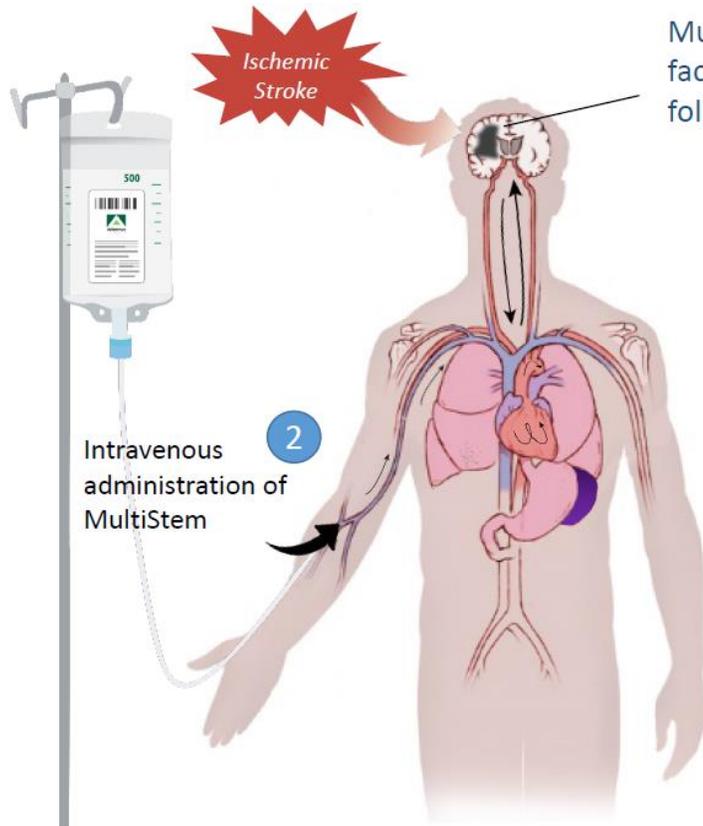
Source: Shichita et al., 2012.

**Treatment options for stroke patients.** There are only two approved options for stroke patients. The only approved drug therapy for stroke is recombinant tissue plasminogen activator (tPA). Considered the “gold standard” by the American Stroke Association, tPA works by dissolving the clot in the cerebral artery, helping to improve blood flow. Most patients must receive tPA within three to four hours of the initial ischemic stroke, as administering tPA after this period is counter-indicated as it the therapy can exacerbate any bleeding within the brain, damaging additional healthy tissue as a result of the inflammatory cascade described above. Owing to the time-dependent nature of tPA and the fact that most patients do not arrive at the hospital with stroke within the three to four-hour time frame, only a small fraction of patients, five to ten percent, are eligible for tPA and actually receive the therapy. Furthermore, tPA is only effective in 30% of patients that receive it.

The second treatment option for stroke patients is a mechanical thrombectomy, where a specialized device on a catheter is typically threaded from a patient’s groin up into his or her brain to remove the blood clot. It is advised that patients receive tPA before this procedure to aid blood flow and recovery. Mechanical thrombectomy is advantageous because it can be used up to six hours after the initial ischemic stroke, but only patients that are able to withstand the procedure are eligible, and only a minority of those patients will see a meaningful benefit.

Fortunately, approximately a third of patients with stroke have rapidly improving stroke symptoms (RISS), deeming that they do not need any therapy. Athersys and Healios as part of their pivotal trial design plans to exclude RISS patients by waiting a certain period of time (up to 18 hours) post-ischemic event, which is typically enough time to detect if a patient may spontaneously recover (RISS) before admitting patients into the trial (TREASURE or MASTERS-2). If MultiStem is approved for stroke, we see the potential for it to be used in all stroke patients, including RISS patients. According to the journal, *Stroke*, up to 30% of RISS patients never fully recover, indicating more patients should receive treatment than do. There are no approved treatments available after the six-hour window, so doctors who do not provide RISS patients any therapy run the risk of that patient never fully recovering. The MultiStem option of treatment out to 36 hours would provide doctors time to evaluate RISS patients while still allowing for treatment should the patient not continue improving.

**Exhibit 4. How Does MultiStem Work?**



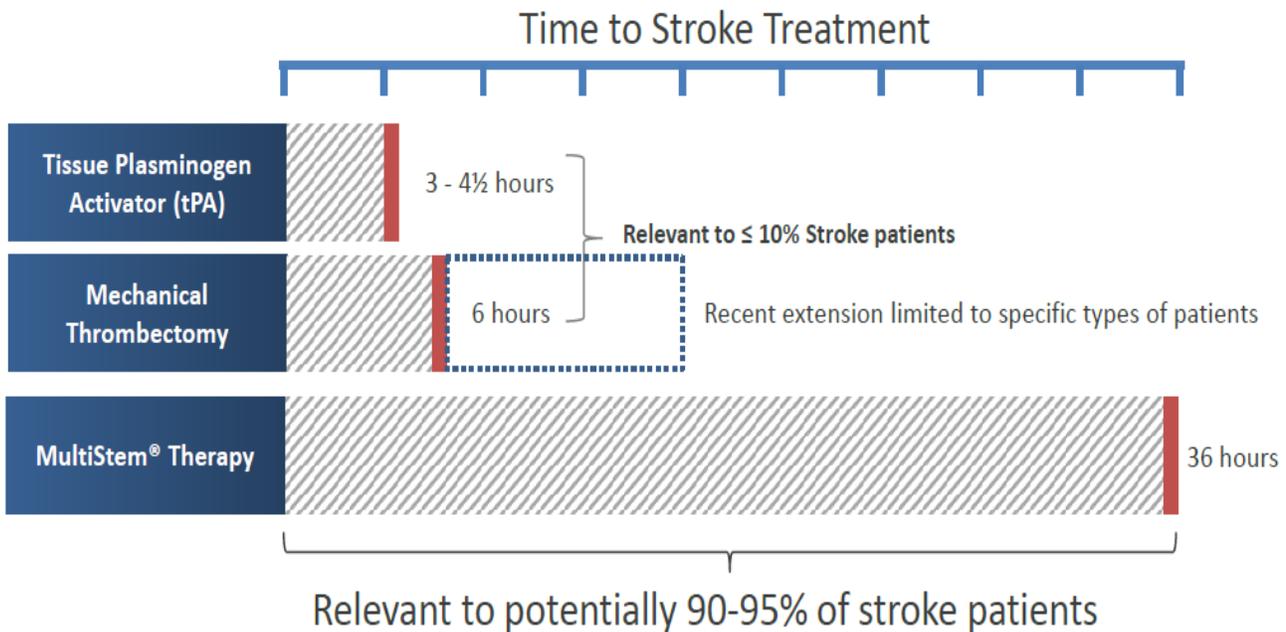
MultiStem works through regulation of multiple factors and pathways important to brain recovery following a stroke.

- 1 Inflammation after stroke leads to greater tissue loss and scarring in the brain. Immune cells coming from the spleen play a major role this response.
- 2
- 3 MultiStem cells migrate to the spleen and peripheral immune system and affect key pathways in the brain.
- 4 Simultaneous downregulation of pro-inflammatory processes and upregulation of reparative immune responses promotes recovery.

**Representative Publication in *Stem Cells* (2017):**  
 MAPC's Enhance Recovery After Stroke by Modulating the Immune Response from the Spleen

Source: Athersys.

**Exhibit 5. MultiStem Hopes to Expand the Stroke Treatment Window.**



Source: Athersys.

**The advantage of MultiStem’s MAPCs.** MultiStem is composed of multipotent adult progenitor cells (MAPCs), which have been shown to reduce inflammation in multiple preclinical disease models. As described, damage following stroke, particularly ischemic stroke, is believed to be partly a result of an inflammatory cascade in the brain that damages both ischemic and healthy tissue. MAPCs do not appear to cross the blood-brain barrier; rather, the cells appear able to exert a systemic anti-inflammatory effect without interfering with the natural healing process. For example, in preclinical stroke models, it was shown that much of the damage related to stroke can be attributed to spleen-derived immune cells; when spleens are removed, strokes are significantly less damaging. The hypothesis is that MultiStem MAPCs are able to seek out the spleen-derived inflammation and dampen the immune response, which decreases the secondary damage related to the primary ischemic insult. MAPCs are systemically delivered via an IV, allowing the cells to circulate and “home” based on signals the cells read, where they appear to then exert a trophic effect, calming the inflammatory reaction. As MAPCs are allogeneic, they can be expanded from a single source to treat multiple patients; they can be cryopreserved, and in this way are, off-the-shelf, readily available to treat patients. Athersys has said that MAPC donation from a single patient can be expanded to millions of doses. These cells can then be shipped to hospitals and clinics to be stored on-site. This is particularly advantageous for time-sensitive acute ischemic diseases such as a stroke or a heart attack.

**Preclinical data for MultiStem in stroke.** To test the thesis that MultiStem is thought to work by downregulating the immune response that results in secondary tissue damage and tissue loss in the brain, Athersys completes a series of experiments. MultiStem was administered within 48 hours of the initial ischemic event, based on the hypothesis that the inflammatory environment peaks at 72 hours. The idea was to see if MultiStem would dampen the inflammatory response through the down-regulation of certain immune cells such as CD3+ T cells and upregulation of anti-inflammatory cells such as M2 macrophages. In 2010, Athersys published the results, detailing the effects of MultiStem in a rat model of stroke. Animals received IV delivery of 400,000 to 20 million MAPC’s one to three days post-stroke and were tested every other week thereafter for eight weeks with the elevated body swing test (EBST) and Bederson tests to determine loco-motor and neurological function. There was a statistically significant dose-dependent improvement seen ( $p < 0.05$ ) in the Bederson scores (a measure of neurological impairment) in animals treated two days post-stroke, with the therapeutic benefit lasting at least 12 weeks. There was also significantly less neuronal damage ( $p < 0.05$ ) compared to control animals’ post-stroke for all rats receiving MultiStem at days one, two and seven post-stroke. In keeping with the anti-inflammatory hypothesis, genetic analysis of animals receiving MultiStem showed reductions in inflammatory marker pathways such as T-cell and lymphocyte activation, inflammatory response and myeloid leukocyte differentiation. Animals also demonstrated increases in genetic markers for neurogenesis, neuronal differentiation and nervous system development, indicating the brain may have started repairing itself post-stroke.

**MultiStem Phase 2 trial in stroke.** In discussions with the FDA, it was decided that since MultiStem had been previously evaluated in multiple other studies Phase 1 and 2 studies in indications such as ischemic cardiovascular disease, that Athersys could move forward directly to a Phase 2 study in stroke. In late 2011 Athersys began enrolling patients in a double-blind, placebo-controlled, Phase 2 study in 140 ischemic stroke patients across 33 sites in the U.S. and U.K. The trial evaluated a high dose of MultiStem (1.2 billion cells) against placebo in patients 24 to 48 hours post-stroke, with endpoints measured after 90 days of follow-up. In results published March 2017, Athersys announced the primary endpoint of Global Stroke Recovery was not met, with 31% of MultiStem-treated patients achieving the endpoint versus 25% of placebo patients. Key secondary endpoints, including modified Rankin Scale (mRS)  $\leq 2$ , NIHSS improvement of  $\geq 75\%$ , and Barthel Index scores of  $\geq 95$ , were also not met but favored MultiStem. Significant results ( $p < 0.05$ ) were seen in other secondary endpoints after one year of follow up, including patients achieving mRS 0 or 1 and patients achieving an Excellent Outcome (a composite of mRS  $\leq 1$  on a scale of 0 to 6; NIHSS  $\leq 1$  on a scale of 0 to 42; and Barthel index  $\geq 95$  on a scale of 0 to 100). The death rate was almost half in the MultiStem arm (8% vs. 15% of control patients), and fewer adverse events, hospital days, and infections for patients treated with MultiStem, which we see as indicating a positive safety profile. The FDA and EMA and PMDA (Japan) only consider Excellent Outcome and mRS shift as approvable endpoints.

**Exhibit 6. Adapted from The February 17, 2016 press release.** Following one-year post-MultiStem therapy patients continue to improve. Below in the exhibits that follow is a summary of Phase 2 data.

Proportion of Subjects with Excellent Outcome at Day 90 and Over One Year

Subjects	Day 90	Day 365
All MultiStem (n=65)	15.4 %	23.1 %
All Placebo (n=61)	6.6 %	8.2 %
Difference with all placebo	8.8 %	14.9%*
Early Treatment with MultiStem (n=31)	16.1 %	29.0 %
Difference with all placebo	9.5 %	20.8%**

\*p = 0.02, \*\*p < 0.01

Source: Athersys.

**Exhibit 7. Improvements Demonstrated One Year After MultiStem Therapy.**

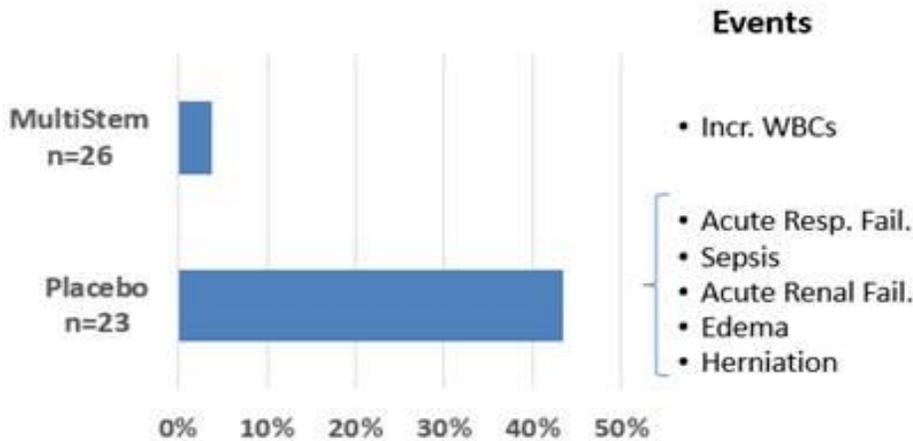
		Day 90	Δ at Day 90	Day 365	Δ at Day 365
ITT (All Subjects)	MultiStem (n=65) vs. Placebo (n=61)	15.4% vs. 6.6%	8.8%	23.1% vs. 8.2%	14.9% p = 0.02
Early MultiStem Treatment (≤36 Hrs) vs All Placebo	MultiStem (n=31) vs. Placebo (n=61)	16.1% vs. 6.6%	9.5%	29.0% vs. 8.2%	20.8% p < 0.01
Early MultiStem Treatment (≤36 hrs) vs Placebo*	MultiStem (n=27) vs. Placebo (n=52)	18.5% vs. 3.8%	14.7%	29.6% vs. 5.8%	23.8% p < 0.01

Source: Athersys.

**Exhibit 8. Phase 2 Data Results:** MultiStem appears to impact not just efficacy (cognition and motor skills) but also clearly has an impact on the normal AE profile experienced by stroke patients.

**Severe Stroke (NIHSS 15+) Subjects**

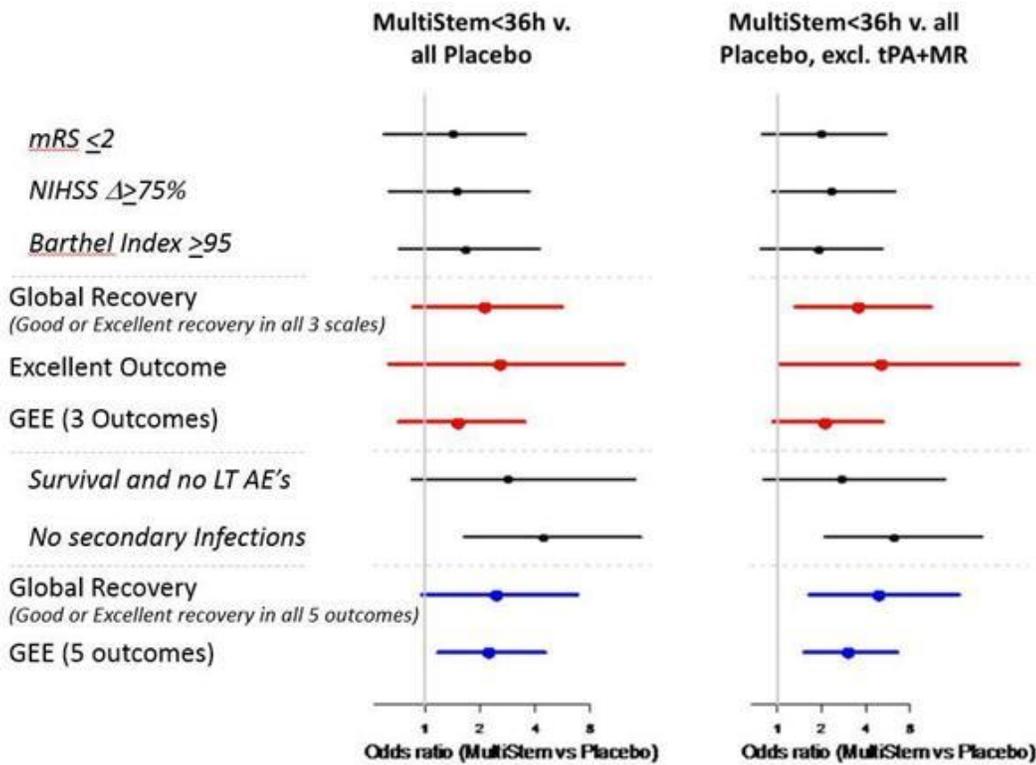
**% Subjects with Grade 3-5 Adverse Events Through Day 30**



Source: Athersys.

**Exhibit 9. Whisker Plot.** The plot shows the odds ratios for a MultiStem-related treatment effect for the outcomes indicated. Numbers greater than 1 are in favor of MultiStem. Each horizontal line represents the 95% confidence interval.

This figure below includes three pre-specified secondary endpoints - modified Rankin Score  $\leq 2$  (disability measure), NIH stroke scale (NIHSS) delta  $\geq 75\%$  (neurological deficit), and Barthel Index  $\geq 95\%$  (activities of daily living) at 90 days following the stroke - and the pre-specified primary endpoint using the "generalized estimating equation (GEE)" method to calculate an integrated assessment of treatment effect between the groups using these three outcomes. An exploratory endpoint, "Global recovery," a combined dichotomous endpoint based on the simultaneous achievement of the three-component endpoints above (mRS $\leq 2$ , NIHSS delta $\geq 75\%$ , and BI $\geq 95\%$ ) is included. Excellent outcome, a combined dichotomous endpoint measuring achievement of mRS $\leq 1$ , NIHSS $\leq 1$ , and BI $\geq 95\%$  and a pre-specified secondary outcome, is also shown. Finally, two important safety outcomes are represented - survival without life-threatening adverse events and secondary infections - and all five components are evaluated together using the approaches above.



Source: Athersys.

**The Phase 3 trials.** Athersys currently has two ongoing Phase 3 trials in Japan (TREASURE) and in the U.S. and Europe (MASTERS-2). The trial in Japan is a placebo-controlled, double-blind, Phase 2/3 trial testing the efficacy and safety of MultiStem in 220 patients with ischemic cortical stroke, randomized 1:1 to either MultiStem or placebo, being conducted by Healios. The study is enrolling patients today and based on current enrollment is estimated to complete (top-line data) by 2H20. The U.S. study is a placebo-controlled, double-blinded, Phase 3 trial of MultiStem in 300 acute ischemic cortical stroke patients randomized 1:1 to MultiStem or placebo, being conducted by Athersys. The trial enrollment is expected to complete in 2H20, with study results in 2021.

There are two study-design aspects that we believe are crucial in determining the probability of success for these trials. First, the intravenous infusions of MultiStem will be given within 36 hours of the stroke diagnosis. As indicated, "time is brain" for these patients, meaning that the longer the inflammatory cascade is able to destroy cells in the patient's brain, the less likely the patient is to successfully recover from the stroke. Athersys (and Healios) have planned the study protocols to have MultiStem administered within a specific therapeutic window that was not only demonstrated to have clinical efficacy in the Phase 2 trial but is backed by years of clinical research on stroke treatment.

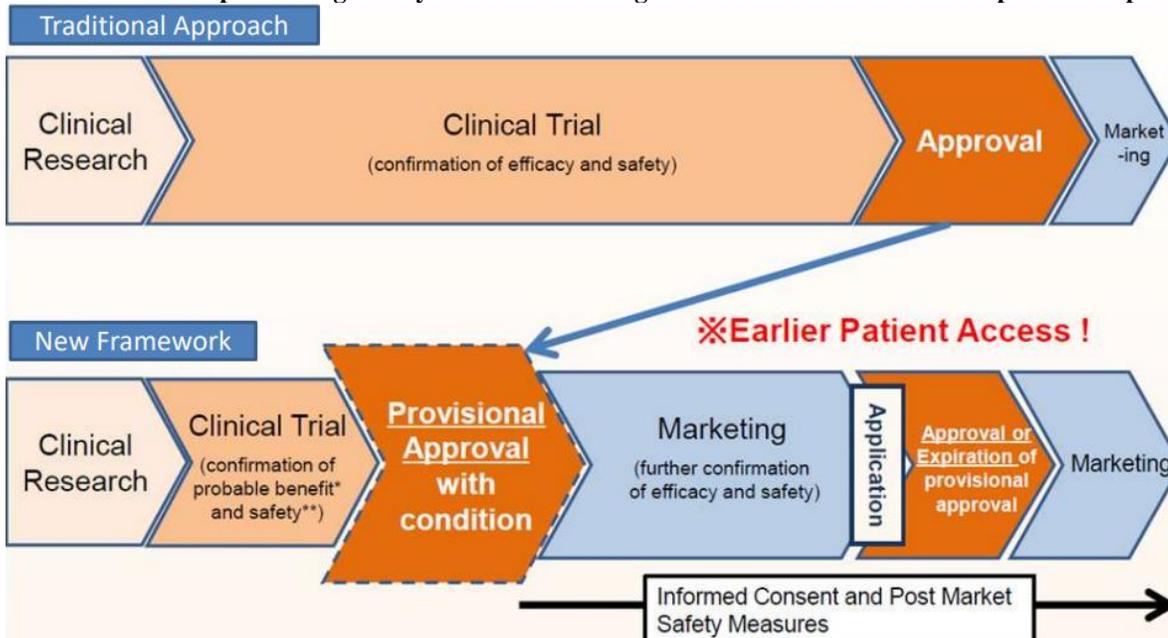
**Market opportunity.** Stroke is the third leading cause of mortality in both the U.S. and around the world. Approximately 800,000 people are victims of stroke annually in the U.S., as well as 15 million globally. The majority of these strokes (85%) are ischemic. According to the Center for Disease Control and Prevention, stroke is a leading cause of death and morbidity in the U.S., with direct costs estimated at \$38.6 billion each year. We model a 45% penetration rate in the ischemic stroke market by 2030, representing a multi-billion dollar opportunity in the U.S. alone. Our 45% penetration rate is a result of what we see as a significant unmet need in ischemic stroke, particularly after the six-hour window closes on the use of tPA or thrombectomy. We model the opportunity in the Japanese market similar to the U.S. market to better understand the potential milestone, royalties and manufacturing payments Athersys may capture from Healios. We do not include China and we have not focused on the opportunity in Europe.

**Athersys is partnered with Healios for Japan.** Healios is a Japan-based manufacturing company that carries out technical development and commercialization of regenerative medicine therapies. Through the umbrella of Healios, the company can contract with multiple smaller companies to provide scale and manufacturing in exchange for rights to developed therapies or milestone payments on sales.

**Healios' mission aligns with Athersys.** Healios is a combination of "Helios," the Greek God of the sun, and the word "heal." Healios aims to provide a "ray of light" to guide the healing of patients with intractable diseases. To do this, the company has developed a manufacturing infrastructure specific to regenerative medicines in an effort to capitalize on emerging therapies around the world. Many of the companies engaging in the development of regenerative medicine therapies are smaller in market cap and may struggle to scale, including Athersys. The opportunity for these smaller companies to partner with a relatively large (about \$700 million market cap) manufacturing company in exchange for milestone payments seems to be an easy decision, in our opinion. Both Athersys and Healios stress the importance of regenerative medicine and view the coming years as a substantial opportunity for patient healing and business growth.

**The opportunity in Japan.** As a result of Japan looking to develop more business directives around healthcare, 2014 and 2015 saw the development of two new laws and the development of a new government agency. The two laws, both passed in 2014, regulate the manufacturing and approval of regenerative medicine therapies. The first law, applicable to both Healios and Athersys, is the Pharmaceuticals and Medical Devices (PMD) Act, which created a new "regenerative medicine approval" subcategory in the Pharmaceuticals and Medical Devices Agency (PMDA). Products designated under this subcategory may be granted expedited conditional approval, where companies are able to bring therapies to market under conditional (early) approval, with full (official) approval coming later after sales have been generated (see the Exhibit that follows). The second law, more applicable to Healios, is the Act of the Safety of Regenerative Medicine (ASRM). This act sets manufacturing standards for regenerative medicine products and develops an outsourcing system for cell processing, allowing companies like Healios to produce cells for medical use where previously only hospitals and research institutes had this privilege. The combination of these two laws, coupled with Japan's national healthcare system and insurance coverage for regenerative medicine therapies, in our view, makes Japan an ideal location to launch a regenerative therapy. Athersys, we believe is additionally advantaged by having a strong, established partner in Healios that can provide "boots on the ground" to guide the regulatory development.

**Exhibit 10. New Japanese Regulatory Guidelines for Regenerative Medicines Work to Speed Therapies to Market.**



Source: Athersys.

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**Broad partnership deal established.** Athersys signed an initial contract with Healios in January 2016 for ischemic stroke in Japan, with Healios receiving access to the MAPC technology underlying MultiStem for its organ bud technology and the option for expansion in two other indications (ARDS and orthopedics) in exchange for \$15 million upfront and \$360 million in potential sales milestones. An evergreen provision was added to allow for continual expansion of the partnership into other indications. In 2016 the PMDA approved Healios' Phase 2/3 clinical trial design testing MultiStem in stroke, triggering two more partnership agreements with Athersys: in January 2017, a clinical trial supply agreement allowing Athersys to provide delivery and manufacturing services to Healios; and in September 2017 Healios agreed to provide financial support to develop an Athersys-led contract manufacturer in Japan.

In March 2018 the partnership with Healios was expanded with a "letter of intent" agreement; (1) expanding the Japanese license to include use of MultiStem in ARDS, and organ buds; (2) receiving a worldwide MultiStem license for treating certain ophthalmological indications; and (3) receiving an option to negotiate a license for MultiStem in China for ischemic stroke, ARDS, and trauma. Athersys received \$20 million with potential for an additional \$360 million in milestones and a tiered double digit royalty. Healios also purchased 12 million Athersys shares at \$1.76 for an equity investment of approximately \$21 million; Healios also received warrants expiring September 2020.

The most recent expansion of the collaboration occurred in June 2018. Healios received a global license to develop and commercialize MultiStem for certain ophthalmological indications, an expansion of the organ bud license to include additional transplantation areas, and rights of first negotiation for licensing deals in China and Japan and for iPSC combination therapies with MultiStem. Healios will also receive a \$10 million credit that may be used towards development milestones in the future. Athersys in exchange received the \$10 million guaranteed from the March 2018 agreement, plus an additional \$10 million to be paid over four quarters beginning 2Q18 and up to \$360 million in aggregate development and commercialization milestones. Royalty payments are between single and low double digits, depending on the licensed indication.

In our view, a final benefit to Athersys came when Dr. Hardy Kagimoto, CEO of Healios, was elected to the Athersys Board of Directors at the annual stockholders' meeting on June 18, 2018. The companies have moved in lockstep since early 2016, and we believe the nomination of Dr. Kagimoto to the Athersys board will further entrench the relationship and help guide the clinical path of MultiStem.

## Modeling Assumptions

1. The MultiStem program is the main platform for the company, and we view it as the driver of the company's success. We assume Athersys continues developing the MultiStem program in neurological, cardiovascular, and inflammation and immunological disease areas and that these programs, like the MultiStem platform itself, are prioritized.
2. For the stroke (neurological) indication, we model approximately 800,000 stroke patients in the U.S. and 340,000 in Japan, with 87% of those classified as ischemic, growing at a rate of 0.1% annual since 2017. By factoring in mortality risk, cortical stroke prevalence, and the effective therapeutic treatment window, we arrive at an addressable market population.
3. Hemorrhagic stroke. Success in ischemic stroke sets the stage for Athersys to develop MultiStem in the small side of the stroke market, Hemorrhagic strokes. Here too, the inflammatory response contributes to additional secondary damage. While the complexities of ischemic stroke are challenging, hemorrhagic can be even more complex and with even fewer options for patients. As such, it makes sense to develop for this indication, only after the ischemic market is realized.
4. For the ADRS (immune) indication, we model the addressable population based on the NHLI estimate figure of 70 per 100,000 in the U.S., denoting an approximate 230,000 patients in 2017 growing at 3.1% annually.
5. For the AMI (cardiovascular) indication, we only model for new heart attacks as we believe they are more likely to be amenable to the trophic and anti-inflammatory effects of MultiStem. We anticipate the annual growth rate and mortality rate quoted by the American Heart Association continue to be high, at 11.1% and 15.5%, respectively, a reflection of the increasing obesity epidemic in the U.S. Considering the lengthy nature of cardiovascular trials, we do not begin to model sales until 2022, and we currently anticipate relatively low (8-10%) peak market penetration as cell therapy is not currently a standard of care in hospitals for treating AMI.
6. For the trauma (inflammatory) indication, we model the treatable population based on a reported 2.5 million trauma-related emergency room visits. Approximately 13% of those visits are due to debilitating ailments, leading to hospitalization. The estimation brings us to over 300,000 addressable patients growing at a rate of 3.1% annually.
7. For the GVHD (inflammatory) indication, we do currently assume any revenues in our model, but we show the model as we believe, with additional resources Athersys may "down the road" re-visit development plans. The population of total U.S. allogeneic stem cell transplants based on 4,265 related and 4,972 unrelated transplants (2017 data) growing at a rate of 3.1% annually. We estimate 90% of that population to desire prophylactic treatment for GVHD.
8. We model a price for MultiStem at \$25,000 initially, growing at 1% per year. Academic literature estimates that therapies such as tPA in stroke should be priced at \$45,800 based on the quality-adjusted life years (QALY) provided to patients. In this instance, should a therapy allow for successful treatment beyond the three to six-hour therapeutic time window, the literature estimates this therapy should command a higher price. We therefore believe our pricing estimates are conservative considering our belief in the upside therapeutic potential of MultiStem. We have seen examples of other cell (for example CAR-T) and gene therapies' command prices anywhere between \$100k and \$2.5M, given the blockbuster size of the stroke market we recognize the therapy must be affordable for the market-size.
9. but are also relatively in-line with other allogeneic cell therapies currently on the market, despite the other allogeneic cell therapies not being approved for the same targeted indications.
10. Our sum-of-the-parts model uses the same probabilities as the product models and the same discount rate as the FCFF. We apply a risk factor of 70% for the trauma and AMI clinical programs as they are in earlier stages (neither beyond Phase 2) and have only been tested in a limited number of patients. We anticipate reducing this risk factor should the trials meet our assumptions of producing data in the next year. For royalties and partnerships, we also use 50% because they are dependent on a third party, Healios, and therefore do not provide transparency in terms of timing of cash flows to Athersys. Lastly, the stroke and ARDS indications have a 50% risk factor as a result of the inherent variability associated with stroke and the fact that the current pivotal programs are based on a post-hoc analysis.
11. Discount rate. We use a 30% discount rate to account for the fact that Athersys is not yet a profitable company, with assets still in clinical development and several years from commercialization. For this reason, we add an additional risk premium to the calculated WACC to arrive at our 30% discount rate.

**Exhibit 11. MultiStem Ischemic Stroke (U.S.).**

Ischemic Stroke (U.S.)	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
No. of Annual Strokes	696,000	696,696	697,393	698,090	698,788	699,487	700,186	700,887	701,588	702,289	702,991	703,694	704,398	705,102
Market Size Growth	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%
Associated Mortality	16.3%	16.3%	16.3%	16.3%	16.3%	16.3%	16.3%	16.3%	16.3%	16.3%	16.3%	16.3%	16.3%	16.3%
Ischemic Strokes Survivors	582,552	583,135	583,718	584,301	584,886	585,471	586,056	586,642	587,229	587,816	588,404	588,992	589,581	590,171
Total cortical ischemic stroke patients (35%)	203,893	204,097	204,301	204,505	204,710	204,915	205,120	205,325	205,530	205,736	205,941	206,147	206,353	206,560
Market Share Penetration	0%	0%	0%	0%	0%	5%	10%	15%	20%	25%	30%	35%	40%	45%
Number of Patients Procedures	-	-	-	-	-	29,274	58,606	87,996	117,446	146,954	176,521	206,147	235,832	265,577
Cost of Therapy	-	-	-	-	-	\$ 25,000	\$ 25,000	\$ 25,000	\$ 25,000	\$ 25,000	\$ 25,000	\$ 25,000	\$ 25,000	\$ 25,000
Risk Factor	-	-	-	-	-	50%	50%	50%	50%	50%	50%	50%	50%	50%
<b>Total Revenue ('000)</b>	-	-	-	-	-	\$ 365,919	\$ 732,570	\$ 1,099,954	\$ 1,468,072	\$ 1,836,925	\$ 2,206,514	\$ 2,576,841	\$ 2,947,906	\$ 3,319,711

Source: Dawson James estimates.

**Exhibit 12. MultiStem Ischemic Stroke (Japan).**

Ischemic Stroke (Japan)	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
No. of Annual Strokes	295,800	296,096	296,392	296,688	296,985	297,282	297,579	297,877	298,175	298,473	298,771	299,070	299,369	299,669
Market Size Growth	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%
Associated Mortality	16.3%	16.3%	16.3%	16.3%	16.3%	16.3%	16.3%	16.3%	16.3%	16.3%	16.3%	16.3%	16.3%	16.3%
Ischemic Strokes Survivors	247,585	247,832	248,080	248,328	248,576	248,825	249,074	249,323	249,572	249,822	250,072	250,322	250,572	250,823
Total cortical ischemic stroke patients (35%)	86,655	86,741	86,828	86,915	87,002	87,089	87,176	87,263	87,350	87,438	87,525	87,613	87,700	87,788
Market Share Penetration	0%	0%	0%	0%	0%	5%	10%	15%	20%	25%	30%	35%	40%	45%
Number of Patients Procedures	-	-	-	-	-	12,441	24,907	37,398	49,914	62,455	75,021	87,613	100,229	112,870
Cost of Therapy	-	-	-	-	-	\$ 25,000	\$ 25,000	\$ 25,000	\$ 25,000	\$ 25,000	\$ 25,000	\$ 25,000	\$ 25,000	\$ 25,000
Risk Factor	-	-	-	-	-	50%	50%	50%	50%	50%	50%	50%	50%	50%
<b>Japan Annual Sales</b>	-	-	-	-	-	\$ 155,516	\$ 311,342	\$ 467,480	\$ 623,931	\$ 780,693	\$ 937,769	\$ 1,095,157	\$ 1,252,860	\$ 1,410,877
Royalty to Athersys	-	-	-	-	-	8%	10%	12%	14%	15%	15%	15%	15%	15%
<b>Total Revenue ('000)</b>	-	-	-	-	-	\$ 12,441	\$ 31,134	\$ 56,098	\$ 87,350	\$ 117,104	\$ 140,665	\$ 164,274	\$ 187,929	\$ 211,632

Source: Dawson James estimates.

**Exhibit 13. MultiStem Hemorrhagic Stroke (U.S.).**

Hemorrhagic Stroke (U.S.)	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
No. of Annual Hem. Strokes (13% of total)	90,480	90,570	90,661	90,752	90,842	90,933	91,024	91,115	91,206	91,298	91,389	91,480	91,572	91,663
Market Size Growth	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%
Associated Mortality	30.0%	30.0%	30.0%	30.0%	30.0%	30.0%	30.0%	30.0%	30.0%	30.0%	30.0%	30.0%	30.0%	30.0%
Hemorrhagic Strokes Survivors	63,336	63,399	63,463	63,526	63,590	63,653	63,717	63,781	63,844	63,908	63,972	64,036	64,100	64,164
Market Share Penetration	0%	0%	0%	0%	0%	0%	0%	15%	30%	50%	55%	60%	65%	70%
Number of Patients Procedures	-	-	-	-	-	-	-	9,567	19,153	31,954	35,185	38,422	41,665	44,915
Cost of Therapy	-	-	-	-	-	-	-	\$ 25,000	\$ 25,000	\$ 25,000	\$ 25,000	\$ 25,000	\$ 25,000	\$ 25,000
Risk Factor	-	-	-	-	-	-	-	50%	50%	50%	50%	50%	50%	50%
<b>Total Revenue ('000)</b>	-	-	-	-	-	-	-	\$ 119,589	\$ 239,417	\$ 399,427	\$ 439,809	\$ 480,271	\$ 520,814	\$ 561,438

Source: Dawson James estimates.

**Exhibit 14. MultiStem Acute Respiratory Distress Syndrome (U.S.).**

Acute Respiratory Distress Syndrome (U.S.)	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
No. of Annual Cases	228,900	235,996	243,312	250,854	258,631	266,648	274,915	283,437	292,223	301,282	310,622	320,251	330,179	340,415
Market Size Growth	3.1%	3.1%	3.1%	3.1%	3.1%	3.1%	3.1%	3.1%	3.1%	3.1%	3.1%	3.1%	3.1%	3.1%
Market Share Penetration	-	-	0.0%	0.0%	0.0%	1%	2%	3%	4%	5%	6%	7%	8%	9%
Number of Patients Procedures	-	-	-	-	-	2,666	5,498	8,503	11,689	15,064	18,637	22,418	26,414	30,637
Cost of Therapy	-	-	-	-	-	\$ 25,000	\$ 25,000	\$ 25,000	\$ 25,000	\$ 25,000	\$ 25,000	\$ 25,000	\$ 25,000	\$ 25,000
Risk adjustment	-	-	-	-	-	50%	50%	50%	50%	50%	50%	50%	50%	50%
<b>Total Revenue ('000)</b>	-	-	-	-	-	\$ 33,331	\$ 68,729	\$ 106,289	\$ 146,112	\$ 188,302	\$ 232,967	\$ 280,220	\$ 330,179	\$ 382,967

Source: Dawson James estimates.

**Exhibit 15. MultiStem Acute Myocardial Infarction (U.S.).**

Acute Myocardial Infarction (U.S.)	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
No. of Annual Heart Attacks	720,000	799,920	888,711	987,358	1,096,955	1,218,717	1,353,994	1,504,288	1,671,264	1,856,774	2,062,876	2,291,855	2,546,251	2,828,885
Market Size Growth	11.1%	11.1%	11.1%	11.1%	11.1%	11.1%	11.1%	11.1%	11.1%	11.1%	11.1%	11.1%	11.1%	11.1%
Associated Mortality	-	-	15.5%	15.5%	15.5%	15.5%	15.5%	15.5%	15.5%	15.5%	15.5%	15.5%	15.5%	15.5%
AMI Survivors	-	750,961	834,318	926,927	1,029,816	1,144,125	1,271,123	1,412,218	1,568,974	1,743,130	1,936,618	2,151,582	2,390,408	
Market Share Penetration	-	0%	0%	0%	0%	1%	2%	3%	4%	5%	6%	7%	8%	9%
Number of Patients Procedures	-	-	-	-	-	10,298	22,883	38,134	56,489	78,449	104,588	135,563	172,127	215,137
Cost of Therapy	-	-	-	-	-	\$ 25,000	\$ 25,000	\$ 25,000	\$ 25,000	\$ 25,000	\$ 25,000	\$ 25,000	\$ 25,000	\$ 25,000
Risk adjustment	-	-	-	-	-	70%	70%	70%	70%	70%	70%	70%	70%	70%
<b>Total Revenue ('000)</b>	-	-	-	-	-	\$ 77,236	\$ 171,619	\$ 286,003	\$ 423,665	\$ 588,365	\$ 784,409	\$ 1,016,724	\$ 1,290,949	\$ 1,613,525

Source: Dawson James estimate.

**Exhibit 16. Trauma (U.S.).**

Trauma (U.S.)	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
Trauma Prevalence	2,500,000	2,577,500	2,657,403	2,739,782	2,824,715	2,912,281	3,002,562	3,095,642	3,191,606	3,290,546	3,392,553	3,497,722	3,606,152	3,717,942
Market Size Growth	3.1%	3.1%	3.1%	3.1%	3.1%	3.1%	3.1%	3.1%	3.1%	3.1%	3.1%	3.1%	3.1%	3.1%
% of Patients Hospitalized	13%	13%	13%	13%	13%	13%	13%	13%	13%	13%	13%	13%	13%	13%
Treatable Population	312,500	322,188	332,175	342,473	353,089	364,035	375,320	386,955	398,951	411,318	424,069	437,215	450,769	464,743
Market Share Penetration	-	0%	0%	0%	0%	0%	1%	3%	5%	7%	9%	11%	13%	15%
Number of Patients Procedures	-	-	-	-	-	-	3,753	11,609	19,948	28,792	38,166	48,094	58,600	69,711
Cost of Therapy	-	-	-	-	-	-	\$ 25,000	\$ 25,000	\$ 25,000	\$ 25,000	\$ 25,000	\$ 25,000	\$ 25,000	\$ 25,000
Risk adjustment	-	-	-	-	-	-	70%	70%	70%	70%	70%	70%	70%	70%
<b>Total Revenue ('000)</b>	-	-	-	-	-	-	\$ 28,149	\$ 87,065	\$ 149,607	\$ 215,942	\$ 286,247	\$ 360,703	\$ 439,500	\$ 522,836

Source: Dawson James estimates.

**Valuation.** Our therapeutic models for MultiStem assume a probability of success (PoS) for all the forecast therapeutic indications. We project our model through the year 2030. For modeling purposes, we use a 30% risk rate (r) in our Free Cash Flow to the Firm (FCFF), discounted EPS, and Some-Of-The-Parts (SOP) models. Our price target is derived from these three models, equally weighting and averaged to the nearest whole number. The result is a one-year price target of \$11.00 per share.

**Exhibit 17. FCFF Model.**

Average of Metrics \$	11
FCFF Price Target \$	12
Year	2019

**DCF Valuation Using FCFF (mln):**

units ('000)	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
EBIT	(46,889)	(53,484)	(46,598)	345,916	762,717	1,369,395	1,983,922	2,656,212	3,257,395	3,893,659	4,569,761	5,291,113
Tax Rate	0%	0%	0%	14%	16%	20%	24%	28%	29%	30%	31%	32%
EBIT(1-t)	(46,889)	(53,484)	(46,598)	297,488	640,682	1,095,516	1,507,781	1,912,473	2,312,750	2,725,561	3,153,135	3,597,957
CapEx	(1,685)	(1,854)	(2,039)	(2,243)	(2,467)	(2,714)	(2,985)	(3,284)	(3,612)	(3,974)	(4,371)	(4,808)
Depreciation	941	1,035	1,138	1,252	1,377	1,515	1,666	1,833	2,016	2,218	2,439	2,683
Change in NWC	(1,546)	-	-	-	-	-	-	-	-	-	-	-
FCFF	(46,088)	(54,303)	(47,500)	296,496	639,592	1,094,316	1,506,462	1,911,021	2,311,154	2,723,805	3,151,204	3,595,832
PV of FCFF	(46,088)	(41,771)	(28,106)	134,955	223,939	294,731	312,103	304,552	283,323	256,854	228,582	200,642
Discount Rate	30%											
Long Term Growth Rate	1%											
Terminal Cash Flow	12,523,414											
Terminal Value YE2030	698,789											
NPV	2,822,506											
NPV-Debt	-											
Shares out ('000)	237,372											
NPV Per Share	\$ 12											

Source: Dawson James estimates.

**Exhibit 18. Discounted EPS Model.**

Current Year	2019
Year of EPS	2030
Earnings Multiple	15
Discount Factor	30%
Selected Year EPS	\$ 8.94
NPV	\$ 7.49

Discount Rate and Earnings Multiple Varies, Year is Constant							
2030 EPS							
Earnings Multiple	7.5	20%	25%	30%	35%	40%	45%
	10	\$15.80	\$10.08	\$6.55	\$4.33	\$2.90	\$ 1.97
15	\$23.70	\$15.13	\$9.83	\$6.49	\$4.35	\$ 2.96	
20	\$31.60	\$20.17	\$13.10	\$8.65	\$5.80	\$ 3.94	
25	\$39.50	\$25.21	\$16.38	\$10.81	\$7.25	\$ 4.93	
30	\$47.40	\$30.25	\$19.65	\$12.98	\$8.70	\$ 5.91	
35	\$55.30	\$35.30	\$22.93	\$15.14	\$10.15	\$ 6.90	
40	\$63.20	\$40.34	\$26.20	\$17.30	\$11.60	\$ 7.88	
45	\$71.10	\$45.38	\$29.48	\$19.46	\$13.05	\$ 8.87	

Source: Dawson James estimates.

**Exhibit 19. Sum of the Parts Model.**

Athersys Sum of the Parts	LT Gr	Discount Rate	Yrs. to Mkt	% Success	Peak Sales	Term Val
MultiStem Ischemic Stroke (U.S.)	1%	30%	3	50%	\$4,742	\$16,353
NPV						\$6.27
MultiStem Hemorrhagic Stroke (U.S.)	1%	30%	3	50%	\$1,123	\$3,872
NPV						\$1.48
MultiStem GI GVHD	1%	30%	3	50%	\$0	\$0
NPV						\$0.00
MultiStem ARDS	1%	30%	6	50%	\$766	\$2,641
NPV						\$0.46
MultiStem AML	1%	30%	5	30%	\$5,378	\$18,546
NPV						\$2.53
MultiStem Trauma	1%	30%	6	30%	\$1,743	\$6,010
NPV						\$0.63
Net Margin						40%
MuslitiStem-Japan Royalties	1%	30%	3	50%	\$423	\$1,460
NPV						\$1.40
MM Shrs OS						237
						\$12.77

Source: Dawson James estimates.

## Risk Analysis

**Clinical Risk:** Athersys is an early-stage biotechnology company currently operating with high expenditures and no product revenues. A significant element of the company's valuation is associated with its lead clinical candidate MultiStem. As such, clinical progress with this stem cell product represents the key risk for the company and shareholders.

**Commercial Risk:** There can be no assurances that the pipeline products will be commercialized, and if they receive regulatory approval, there is a risk that Athersys will not be able to reach the projected market share potential.

**Employee Risk:** Athersys has an experienced management team, which plans to ideally bring MultiStem to market within the next three years. The success of the company may depend on the expertise, abilities, and continued services of its senior officers, sales staff, and key scientific personnel.

**Financial Risk:** Athersys has a high burn rate and is currently not a profitable company. The company might face multiple dilutions in the future to raise capital to fund its operations.

**Intellectual Property Risk:** The company may have to defend its patents and technical know-how, and there can be no assurances that the patents will not be infringed upon or will be held as valid if challenged, and the company may infringe on third party's patents.

**Partnership Risk:** The potential benefits from the partnership with Healios are subject to certain milestones, which if not achieved may delay commercialization in Japan and fail to provide payments to Athersys.

**Regulatory Risk:** There are no assurances that Athersys' products will be approved in the U.S., Japan, Europe, or other markets.

**Exhibit 20. Income Statement.**

Athersys, Inc. Income Statement (\$ '000)	BI	BN				BS	BX	CC	CH	CM	CR	CW	DB	DG	DL	DQ	
ATHX: YE Dec. 31	2018A	1Q19A	2Q19A	3Q19E	4Q19E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
<b>Product Revenue (000's)</b>																	
MultiStem Ischemic Stroke (U.S.)									365,919	732,570	1,099,954	1,468,072	1,836,925	2,206,514	2,576,841	2,947,906	3,319,711
% Chg																	
MultiStem Ischemic Stroke (Japan) - Royalty									12,441	31,134	56,098	87,350	117,104	140,665	164,274	187,929	211,632
% Chg																	
MultiStem Hemorrhagic Stroke (U.S.)									-	-	119,589	239,417	399,427	439,809	480,271	520,814	561,438
% Chg																	
MultiStem ARDS									33,331	68,729	106,289	146,112	188,302	232,967	280,220	330,179	382,967
% Chg																	
MultiStem AMI									77,236	171,619	286,003	423,665	588,365	784,409	1,016,724	1,290,949	1,613,525
% Chg																	
MultiStem Trauma									28,149	87,065	149,607	215,942	286,247	360,703	439,500	522,836	
% Chg																	
<b>Total Revenues (Product Sales, Grants &amp; Milestones)</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>-</b>	<b>488,928</b>	<b>1,004,052</b>	<b>1,754,997</b>	<b>2,514,223</b>	<b>3,346,065</b>	<b>4,090,610</b>	<b>4,879,033</b>	<b>5,717,278</b>	<b>6,612,108</b>
Contract revenues from Healios	22,276	1,441	4,193	1,441	1,441	8,516	-	-	-	-	-	-	-	-	-	-	-
% Chg																	
License Fees - Contract revenues	1,461	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
% Chg																	
Grant Revenues	554	4	69	70	70	213	16	17	17	17	17	17	17	18	18	18	18
% Chg																	
Pfizer Milestones																	
% Chg																	
<b>Total Revenues (Product Sales, Grants &amp; Milestones)</b>	<b>24,291</b>	<b>1,445</b>	<b>4,262</b>	<b>1,511</b>	<b>1,511</b>	<b>8,729</b>	<b>16</b>	<b>17</b>	<b>488,944</b>	<b>1,004,069</b>	<b>1,755,014</b>	<b>2,514,240</b>	<b>3,346,082</b>	<b>4,090,628</b>	<b>4,879,051</b>	<b>5,717,296</b>	<b>6,612,126</b>
<b>Expenses</b>																	
COGS (excludes royalties)	-	-	-	-	-	-	-	-	95,297	194,584	339,780	485,374	645,792	789,989	942,952	1,105,870	1,280,095
COGS % Product Sales		20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%
R&D	38,656	11,415	11,139	11,000	10,500	44,054	42,000	35,000	36,000	34,920	33,872	32,856	31,871	30,914	29,987	29,087	28,215
R&D % Revs																	
G&A	10,442	3,106	2,867	2,600	2,650	11,223	11,500	11,615	11,731	11,848	11,967	12,087	12,207	12,330	12,453	12,577	12,703
G&A % Revs																	
Other (depreciation)	855	184	157	-	-	941	-	-	-	-	-	-	-	-	-	-	-
<b>Total expenses</b>	<b>49,953</b>	<b>14,705</b>	<b>14,163</b>	<b>13,600</b>	<b>13,150</b>	<b>55,618</b>	<b>53,500</b>	<b>46,615</b>	<b>143,028</b>	<b>241,352</b>	<b>385,619</b>	<b>530,317</b>	<b>689,870</b>	<b>833,233</b>	<b>985,392</b>	<b>1,147,534</b>	<b>1,321,013</b>
Oper. Inc. (Loss)	(25,662)	(13,260)	(9,901)	(12,089)	(11,639)	(46,889)	(53,484)	(46,598)	345,916	762,717	1,369,395	1,983,922	2,656,212	3,257,395	3,893,659	4,569,761	5,291,113
Gain from sale of insurance proceeds, net	617																
Oper. Inc. (Loss)	(25,045)																
Oper Margin	NM	NM	NM	NM	NM	NM	NM	NM	71%	76%	78%	79%	79%	80%	80%	80%	80%
Other Income Expense (net)	762	304	213														
Other Income (loss of unconsolidated affiliate)																	
Equity Earnings (loss) of unconsolidated affiliate																	
Expense from change in fair value of warrants, net																	
Preferred Stock Dividends																	
Change in Warrant valuation																	
Deemed dividend resulting from induced conversion of convert p.stock																	
<b>Pre-tax income</b>	<b>(24,283)</b>	<b>(12,956)</b>	<b>(9,688)</b>	<b>(12,089)</b>	<b>(11,639)</b>	<b>(46,372)</b>	<b>(53,484)</b>	<b>(46,598)</b>	<b>345,916</b>	<b>762,717</b>	<b>1,369,395</b>	<b>1,983,922</b>	<b>2,656,212</b>	<b>3,257,395</b>	<b>3,893,659</b>	<b>4,569,761</b>	<b>5,291,113</b>
Taxes	-	-	-	-	-	-	-	-	48,428	122,035	273,879	476,141	743,739	944,645	1,168,098	1,416,626	1,693,156
Tax Rate	0%	0%	0%	0%	0%	0%	0%	0%	14%	16%	20%	24%	28%	29%	30%	31%	32%
<b>Net Income</b>	<b>(24,283)</b>	<b>(12,956)</b>	<b>(9,688)</b>	<b>(12,089)</b>	<b>(11,639)</b>	<b>(46,372)</b>	<b>(53,484)</b>	<b>(46,598)</b>	<b>297,488</b>	<b>640,682</b>	<b>1,095,516</b>	<b>1,507,781</b>	<b>1,912,473</b>	<b>2,312,750</b>	<b>2,725,561</b>	<b>3,153,135</b>	<b>3,597,957</b>
Net Margin	NM	NM	NM	NM	NM	NM	NM	NM	61%	64%	62%	60%	57%	57%	56%	55%	54%
EPS	(0.18)	(0.09)	(0.06)	(0.08)	(0.07)	(0.31)	(0.31)	(0.24)	1.39	2.77	4.37	5.56	6.52	7.28	7.93	8.47	8.93
Non GAAP EPS (dil)	(0.16)	(0.08)	(0.06)	(0.07)	(0.07)	(0.28)	(0.29)	(0.22)	1.41	2.79	4.39	5.58	6.53	7.30	7.94	8.49	8.94
Wgtd Avg Shrs (Bas) - '000s	136,641	145,964	150,163	150,914	151,668	149,677	167,213	181,408	186,909	192,577	198,417	204,435	210,635	217,022	223,604	230,385	237,372
Wgtd Avg Shrs (Dil) - '000s	136,641	145,964	150,163	153,166	156,230	151,381	174,615	197,317	213,582	231,188	250,245	270,873	293,202	317,371	343,533	371,851	402,504

Source: Dawson James estimates.

Companies mentioned in this report:

Healios (TYO-4593: Not Rated)

Important Disclosures:

**Price Chart:**



Price target and rating changes over the past three years:

Initiated – Buy – August 26, 2019 – Price Target \$11.00

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Market Underperform (Sell)	0	0%	0	0%
Total	53	100%	13	25%

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