Company Profile

Athersys

Athersys (Nasdaq: ATHX) is a biopharmaceutical company engaged in the discovery and development of novel therapies designed to treat significant unmet medical needs. The company is heavily focused on the regenerative medicine area, with multiple clinical and preclinical stage programs. The most advanced programs at the company are focused on the development of MultiStem®, a clinical stage allogeneic stem cell therapy that has demonstrated potential for treating a range of conditions and is believed to have widespread application in the field of regenerative medicine. The company has internal programs applying MultiStem across multiple therapeutic areas including cardiovascular, neurological, immune dysfunction and other disease areas, and partnered programs with Pfizer (applying MultiStem to treat inflammatory bowel disease) and Angiotech Pharmaceuticals (acute myocardial infarction). Athersys has a broad network of collaborative relationships with leading research and clinical institutions and is committed to developing a pipeline of novel 'best-in-class' medicines.

Gil Van Bokkelen

Athersys, Inc., 3201 Carnegie Avenue,
Cleveland, OH 44115, USA
Tel.: +1 216 431 9900
gilvb@athersys.com

Athersys is a biopharmaceutical company engaged in the discovery and development of therapeutic product candidates designed to extend and enhance the quality of human life. The company was established in 1995, and is based in Cleveland, OH, USA, near the Cleveland Clinic, Case Western Reserve University and several other clinical and research centers. The company also has operations in Leuven, Belgium, and has approximately 45 employees. Through the application of proprietary technologies, Athersys is committed to establishing a pipeline of highly differentiated, 'best-in-class' candidate therapeutics to treat significant, unmet medical needs. The lead programs are focused on the development of MultiStem®, a patented and proprietary nonembryonic stem cell therapy that has demonstrated potential for treating a range of diseases, including in the cardiovascular, neurological and immune system dysfunction areas. In December 2009 Athersys announced a global strategic partnership with Pfizer (NYSE: PFE) focused on the collaborative development and commercialization of MultiStem for the treatment

of inflammatory bowel disease (IBD), and is also partnered with Angiotech Pharmaceuticals (Nasdaq: ANPI) to treat certain types of cardiovascular disease. In addition, we are developing novel pharmaceuticals to treat indications such as obesity, as well as certain conditions that affect cognition, attention and wakefulness.

MultiStem is a proprietary adherent stem cell product that is produced by obtaining a special class of early progenitor or stem cells from healthy, consenting donors. Typically these cells are obtained from bone marrow, although they may also be found in other tissue and organ systems. The clinical product consists of a pharmaceutical grade composition of cells that have been specially formulated for clinical use, and that may be delivered either systemically (i.e., intravenously) or locally (e.g., using direct injection or a catheter-based delivery approach). MultiStem behaves in a drug-like fashion by expressing proteins and other factors involved in tissue repair and immune system regulation, and acting through multiple mechanisms such as protecting damaged or injured cells, reducing

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inflammation and promoting new blood vessel formation in areas of ischemic injury (FIGURE 1). While produced on an industrial scale in a manner similar to traditional biologics, MultiStem has distinctive multimodal therapeutic value.

Several factors have limited the clinical impact of traditional bone marrow or hematopoietic transplants, such as the need to tissue match donor and recipient, administering immunosuppressive drugs to reduce the risk of rejection or other immunological complications (e.g., graft-versus-host diseases [GvHD]), and the lack of ability to expand stem cells so that material from a single healthy donor can be used for more than one patient. In contrast to traditional approaches, MultiStem has shown the potential to address each of these limitations. Using cells obtained from a healthy consenting donor to establish master and working cell banks, millions of uniform doses of MultiStem may be manufactured using state of the art closed system manufacturing processes, and the cells may then be cryogenically preserved for at least several years. Furthermore, MultiStem may be administered like type-O blood – without the need for tissue matching or administration of immunosuppressive drugs (FIGURE 2).

A key part of the research and development strategy at Athersys is to establish collaborative alliances with other research

institutions, clinical centers and commercial organizations. Over the past several years, the company has established collaborations with more than 30 research and clinical institutions across the USA and Europe. Through these collaborations, the company has been systematically exploring the potential application of MultiStem to treat cardiovascular disease conditions such as damage from acute myocardial infarction, peripheral vascular disease or vascular injury, chronic ischemic conditions and a range of other conditions. Recently, the company announced data from a Phase I clinical study involving administration of MultiStem to patients who had suffered an acute myocardial infarction. MultiStem was delivered into the heart using a proprietary micro-infusion catheter that enables rapid efficient placement of the cells directly into the region of ischemic damage following a heart attack (FIGURE 3). Top-line data from the study showed that administration of MultiStem was safe and well tolerated, and there were also encouraging signs of improvement in multiple measurements of cardiovascular performance including left ventricular ejection fraction, left ventricular end systolic volume and wall motion. The company intends to initiate a Phase II clinical trial with its partner, Angiotech Pharmaceuticals, in 2011.

Figure 1. Potential mechanisms of benefit of MultiStem® – a proprietary stem cell therapeutic.

Working collaboratively with other academic labs, the company has published promising results in various preclinical models of vascular injury, and has also conducted work in models of chronic ischemia. Administration of MultiStem in various cardiovascular models has shown a corresponding reduction in inflammation in the region of ischemic damage, along with cardioprotective or cytoprotective benefits, as well as proangiogenic and vasculogenic effects. These effects appear to be achieved primarily through trophic mechanisms, as opposed to direct tissue replacement.

Another area where MultiStem has shown promise involves treatment of certain neurological conditions, such as ischemic stroke, traumatic brain injury, neonatal hypoxic ischemia or other conditions, which represent significant unmet medical needs. Stroke represents the leading cause of serious disability globally, with approximately 800,000 patients suffering a stroke each year in the USA alone, and an estimated 15 million stroke victims globally. The vast majority of these strokes are ischemic (as opposed to hemorrhagic) in nature. The only therapeutic currently approved for stroke is the thrombolytic tissue plasminogen activase, which must be administered within approximately 3 h of the occurrence of the ischemic stroke. Unfortunately, most stroke victims are unable to get to a hospital within that time frame, and it's estimated that less than 5% of stroke patients receive treatment with tissue plasminogen activase.

Published research has shown that intravenous administration of MultiStem in preclinical models can protect and help repair the damage caused by a stroke or similar ischemic event, such as neonatal hypoxic ischemia (a leading cause of cerebral palsy), even when administered several days after the initial event. Similarly, MultiStem can

Figure 2. MultiStem® production process. Material is isolated from a healthy donor, cells are expanded, concentrated and banked, and then used to treat many patients without the need for tissue matching and immune suppression.

apparently help limit or reduce the damage caused by a traumatic brain injury, by reducing inflammation that occurs after the injury, helping to restore the integrity of the blood–brain barrier and other mechanisms (FIGURE 4). The US FDA has authorized a double-blind, placebo-controlled study involving administration of MultiStem to ischemic stroke patients, which the company intends to initiate in 2011.

The immunomodulatory effects of MultiStem suggest potential relevance across a range of conditions involving immune system dysfunction. Preclinical studies suggest that MultiStem can help reduce the incidence and severity of GvHD, which is commonly seen in bone marrow

Figure 3. Catheter delivery and retention of MultiStem® in ischemic region in an acute myocardial infarction patient at (A) 5 s, (B) 30 s and (C) 60 s; vessel patency after delivery is shown in (D). The arrow marks the catheter-based transarterial delivery of the stem cell product.

Figure 4. MultiStem® (green) supports axonal growth (red) and reverse axonal inhibition by proteoglycan scar components (blue).

transplant recipients. The company is currently conducting a Phase I clinical trial involving administration of MultiStem to leukemia and lymphoma patients that are at risk for GvHD, and MultiStem was recently granted Orphan Drug status by the FDA for this indication.

Inflammatory bowel disease is another immune system disorder that MultiStem may have potential relevance for treating. It is estimated that more than 2 million individuals in the USA, core European markets and Japan suffer from various forms of IBD, including Crohn's disease and ulcerative colitis, which are the most commonly diagnosed forms of IBD. Patients with IBD may experience a range of symptoms, including diarrhea, urgency, rectal bleeding and abdominal pain. Patients may also experience fatigue, fevers, weight loss and dehydration. The symptoms can be incapacitating.

Current approved treatments for IBD consist of corticosteroids or other immunosuppressive drugs that may have certain side effects or risks associated with their extended use. Furthermore, many individuals suffering from IBD become resistant to currently available therapies. As a result, many patients progress to surgical intervention in order to remove damaged sections of the GI tract. Unfortunately this approach is typically not curative, since it does not address the underlying immune system dysfunction that is responsible for causing the disease and the corresponding tissue damage. Furthermore, surgical intervention has significant associated risks, and is extremely expensive.

Athersys and Pfizer are co-developing MultiStem as a new potential treatment for IBD, and recently initiated a Phase II clinical trial involving administration of MultiStem to patients suffering from ulcerative colitis, the most common form of IBD. The partners believe this represents a mechanistically novel approach, with potential for improved efficacy and reduced side effects compared with existing treatments. MultiStem appears capable of delivering a therapeutic benefit through more than one mechanism of action. Factors expressed by MultiStem are believed to reduce inflammation and regulate immune system function, protect damaged or injured cells and tissue, and augment tissue repair and healing in other ways.

Future perspective

The future of regenerative medicine will involve a variety of approaches, including stem cells, engineered tissue, small-molecule therapeutics and biologics that promote tissue repair and healing, and lead to safer and more effective therapies. Athersys believes that regenerative medicine technology could transform current medical practices in multiple ways, and has the potential to both improve clinical outcomes and reduce overall healthcare costs. The company is committed to developing MultiStem as an 'off-the-shelf' allogeneic cell therapy product for multiple disease areas. The company has ongoing or planned clinical trials for treating cardiovascular disease (e.g., acute myocardial infarction), neurological conditions (e.g., ischemic stroke) and immune system disorders (e.g., IBD and GvHD). Working with established commercial partners like Pfizer and Angiotech, as well as a broad network of collaborators at leading research and clinical institutions in the USA and Europe, the company has demonstrated that MultiStem exhibits a consistent safety profile and can achieve therapeutic effectiveness in multiple ways.

Information resources

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Executive summary

- Athersys is a biopharmaceutical company that has multiple regenerative medicine programs, as well as traditional drug development programs.
- The company is focused on the clinical development of MultiStem®, an allogeneic stem cell product.
- Primary areas of focus include applying MultiStem to treat cardiovascular disease, certain neurological conditions and immune system disorders.
- Unlike traditional bone marrow or stem cell transplants, MultiStem may be manufactured on an industrial scale, with millions of doses produced from material obtained from a single healthy, consenting donor.
- The product can be safely and stably cryopreserved for an extended period of time.
- MultiStem is administered like type-O blood, without the need for tissue matching or administration of immunosuppressive drugs.
- MultiStem exhibits a drug-like profile, conveying a therapeutic benefit through multiple trophic pathways.
- Studies have shown that MultiStem reduces inflammation, conveys cytoprotective effects, and exhibits proangiogenic and vasculogenic effects in ischemic injury models.
- Following administration, cells are cleared from the body over time, and do not act as a permanent transplant.
- Athersys has multiple clinical stage programs, and has established partnerships with several companies, including Pfizer, Angiotech Pharmaceuticals and RTI Biologics.