MAXIM GROUP

EQUITY RESEARCH INDUSTRY REPORT

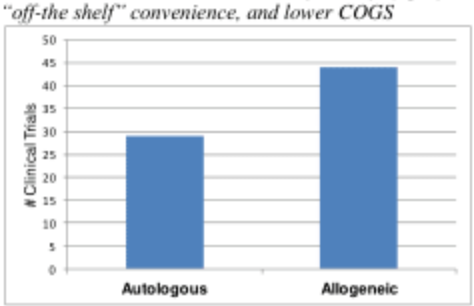
July 8, 2013

Regenerative Cell Therapy: Autologous versus allogeneic is the wrong question?

It's pre-clinical, manufacturing, and clinical data that drive safety.

Companies mentioned include:
Athersys, Inc. (ATHX) – $1.68 – Buy
Baxter (BAX) – $69.88 – NR
Capricor (private)
Cardio3 Biosciences (private)
Cytomedix (CMXI) – $0.42 – NR
Cytori Therapeutics (CYTX) – $2.43 – Buy
Dendreon (DNDN) – $4.48 – Sell
IntellicellBioScience (SVFC)-$0.05 - NR
Lonza (LONN.VX) – CHF72.30 -NR
Mesoblast Ltd. (MBLTY) – $25.14 – Buy
NeoStem, Inc. (NBS) – $0.57– NR
Osiris (OSIR) – $10.40 – NR
Pfizer (PFE) – $27.97 – NR
Pluristem (PSTI) – $2.98 – Hold
Teva Pharmaceuticals (TEVA) – $38.94 – Buy
**Closing prices (7/05/2013)*

More clinical trials are taking place with allogeneic cells, which we believe is due to a good safety profile, "off-the shelf" convenience, and lower COGS



Source: Clinicaltrials.gov and Maxim Group estimates

Jason Kolbert
[redacted]

Source: [redacted]

- **"What the eyes see and the ears hear, the mind believes" – Harry Houdini.** In the wake of Pluristem's clinical hold, some investors have been asking if there are implications for other allogeneic companies. NeoStem closed its presentation at the Alliance for Regenerative Medicine (ARM) conference in April 2013, with a slide that autologous cells are safe. Well, that depends? Were the autologous cells manipulated, enriched, exposed to media, or expanded? The NeoStem product is "manipulated." In this report, we review the safety data for allogeneic cells and claims from autologous companies like NeoStem that allogeneic cells are less safe or not safe. In fact, we believe this is misdirection on the part of autologous companies.
- **Manipulation?** Generally speaking, both autologous and allogeneic cells are manipulated. The definition of manipulation varies from minimally manipulated to manipulated, but it is a misnomer to claim that no manipulation occurs.
- The clinical hold on Pluristem has become fodder for some who want to raise the allo safety question. We spoke with Athersys and Mesoblast (allogeneic cells), and both companies told us that they have had zero immune-related AE's. All of these companies (allogeneic and autologous) are using different cell types, isolation procedures, product composition, and delivery. Both types are manipulated. Athersys has safely delivered doses of more than 1 billion cells systemically with no reported immune reactions. Mesoblast has tested its products in hundreds of patients with no allo-related AEs. The only company on the landscape that we see that is truly minimally manipulated is IntelliCell Bioscience (SVFC).
- **Our conclusion:** We believe both allogeneic and autologous with few exceptions qualify as manipulated products; therefore, the safety of both products must be assessed in pre-clinical, manufacturing, and clinical studies. We believe both allogeneic and autologous products will be approved for various indications. Most importantly, if the outcome is initially binary (it works or it doesn't), then patient convenience and cost of goods are likely to be major market factors. In this case, allogeneic has multiple advantages over the autologous process, which is more expensive and less patient friendly.

INVESTMENT SUMMARY

The discussion in regenerative medicine has more recently and increasingly—(and shortsightedly in our opinion) been focused on the debate of safety of autologous versus allogeneic. We believe Pluristem's clinical hold is not an allogeneic problem but a Pluristem problem. The company is using a cryopreserved formulation of its placental-derived cells. This formulation includes DMSO as a preservative and albumin in a light saline solution. DMSO is an immune stimulator, (commonly used). It's possible that the immune response seen in the patients is due to the formulation versus the cells, themselves. We don't have the data yet to know the cause of the immune reaction in the Pluristem patient that triggered their clinical hold.

We have spent some time discussing risk with the allogeneic CEOs, as some of the autologous companies have attempted to maximize the risk of the allogeneic approach. We see this as a scare tactic that's not based on science. **Mesoblast and Athersys have reported no immune responses associated with their allogeneic cell therapies.** In fact, Pluristem, Mesoblast, and Athersys use different cell types and process them differently. Mesoblast is using mesenchymal precursor cells (MPCs), and Athersys is using multipotent adult progenitor cells (MAPCs). Both MPCs and MAPCs are isolated from the bone marrow, while Pluristem uses placental-derived cells. Athersys has delivered more than 1 billion cells safely to multiple patients in their Phase II stroke trial. Mesoblast has treated hundreds of patients with no reported immune related AE's. We have not seen any evidence so far pointing toward these allogeneic cells (from Mesoblast and Athersys) as being unsafe. Osiris Prochymal is another example of a safe (approved) allogeneic product.

To really understand the allogeneic vs. autologous debate, we need to look at how the products are derived. Regardless of the source (allogeneic or autologous) of the cells, the cells are put through a series of manipulations before they are delivered back into the patient. We consider the purifying of the cells a technique used by most cell therapy products as a manipulation. For example both Baxter and NeoStem, enrich their products for CD34+ cells. These process select cells with either, and, or antibody-magnetic bead process (a column); hence, in the eyes of the FDA the cells have been manipulated. Furthermore, these cells are stored in different formulations of various mediums before being injected back into the patients. With each manufacturing process step, there is a chance of variability that can induce an immune response in a patient. This variability is inherent in all isolated stem cells, whether they are autologous or allogeneic. Therefore, a stringent quality control of the manufacturing steps and release criteria are needed as early as the pre-clinical stage to demonstrate the safety of the cells. The only process that we are aware of that truly qualifies as minimally manipulated (both are autologous) is depending on definitions, the Cytori (CYTX) process (which does add an enzyme that is later removed, so technically it does not qualify) leaving the IntelliCell Bioscience process (which adds nothing, is done on-site, (sonification to separate cells and create a stromal vascular fraction) and is then checked for contamination and "quality controlled" before being returned to the patient) all within an hour. The cells never leave the premises. This process does appear to meet current FDA guidelines as "minimally manipulated" and as such likely falls under "practice of medicine" guidelines.

The issue by how clinicians are able to treat patients today continues to surface. To that end we take a moment to try to understand what are the current specific regulations that allow IntelliCellBioScience to operate and treat patients. IntelliCell's position on the legal/regulatory status of SVFC (stromal vascular fraction cells) is that the product is a human cell, tissue, and cellular and tissue-based product ("HCT/Ps") and is regulated under the regulations created under 21 C.F.R. § 1271. The Company maintains that the SVFC product fall within the exemption from FDA regulation found under 21 C.F.R. § 1271.15(b). This is because the HCT/Ps are removed from and reintroduced into the same patient during the same surgical procedure as that term is used in the practice of medicine. The cells that are reintroduced are exactly the same cells (i.e., "such cells") as the cells removed from the autologous patient. Thus, the SVFC product falls under an exemption to FDA regulation.

The SVFC product and the procedures used for the product are similar to those used in autologous bone marrow aspirate transplants, skin grafts, knee ligament replacement, and cardiac bypass procedures. FDA regulation of the SVFC product as a drug would require consistent interpretation and application of the regulatory requirements, and would mandate that these other medical products and procedures should also be regulated as drugs requiring FDA pre-approval.

Alternatively, even if the SVFC product is not exempt under 21 C.F.R. 1271.15(b), the company maintains that it meets the requirements in 21 C.F.R. § 1271.10(a) for regulation solely under PHS Act § 361 and Part 1271 as a "361 HCT/P" and not as a drug, device, and/or biologic requiring an approved application. Under that section of the regulation, HCT/Ps that are from an autologous source, minimal manipulation, and for homologous use, and do not include added components (with some minor exceptions) are exempt from FDA pre-approval as a drug.

Under these guidelines IntelliCell Bioscience is empowering clinicians to treat patients today for everything from orthopedic injuries to multiple sclerosis. The company has treated over 300 patients and in some cases with dramatic results. We went so far as to review patients stories and case histories, publications and even met with the company's attorneys (ex-FDA reviewers) to understand the definitions of minimally manipulated and the legal guidelines by which the company's process allows physicians to treat patients. We left believing that this is the only company, at the moment that qualifies with a process that meets current guidelines.

The next step in our research process was to review the current published and unpublished data comparing the safety of the allogeneic cells. Some of these studies have included side-by-side comparisons of the allogeneic and autologous cells. In our literature search we also came across numerous examples of blood transfusions (hundreds of thousands that have been accomplished "allogenically" with little to no immune reaction concerns. Conversely there are also multiple examples of autologous transfusions that have resulted in immune reactions. This goes to our point that it is the process and handling that has everything to do with the safety of such procedures.

Hare et. al published data in *JAMA* on POSEIDON—one of the first trials comparing allogeneic versus autologous bone marrow-derived mesenchymal stem cells delivered by transendocardial injection in patients with ischemic cardiomyopathy (ICM)[1]. In the trial, 30 patients were randomized between an allogeneic and autologous arm. The patients were further assigned to three increasing dose levels of 20, 100, and 200M cells. The primary endpoint of the study was the 30-day event rate of predefined treatment emergent serious adverse events (SAE). One patient in each group had an SAE (hospitalization for heart failure) in 30 days. Three patients in the allogeneic group and nine patients in the autologous group experienced adverse events (AEs). Over the 12-month period, 10 patients in the allogeneic group and 11 patients in the autologous group experienced AEs. Major adverse cardiac events (MACE) for the 12-month period occurred in three patients in the allogeneic group and four in the autologous group. Overall, both treatments demonstrated reduced infarct size, improved ventricular remodeling, and similar safety profiles.
This data mirrors what Mesoblast has seen with its own side-by-side comparison of allogeneic and autologous MPC. In pre-clinical studies, Mesoblast has shown that sheep had an identical stromal receptor found in humans, making the sheep an ideal preclinical model for Mesoblast's MPC product (for human studies, Mesoblast isolated MPC cells with a stromal receptor). When allogeneic and autologous MPC were used for treatment, the company found that there was no difference in efficacy.

[1] Hare, et. al. Comparison of allogeneic vs. autologous bone marrow-derived mesenchymal stem cells delivered by transendocardial injection in patients with ischemic cardiomyopathy. 2012. JAMA 308(22).

In addition, Mesoblast performed two pilot studies in cardiac and orthopedic indications in which autologous and allogeneic cells were generated in a similar fashion. The only difference was that the cell and all other manufacturing variables were the same. These side-by-side studies showed no immunogenicity concerns, and the efficacy was same between autologous and allogeneic cells.

Athersys has also shown that, when used side by side, MultiStem derived from allogeneic or autologous cells did not show any differences in safety or efficacy. In addition, Athersys's many collaborators, including Pfizer, have demonstrated the safety of allogeneic (and xenogeneic) MultiStem in immune-competent animal models of disease and injury.

Capricor, Inc. (private) is a unique company in the cardiovascular space. The company has transitioned from an autologous to an allogeneic model based on a vision of commercialization and COGS, combined with the science that suggests allogeneic is equally safe and even potentially more effective than autologous. The company uses homologous-tissue-derived stem cells (cardiac). It isolates progenitor cells from an allogeneic heart that is destined to become cardiac cells. In its phase I "CADUCES" trial, Capricor has shown its autologous cardiosphere-derived stem cells (CDC) reduce infarct size and generate new myocardium, in principle repairing the heart. However, Capricor found the autologous method cumbersome (manufacturing). Mechanistically, the company reasoned that it is the cell cytokines that were affecting the local environment and not the cells themselves. As such, allogeneic should work as well—and, thus far, that reasoning has proved valid.

The safety of allogeneic cells is not just limited to pre-clinical studies but has been validated in clinical trials in multiple indications in cardiovascular, autoimmune, and neurological conditions. Interestingly, the majority of the studies registered on clinicaltrials.gov use allogeneic stem cells (~44). In contrast, only ~29 studies are using autologous stem cell therapy. We believe the reason for such interest in allogeneic treatment is due to its safety, efficacy, and, most importantly, convenience as an "off-the-shelf" treatment.

The safety of the allogeneic MSCs has also been documented in a meta-analysis of published and clinical trials. Lalu et. al recently published results of a systemic review of clinical trials that used MSCs to evaluate their safety[2]. The authors reviewed 2,347 publications and 37 clinical trials. These studies recruited a total of 1,012 participants with clinical conditions ranging from cardiovascular diseases to autoimmune diseases, as well as healthy volunteers. The authors found that eight of the studies were randomized control trials and had enrolled 321 participants. The randomized control trials showed no association between acute infusional toxicity, organ system complications, infection, death or malignancy. **Overall, the allogeneic MSC clinical trials have shown to be safe.**

This drives us to our first conclusion: *When allogeneic and autologous cells of the same phenotype are compared side by side, they show similar efficacy and safety profiles. In addition, a meta-analysis shows overall safety of the MSCs. Therefore, the argument on safety and efficacy of autologous vs. allogeneic has no scientific basis, in our opinion.*

Manipulation exists for both autologous and allogeneic cells? Mesoblast and Cardio3 Bioscience (private) use bone-marrow-derived cells for treatment of heart failure; however, the end product used in patients is markedly different. Mesoblast uses allogeneic expanded MPC, while Cardio3 uses autologous bone marrow-derived mesenchymal cells treated with cardiopoietc growth factors.

[2] Lalu et. al. Safety of Cell Therapy with Mesenchymal Stromal cells (SafeCell): A systematic review and meta-analysis of clinical trials. (2012) PLOS one, 7(10).

Mesoblast believes that the best solution is a single potent cell type that is multi-factorial in its ability to regulate inflammation and neoangiogenesis. The company has shown that its MPCs can respond and act according to what the tissue is demanding. In the cardiac space, MPCs appear to stimulate angiogenesis (revascularization of the heart muscle) and, as a result, enhance the survival of cardiac cells. At the same time, the cells are also modulating the local immune system by polarizing pro-inflammatory cells toward a non-inflammatory state and activated T cells toward regulatory T cells.

Cardio3's C-Cure differentiates autologous bone marrow mesenchymal stem cells toward cardiopoietic cells by treatment with the cardiopoietic growth factors. The C-Cure cells proliferate, engraft, and differentiate into heart muscle cells. The cells also have an indirect effect through the release of trophic factors. In a phase II trial, the treatment showed significant improvement in both a 6-minute walk test and Left Ventricular Ejection Fraction (LVEF) versus baseline. C-Cure is in a European phase III "CHART-1" trial to treat CHF secondary to ischemic cardiomyapathy. The company expects to obtain an IND in the United States by mid-2014 for a phase III CHART-2 trial.

This drives us to our next conclusion: *Both Mesoblast and Cardio3's starting material is bone marrow cells. Where Mesoblast isolates MPCs, Cardio3 drives the mesenchymal stem cells toward cardiopoietic cell differentiation. Both methods use different manufacturing techniques to generate the product. While Cardio3 is an autologous product, the original product has been modified to differentiate ex-vivo into cardiopoietic cells. Is this newly-derived differentiated autologous cell safer than the starting material? That can only be answered in the preclinical and clinical studies. Mesoblast has shown in preclinical and clinical trials that its cells are not only safe but efficacious, and so has Cardio3. Therefore, the differentiation factor between these two markedly different cells is their efficacy in the patients.*

Is one cell type (autologous vs. allogeneic) more efficacious than another? We believe companies like NeoStem are trying to maximize the risk of allogeneic approaches using misdirection from the real issues of SWOT (strengths, weakness, opportunities, and threats). We look at the pros and cons of allogeneic vs. autologous models based on the science and data. The discussion in cell therapy is being directed toward the safety of the cell source rather than the science behind the cell source. We believe that this is a grave mistake since each product is unique with its own pros and cons for their indications.

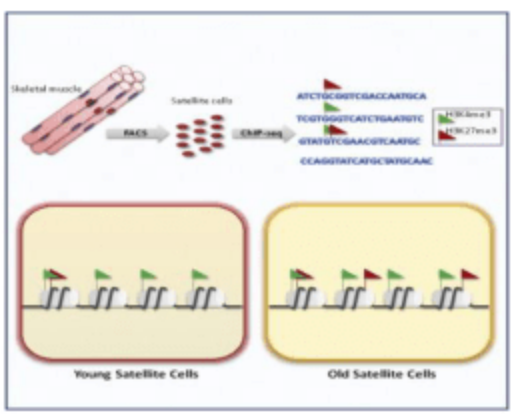


Exhibit 1. All cells contain the same genetic information; however, the identity of distinct cells is established at epigenetic levels (consisting of chemical changes to the DNA and histone). These "histone signatures" determine which genes are turned on or off. A recent paper in the *Cell Reports* showed that muscle stem cells from old mice had different histone signatures than the young mice[3]. What this means is that the older mice have more stop signals (genes locked in off position) than go signals (on position). In layman's terms, with age, changes in histone signatures are linked to the functional decline of stem cells. A younger stem cell has potential to express and seem ready to become all kinds of different tissue cells compared to its older stem cells, which are more restricted.

*Source: Liu, L. et al. Cell 2013*3

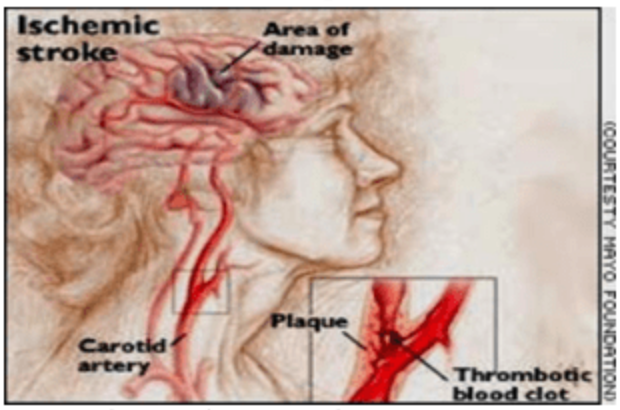
[3] Liu, L. et al. Chromatin Modifications as Determinants of Muscle Stem Cell Quiescence and chronological aging. (2013) Cell Reports. (4).

Another report from a paper in *Nature* showed that the accrual of DNA damage from ageing in hematopoietic stem cells of mice may result in functional decline and contribute to the diminished capacity of aged tissues to return to homeostasis after an injury (such as heart attack)[4]. These studies will need to be confirmed in humans, but if they show the same conclusion as in animal studies, it will have a profound effect on development of autologous versus allogeneic treatments in cardiovascular space.

This brings us to our next conclusion: *Autologous companies like NeoStem use hematopoietic stem cells (purified CD34+) for their treatment. The autologous stem cells are great in your 20s, but when you need a cell therapy in your 60s or 70s, will these stem cells with "stop signals" be of any use? On the other hand, Mesoblast's MPCs from a healthy 20-year-old have "go signals" and are off the shelf, ready to home to the affected area and ameliorate disease condition. Compare all of this (plus, no patient discomfort) for an off-the-shelf, readily available product to companies like NeoStem, which require two additional return trips to the hospital, one to harvest the product (12 bone punctures with four needle pulls on each puncture), which requires extracting 300cc's of bone marrow—and then processing it and returning to the patients (which must be within 72 hours).*

Are autologous and allogeneic therapeutics in competition? Not necessarily. We believe that these two broad therapeutics are distinct, and they even may be complimentary in some indications.

Exhibit 2. A classic example of an ischemic stroke



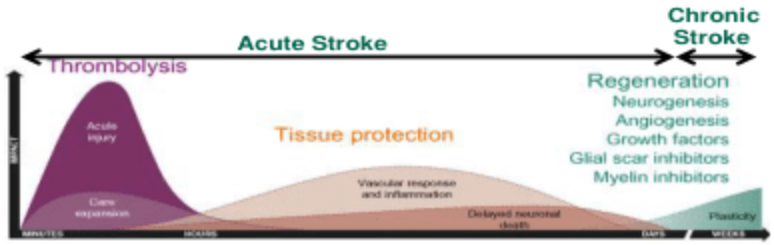
Source: Athersys and Mayo Foundation

A stroke occurs when blood flow to the brain is interrupted This can occur due to either ischemia (lack of blood flow) caused by blockage (thrombosis, embolism) or a hemorrhage (rupture of blood vessel in the brain). Loss of blood in the brain results in cell death, causing neurological deficit, which is usually unilateral (affecting one side of the body) and triggers the inability to move one or more limbs, understand, speak, or see on one side of the visual field.

The only approved viable therapy today is recombinant tissue plasminogen activator (rtPA). It has limitations, as it must be administered within three to four hours of the initial ischemic stroke. If administered after this time, it can cause or exacerbate cerebral bleeding (i.e. hemorrhage), resulting in a worsening of damage or even death. As such, it is only used on ~5% to 8% of treatable patients.

[4] Rossi, DJ. et. al. Deficiencies in DNA damage repair limit the function of hematopoietic stem cells with age. (2007) Nature (447), 725-729

Exhibit 3. Phase of injury and changes in tissue architecture targeted by cell therapy



Treatment	Tissue plasminogen activator	MultiStem (Athersys)	ALD-401 (Cytomedix)
Time	<4 hrs	1-2 days	13-19 days
Clinical Stage	FDA approved	Phase II	Phase II

Source: Maxim Group modified from Sinden et. al. Intr. J of Stroke, (2012)[5]

A stroke injury is a progressive injury. In the early days of the stroke after acute injury, there is inflammation; at later point in time, there is delayed neuronal cell death. Therefore, a treatment for a stroke patient would be multi-modal and would require different approaches. In the early acute phase of stroke (72 hours post stroke), there is an increase in inflammation and vascular response. Athersys's cell therapy MultiStem is administered during this time period. The hope is that MultiStem can shift the immune system into repair mode (e.g. through stimulation of reparative Tregs and M2 macrophages). Days after stroke, there is a delayed neuronal death. Cytomedix's cell therapy (autologous ALDH bright cells, or "ALDH^{br}" cells) is administered during this window, since it promotes tissue protection and repair through angiogenesis and neurogenesis. These approaches are dramatically different—so much so that they may even be complimentary. MultiStem is given systemically in a large dose (possibly >billion cells) prior to 48 hours post injury to modulate inflammation, while the Cytomedix therapy is given locally 13-19 days after stroke in a small dose, targeting the brain.

Athersys's MultiStem is given at the earliest time, just days after stroke. Being an allogeneic product, it can be produced and is readily available. The mechanism of MultiStem appears to be primarily through immunomodulation, which is most likely occurring through its sequestering of immune cells in the spleen after stroke. The choice of intravenous injection makes an ideal delivery for administration of the increased number of cells. We believe the window of opportunity for MultiStem treatment is also ideal, since the patient will already be hospitalized and the therapy does not require either patients' cells or an invasive inoculation. Most importantly, cell therapy does not require immunosuppression with treatment.

Unlike Athersys, Cytomedix's ALD-401 cell therapy is dependent on autologous unexpanded ALDH^{br} cells. The ALDH^{br} cells are administered through intracarotid infusion, and the theoretical treatment window for Cytomedix is longer compared to Athersys. The ALD-401 mechanism of action is not immunomodulation like Athersys' MultiStem. Cytomedix actually suggests that its cells would be of no benefit if given right after stroke. Since ALD-401 promotes angiogenesis, we believe the timing of intervention makes sense. After 13-19 days post stroke, the cells can initiate angiogenesis and tissue regeneration. We see MultiStem and ALD-401 as complimentary treatments—MultiStem is immunomodulatory and is given to curb the inflammatory peak prior to 72 hours post stroke, while ALD-401 promotes angiogenesis and is given 2 weeks post stroke when angiogenesis and tissue regeneration can occur.

How about in cardiovascular disease: Is timing of the treatment a factor? The autologous companies will argue that one should wait some period of time for the hypoxic signals to peak so that cells can appropriately home to the heart. Delivering cells too early minimizes their effect as they become destroyed in the ensuing cytokine—inflammatory chaos of the initial ischemic event. We find this argument flawed.

[5] Sinden et. al. Stem cells in stroke treatment: the promise and the challenges. Intr. J of Stroke, (2012) 7 (5): 426-434

The inflammatory cascade creates secondary damage that, if turned off, effectively limits consequential damage. That's exactly what allogeneic cells do, but that's only their first mission. These cells persist for weeks. They do home along the same SDF-1 gradient and will follow as the hypoxic signal (hypoxic induced factor or HIF) builds. The cells are in effect "on board" and ready to respond as needed. Also, the SDF-1 gradient naturally is only expressed for the first few days, a time frame that is more suited for an "off-the-shelf" allogeneic treatment than the autologous treatment.

This drives us to our next conclusion: *It is unknown whether most of the damage occurs initially or over time, and the reality is probably that it is a deadly combination of both—the immediate inflammatory cascade and the secondary ischemic stress. We believe that, in certain indications, allogeneic may be more preferable (such as in an acute phase in stroke with Athersys' MultiStem), while autologous cells may be more appropriate later in time (such as weeks after stroke). The clinical data will drive these conclusions.*

We believe clinical trial strategy is important. Mesoblast is the leader in cardiovascular space. With its partner Teva, the company is preparing to launch a global phase III program in congestive heart failure (CHF) (n=1,700). Mesoblast believes that a single potent cell type that is multi-factorial in its ability to regulate inflammation and neoangiogenesis is the best solution. Mesoblast and Teva are planning for a two-year, $130 million program. Cytori believes it may be possible to do single, modestly sized clinical trial (consistent with the PMA guidelines). We believe that NeoStem will need to do two large pivotal trials (because these are processed, or manipulated, cells in a non-orphan setting) and will have to raise ~$150M for a phase III trial. Given the SWOT analysis for NeoStem's products, we believe this level of financing will be a difficult challenge.

This drives us to our next conclusion: *We believe that, eventually, we will see both autologous and allogeneic treatments approved, but each will need to show its benefits. If the allogeneic and autologous therapies are equivalent for most regenerative indications (which our key opinion leaders believe is most likely), the COGS and patient convenience will become critical factors.* ***We believe that's the reason for Baxter's decision to look for buyers for its cell therapy division. By default, this does not bode well for NeoStem, which has a similar cell therapy and the same high COGS.***

If all things are equal (efficacy and safety), then manufacturing is the critical factor. There are multiple late-stage clinical trials underway evaluating the use of stem cells as a therapeutic to either arrest the progression of heart disease or to even reverse disease. Some of these trials include Mesoblast's trial evaluating purified bone marrow cells (MPCs), Athersys' MAPC, Osiris's expanded mesenchymal stem cells (MSC), and Capricor's cardiosphere-derived stem cells (CDC). These are cells in a bottle, or allogeneic sources. In this case, the cells are initially developed from a donor source, processed at a cGMP factor, and cryopreserved. These cells are in effect an active biological therapeutic—an off-the-shelf ready product with zero patient discomfort. The cost of goods of a mass-produced, allogeneic product is likely to be the lowest in the industry.

Some of the companies with autologous therapies are using bone marrow harvest—for Baxter, a small dose at 50cc; for NeoStem, it is large at >300cc of bone marrow. Cytomedix is also using bone marrow to isolate ALDH bright cells. The use of adipose tissue (fat) by Cytori has come into focus as a rich source of cells that can be harvested via liposuction. More recently, Cardio3 Biosciences (private) uses bone marrow cells that have been treated with the cardiopoietic growth factors. These methods are all autologous—your own cells, but manipulated. Generally speaking, autologous methods are expensive as they involve offsite processing of the cells—in some cases, in cultures (expanded), and in other cases, enriched for a specific cell type. In the case of adipose stem cells, they are processed "while you wait" (on site in an hour or less), and at a very low cost of goods. But, in general the allogeneic cells have the lowest cost in the industry versus a custom-produced, offsite-manufactured product, which will likely have the highest cost of goods.

However, not all companies have strategies in place to move from clinical stages to commercialization. As we have mentioned, variability in any step of the process can lead to an immune response. This is true for manufacturing both allogeneic and autologous therapies.

For allogeneic companies, manufacturing will be a critical success factor. Mesoblast and Athersys both appear to have well placed manufacturing strategies. Mesoblast's clinical trial and commercial product are being produced by Lonza (Singapore), and we know that Athersys is also working with Lonza. Our understanding is that Lonza is now producing clinical supply for Mesoblast. As such, there is little concern in product manufacturing or "tech transfer," which has been accomplished. This is critical since variability in any step of the process can lead to an "immune reaction." We know that the Mesoblast cell line is a precursor MSC, is very potent, and is expanded, with tight controls in place. We also know that with Lonza, Mesoblast has developed certain strategic tax advantages that complement its manufacturing process, thinking ahead towards commercialization.

Athersys (also working with Lonza) has a robust process in place. Athersys is prepared to develop systemic high-dose therapy (cell doses> 1 billion). In this regard, Athersys believes it is in a strong position to treat certain conditions (GvHD and stroke) in which high-dose systemic therapy is needed to develop a consistent effect. From prospective of treatment, these products are truly "off-the-shelf" ready and can be delivered to the patient with no prior intervention. We expect COGS to be below $1,000 per dose.

We believe that Baxter has concerns regarding the treatment paradigm (autologous) and the cost of goods sold. Dendreon's problems have been keenly watched by major pharma and biotech companies that shun the concept of personalized autologous therapy. Once identified as candidates for therapy, patients need to have their cells extracted and processed. This process requires aphaeresis (single site), manufacturing at a central location (which is labor- and process-intensive), and a subsequent return to the clinical site for patient injection. We estimate this process at a commercial scale to be $10,000 per unit or higher.

We believe NeoStem has similar issues to Baxter. NeoStem utilizes an autologous selected bone marrow cell (CD34+), where CXCR4 is a chemokine receptor specific for stromal derived factor-1 (SDF-1). As such, these cells can home along an SDF-1 gradient to the infarct. The cells are delivered into the infarct related artery (IRA) with the hope that they then drive new blood vessel formation (positively impacting or arresting the progression of the infarct size). The product begins with approximately a 300 cc bone marrow aspirate (12 needle stocks, four pulls on each needle) and is then sent to the company's manufacturing plant, where the product is enriched for the presence of CD34+CXCR4+ cells. The turnaround time has a 72-hour window. The COGS are likely the highest versus the other companies mentioned, at commercial scale of at least $10,000 per unit.

Cytori is an exception to high COGS in autologous therapy. Cytori processes autologous cell locally—that is, patient samples processed on site at the hospital and then immediately delivered back to the patient. This is the Cytori process, in which patients undergo a modest liposuction and then cells are processed and returned. We estimate the COGS of this process to be a minimal $250-$500 per unit. We estimate the process time to be approximately one hour.

This drives us to our next conclusion: *If a single homogeneous cell therapy is proven clinically to be the best treatment modality in cardiovascular disease, than allogeneic wins over autologous based on cost of goods, off-the-shelf availability (no waiting or processing), high consistency (homogeneity gives MPC batch-to-batch consistency), and patient convenience. If heterogeneous is best, Cytori is ideally positioned.*

So what does all of this mean? NeoStem has said "autologous cells are safe," suggesting that allogeneic are not. We believe neither claim is true and both are misleading. We assert that, based on the available pre-clinical and clinical data, allogeneic cells are neither more nor less safe than autologous.

Allogeneic and autologous are two broad subtypes of cell therapy. Each company with allogeneic and autologous products uses different sources of cells—whether bone marrow, cardiac stem cells, reprogrammed bone marrow cells, or placental cells. These cells are all manipulated differently giving them variability. Hence, an immune response in Pluristem's placental-derived cells does not lead to a problem for all allogeneic cells, in our opinion. This is simply a Pluristem problem. So far, Mesoblast and Athersys have seen zero serious adverse events with their cells. Strong pre-clinical and clinical data—not just from Mesoblast and Athersys, but other companies and institutions—has shown that allogeneic cells are well tolerated in thousands of patients, efficacious, and, most importantly, safe. Autologous and allogeneic cells (we believe) act trophically and not directly. If this is true, and the cell types that companies like Mesoblast and Athersys are working with are potent and not immunogenic, than the allo companies have several strategic advantages.

1. Lower cost of goods
2. Off the shelf, readily available. No waiting for your cells.
3. No patient discomfort in any way, shape, or form.

Exhibit 4. Some of the approaches of public companies in cardiology and other indications

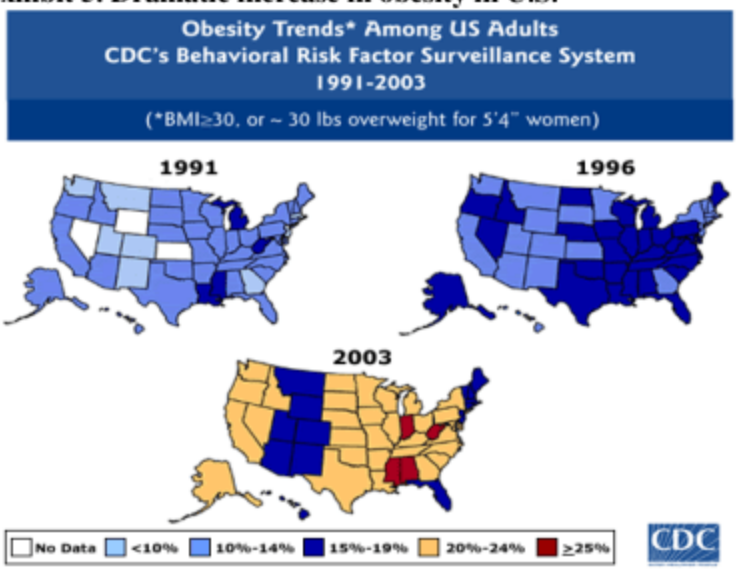
Company	Cell Type	Source	Type and COGS	Manufacturing	Development Status
Athersys	Multipotent adult Progenitor Cells (MAPC), expanded ex-vivio and highly enriched	Single Donor , Expanded in culture	Allogeneic-universal compatibility, LOW COGS	cGMP manufacturing able to produce millions of doses from a single batch of cells processed	Phase II trial for ulcerative colitis. Phase II trial for Stroke. Phase I proof of concenpt in MI completed
Baxter	CD34+ GCSF derrived Messenchymal stem cells	Adult peripheral blood	Autologous adult cells, High COGS	Validated industrial scale production, millions of doses of cells from a singel donor	Phase III trial in CMI
Cytomedix	ALDHR bright cells isolated from bone marrow	Adult bone marrow	Autologous adult cells, High COGS	cell type selected for ALDHbright. Cells are not expanded	Phase II trial for stroke
Cytori	Adherrent stromal cells (ASC) derived from adipose tissue, on site	Adipose tissue	Autologous adult cells, Low COGS	on-site in 60 minutes or less, minimal manipulation	Phase III trial in STEMI. Phase II in CMI
Mesoblast	Highly selected precursor MSC cells that are immune-priviledged and believed to be up to 10,000x potency than MSC's	Single Donor , Expanded in culture	Allogeneic-universal compatibility, LOW COGS	Large Production facility in Singapore where cells are expanded and tightly monitored for passages. Cell type selected with mAb technology	Large Phase III (n=1700) in CHF. Phase II in AMI
NeoStem	Bone marrow derived >300cc (invasive procedure) and processed with 72 hours life from harvest to return. Process enriches CD34+CXCR4+ cell type	Adult bone marrow >300cc	Autologous adult cells, High COGS	Cells are harvested from bone marrow for up to >300cc. Cells are processed over 24-72 hours and returned to patient. Cells are enriched for CD34+CXCR4+ cells	Phase II in STEMI
Osiris	MSC expanded ex-vivo	Single Donor , Expanded in culture	Allogeneic-universal compatibility, LOW COGS	cells from a single donation can be expanded to >10,000 doses, cGMP manufacturing	Phase III in steroid refractory GvHD. Phase II in AMI

Source: Maxim Group

Cardiovascular diseases. The World Health Organization (WHO) has labeled chronic disease the number one priority for this decade due to prevalence, health economics, and patient morbidity. In the U.S. alone, the American Heart Association (AHA) estimates that 80 million American adults (approximately one in three) have one or more forms of cardiovascular disease (CVD). According to our key opinion leader, Dr. Leslie Miller, CVD is associated with 1 million deaths, 1 million heart attacks, 400,000 strokes, and 350,000 sudden deaths in the United States each year. Worldwide, the problem magnifies. Saying CVD is a huge unmet need is an understatement. The economic costs are even more staggering, with $280 billion spent on CVD each year. Based on age prediction, costs are projected to triple to $850 billion by 2030.

Unfortunately, the future is not looking better, due to the increase in the risk factors associated with CVD, such as hypertension and obesity. According to the CDC, there has been a dramatic increase in obesity in the U.S. More than one third of adults and approximately 12.5 million children and adolescents are obese.

Exhibit 5. Dramatic increase in obesity in U.S.



Source: CDC and Dr. Leslie Miller, I[st]Regenereative Medicine Investor Day, April 17, 2013 New York City, NY

Heart failure. Heart failure occurs when the heart is unable to sufficiently pump blood to meet the needs of the body. Common causes of this heart disease include myocardial infarction, ischemic heart disease, diabetes, hypertension, and cardiomyopathy. According to Dr. Miller, it has been estimated that there are approximately 7 million and 20 million heart failure patients worldwide—and one-third of this population has advanced heart failure. Heart failure is considered advanced when conventional heart therapies no longer work.

The New York Heart Association (NYHA) classification system grades the severity of these symptoms on a I to IV scale. This provides a simple way of classifying extent of heart failure based on limitation on the physical activity and the symptoms during the activity such as breathing and angina pain. Patients with NYHA Class I have cardiac disease with no limitation on physical activity, while Class IV patients have severe limitations, even at rest. Basic heart-failure-related symptoms begin with shortness of breath, even at rest.

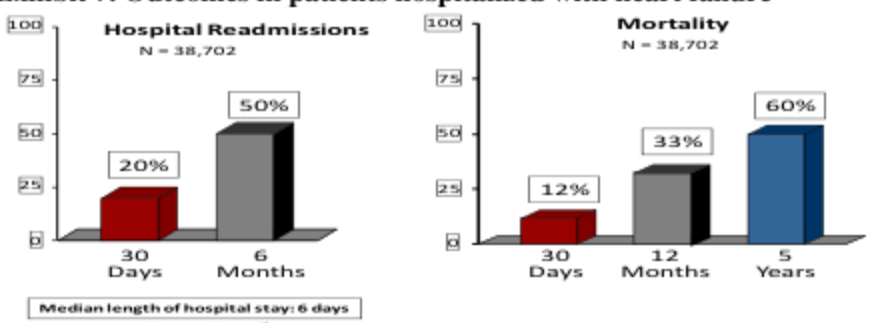
Exhibit 6. NYHA classifies patients based on their ability to do physical activity with the presence of physical symptoms

Class	Functional Capacity: How a patient with cardiac disease feels during physical activity
I	Patients with cardiac disease but resulting in no limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea or anginal pain.
II	Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea or anginal pain.
III	Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea or anginal pain.
IV	Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of heart failure or the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort increases.

Source: Maxim Group and AHA

Dr. Miller also talked about the global impact of heart failure, stating that there are more days spent for the care of heart failure than any other diagnosis. There are an estimated 7 million patients in the U.S. suffering from HF, and around 20 million worldwide. Of those 7 million patients, around 250,000-300,000 patients have advanced HF (Class III or IV). **There is no therapy for advanced HF**. There is nothing present today that changes the natural history of these patients. According to Dr. Miller, the incidence of new cases of advanced HF each year is rising sharply. These are patients who have become more refractory after being on defibrillators and other strategies. Once a patient has been admitted into the hospital for HF, there is a 20% chance they will be back in hospital in a month and a 50% chance in 6 months. Of these patients, 12% will die in a year and 60% in 5 years. This underscores the huge unmet medical need of CVD.

Exhibit 7. Outcomes in patients hospitalized with heart failure



Source: Dr. Leslie Miller, I[st]Regenereative Medicine Investor Day, April 17, 2013 New York City, NY

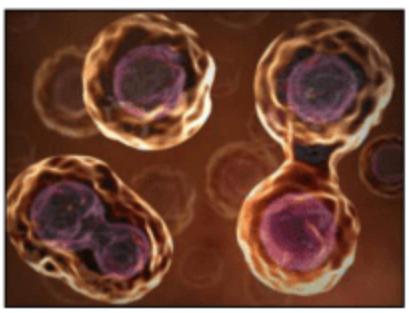
Dr. Miller mentioned that the pharmacological treatment paradigm for these patients is not adequate. The best drugs available in the market are ACE inhibitors, and they only have an absolute reduction in mortality of 2% per year. Dr. Miller referred to CVD as the graveyard of the pharmaceutical industry. Thirteen drugs have gone into phase III trials in the last 12 years without being successful. Treatments such as transplants are an alternative, but there were only 2,200 transplants in U.S. last year with a need of 25,000. Mechanical assist devices are not cost effective, especially if you consider the global impact of CVD. In addition, one of the central problems of pharmacological drugs is compliance, and almost 20% of patients drop out due to adverse events. Biologics, on the other hand, are cost effective, do not have a compliance issue, and are administered as a one-time treatment (making them an attractive therapy—albeit, only if they can show no cardiac death and HF-related hospitalization in trials).

There is a focus in cardiology with cell therapy. We believe that 2013 will be the year that we start seeing results from multiple late-stage PII trials and the start of pivotal programs. These trials are evaluating the use of stem cells as a therapeutic agent to either arrest the progression of heart disease or to reverse the disease state itself. The largest heart cell therapy trial ever undertaken is the endeavor of an EU consortium funded public trial, known as BAMI—a 3,000 person trial that will use bone marrow cells (autologous) injected into the heart five days post infarct. While BAMI is exciting, it is doubtful that this trial will be completed in a timely manner, in our opinion, and it's not clear how a therapy will be developed from the trial. The trial, however, is intended to prove that stem cells can repair and arrest the progression that typically follows severe heart attacks. The more interesting commercial trial we would focus upon is the Mesoblast (partnered with Teva) 1,700-patient global trial in CHF with allogeneic antibody purified bone marrow cells—mesenchymal progenitor cells (MPCs), or Revascor. MPCs are initially developed from a donor source, processed at a cGMP factor, fully tested for potency and safety, and cryopreserved so that they can be administered to the patient when needed, especially true in an acute setting. Teva's CEO Dr. Jeremy Levin has openly stated Teva's support and intention to move forward with this trial.

We believe Revascor has the potential to make the autologous approaches to heart failure and cardiac related conditions obsolete—*with a few exceptions (one of which may be Cytori).*

Mesenchymal—or human stromal—stem cells are non-hematopoietic progenitor cells that have the ability to transform into a variety of structural tissues in the laboratory. Although the precise signals necessary to direct cell differentiation to specialized cells are not known, placement of a precursor cell into the appropriate environment is believed to trigger the secretion of a number of cytokines (growth factors) that then exert an endogenous response, allowing the body to initiate the repair mechanisms. In our discussions with management, we have come to appreciate that these cells are in fact more potent than MSCs further downstream in the cell lineage. They are selected via unique expression of STRO-3, a surface marker only found in the earliest precursors of the mesenchymal lineage. These cells have multipotential capabilities. The resulting cell type is able to secrete potent cytokines that then allow an endogenous repair and regenerative response.

Exhibit 8. Human stromal cells



The MPCs act as micro-drug factories, providing the secretion of trophic factors that then exert multiple mechanisms of action including (but not limited to) anti-apoptosis (anti-death) of cells, anti-fibrotic, anti-inflammatory, and immunomodulatory, by shutting down specific T-cell subsets driving autoimmunity. As a result, the cells allow the regeneration of damaged tissue through the recruitment of the body's own tissue-specific precursor cells.

Source: Mesoblast

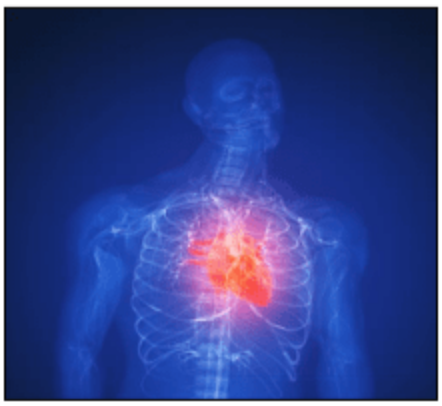
Congestive heart failure (CHF). The most recent statistics from AHA suggest that up to 6.6 million people in the United States suffer from heart failure, with an additional 670,000 new cases diagnosed each year. This is the No. 1 cause of mortality and hospitalization in the Western world.

CHF is a chronic condition characterized by an enlarged heart and insufficient blood flow to the extremities of the body. The condition develops over time and can be caused by many factors that put an excess demand on the heart muscle, including high blood pressure, incompetent valves, infections of the heart muscle or valves, or congenital heart problems. The heart itself becomes enlarged and the muscle walls thin.

Exhibit 9. An Enlarged Heart

Although patients are initially treated with drug therapy, the only current method of treating end-stage disease is a heart transplant or mechanical assist device. Only around 2,000 heart transplants are performed annually in the United States, leaving a large unmet medical need.

Mesoblast's target market is CHF patients in NYHA class II to IV with an ejection fraction of less than 35%. According to the company, the estimated market size in the United States alone is currently 2.5 million patients (41% of 6.2 million pre-existing sufferers), with 201,000 newly diagnosed (30% of 670,000) each year. Our estimates are slightly more conservative.



Clinical trial in CHF. The Phase II data was very strong for a small study, with significant p-values (which it was not powered to show) and, more importantly, "no deaths" in the treated group over a 30-month time frame.

The Phase II trial (n=60) was randomized, multi-centered, and placebo-controlled. The goal was to compare the safety and efficacy of three doses of Revascor on top of maximal approved therapies versus maximal therapies alone. Patients had to be classified as "moderate to severe," according to the New York Heart Association (NYHA) class II or III status, with ejection fractions below 40%. The trial enrolled both ischemic and non-ischemic heart failure patients.

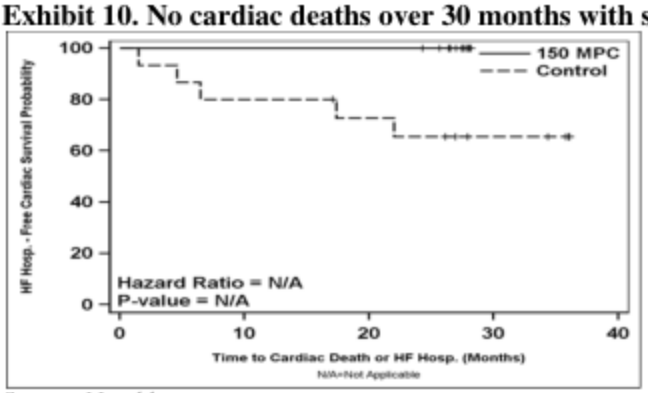
Source: http://www.cochrane.org/features/stem-cell-treatment-acute-myocardial-infarction

All patients were randomized 3:1; controls to MPCs at 25M, 75M, or 150M cell doses. Cells were locally injected using the NOGA Myostar catheter system in a single injection. The primary stated endpoint of the trial was safety and feasibility, which was met (meaning that there were no adverse events associated with MPCs at any dose and no clinically relevant immune responses to donor cells as reported by the company).

A single administration of MPC (150M cell dose) induced sustained improvement in heart-failure-related hospitalization and no cardiac death in the 30-month time frame. It is our understanding that three out of the 15 (20%) of the controls and six out of the 30 (20%) patients who received low (25M) or mid-range (75M) doses of MPC had either been hospitalized with heart failure or had died.

According to the FDA guidelines, the Phase III studies should use endpoints such as mortality and heart-failure-related hospitalizations rather than ejection fraction. Mesoblast was able to show both improvement in hospitalization and no cardiac deaths in a Phase II trial.

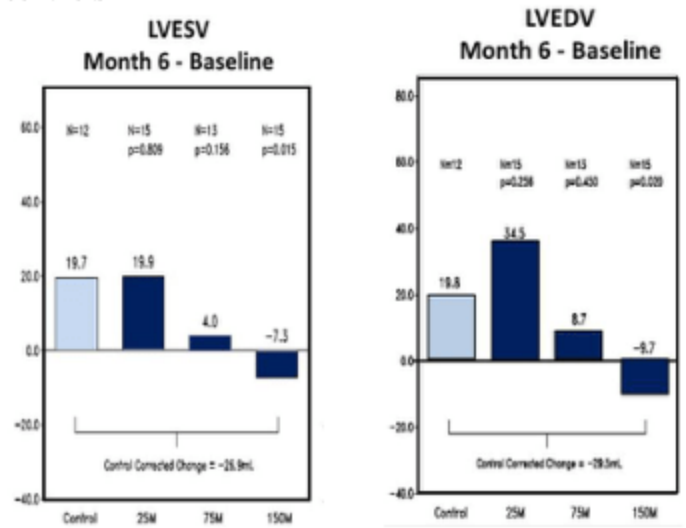
Exhibit 10. No cardiac deaths over 30 months with single administration of 150M MPC



Source: Mesoblast

In addition to no cardiac deaths, Mesoblast also looked at the surrogate markers' decrease in systolic and diastolic volume. Treatment with 150M cells resulted in decreases in systolic and diastolic volume changes, showing that the cells caused a remodeling of the heart tissue. Decreases in volume change translated to upstream results, no cardiac death, or HF-related hospitalization. In addition, there was an improvement in quality of life measures, such as six-minute walk over 12 months.

Exhibit 11. 150M MPC dose resulted in improved systolic and diastolic volume change compared to controls



Source: Mesoblast

Phase III with a partnership with Teva. A Phase III trial of Revascor will be evaluated to treat moderate to severe congestive heart failure patients. We anticipate the trial to be highly powered (N=1,700) and to take up to two years to enroll. Our assumption is 90% for a 10% difference in all-cause mortality. We believe the trial strategy here is twofold: 1. Run one global trial that is well designed and well powered, with accepted endpoints (mortality and hospitalizations); and 2. leverage the data base from that trial to leap-frog the product to other indications with smaller, faster follow-on trials.

Heart attacks – AMI. At the other end of the disease spectrum, Mesoblast is evaluating the MPC technology for the treatment of acute coronary artery disease and heart attacks.

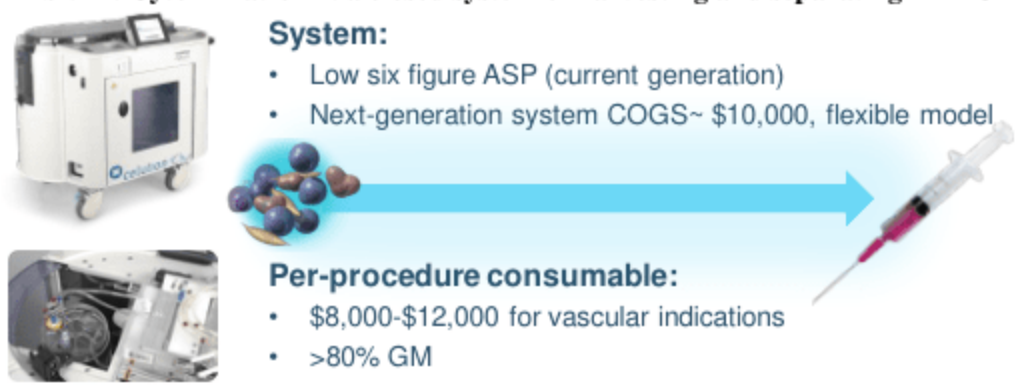
Mesoblast initially started with a 90-patient Phase II trial. Teva determined that the trial was not adequately powered, so Mesoblast and Teva increased the clinical trial to 225 patients. According to Mesoblast, Teva gave funds beyond contractual obligation for the expansion of this trial.

Being an allogeneic product, every emergency room in the country can have ready access to Revascor, and it can be used in conjunction with all the standard life-saving procedures, such as clot-busting and stent technologies, at the earliest and most effective time. As such, the treatment paradigm allows the interventional cardiologist to inject a small volume of liquid cells (a few cc) that contains the active dose right at the time of stent placement.

Manufacturing is critical. Mesoblast is emphatic that its manufacturing operation through Lonza is now ready to supply the clinical needs of a 1,700-person global CHF trial. We know that the Mesoblast cell line is a precursor MSC, is very potent, and is expanded, with tight controls in place. We also know that with Lonza (Singapore), Mesoblast has developed certain strategic tax advantages that complement its manufacturing process.

Cytori has an interesting product, since it is not being marketed as a cell therapy but more along the lines of a device pathway. From a patient's fat tissue, adipose-derived stem and regenerative cells (ADRCs) are isolated in less than one hour and injected back into the patient. The company plans to make the capital investment in the system below $100,000, allowing penetration of the machine in hospitals and clinics. The main driver of the revenue will be the consumables. This is a completely different strategy than any of the other cell based therapies in this space. Even though it's an autologous therapy, liposuction is viewed as "patient friendly." We do not believe that liposuction is a big deal, and it seems patients are actually excited to have it done. Get a love handle busted in the process of having your heart fixed.

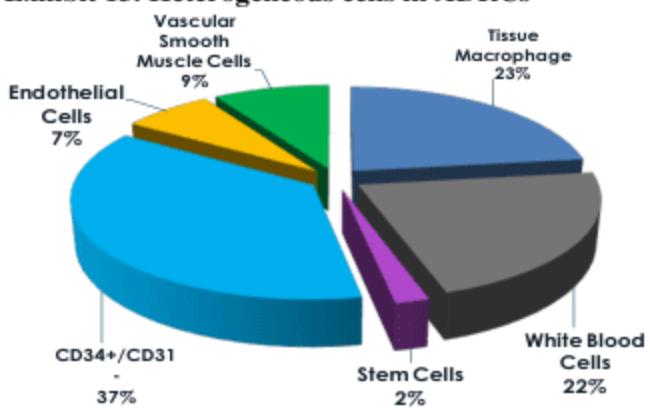
Exhibit 12. Cytori Platform: a closed system of harvesting and separating ADRC in an hour



Source: Cytori

ADRCs are a heterogeneous or mixed population of cells including adult stem cells, endothelial progenitor cells, leukocytes, endothelial cells, and vascular smooth muscle cells. Cytori believes this mixed population influences the local environment via immune modulation, secretion of trophic factors, and differentiation of stem cells.

Exhibit 13. Heterogeneous cells in ADRCs



Source: Cytori

Cytori is currently working with EU regulators to develop a label indication for Celution, a proprietary device which separates ADRCs from adipose tissue for the treatment of acute heart attack patients. Cytori is working in Europe (like in the United States) along a device pathway with a "notified body." Recall that in Europe, Celution is already approved for the reinfusion of cells treating tissue ischemia. As such, we believe that Cytori has a unique opportunity to win European approval based on one pivotal study (ADVANCE trial, N=216 patients) with preparations now underway and the first enrolled patient by Thanksgiving, according to our estimate.

Does the Cytori model make sense in the acute MI setting? We believe so. The initial ischemic event, a blockage in a blood vessel to a coronary heart artery, creates the ischemic crisis. The trauma-ER team knows that "the clock is ticking," and the goal is to unblock the artery and restore blood flow as soon as possible. Restoring blood flow, however, has its own sets of complications, such as reperfusion injury. Administering cells at the time in which the artery is unblocked may not be ideal. It may in fact be better to wait 24-72 hours. This allows patients to be evaluated at the 72-hour mark to see if they are recovering on their own, or if the heart is beginning to scar (become fibrotic) and lose tissue. Cytori's autologous cells and process fits this paradigm neatly. The cells can be administered at the 48-72 hour mark. The cells are safely harvested using liposuction, processed in under an hour, and returned via infarct related artery – all of this at a cost of goods that is similar to allogeneic products (sub $1,000). The cells (your own, or autologous cells) can then work to ameliorate the deleterious localized inflammation and, more importantly, fibrosis, as well as promote neo-angiogenesis in a longer-term integrated fashion.

APOLLO. Cytori's European clinical trial evaluated adipose-derived stem and regenerative cells (ADRCs) in patients with acute myocardial infarction (heart attack or AMI). APOLLO was a small trial (N=14-patient) that was a prospective, randomized, double-blind, placebo-controlled, feasibility trial. In the trial, all patients were treated with the standard of care and subsequently underwent an abdominal liposuction. Each patient's adipose tissue was processed by the Celution System. ADRCs were extracted, washed, and concentrated into a syringe of clinical grade cells. Within 36 hours of the myocardial infarction and no longer than 24 hours after undergoing percutaneous coronary intervention, patients received an injection of either 20 million ADRCs (n=10) or a placebo (n=4).

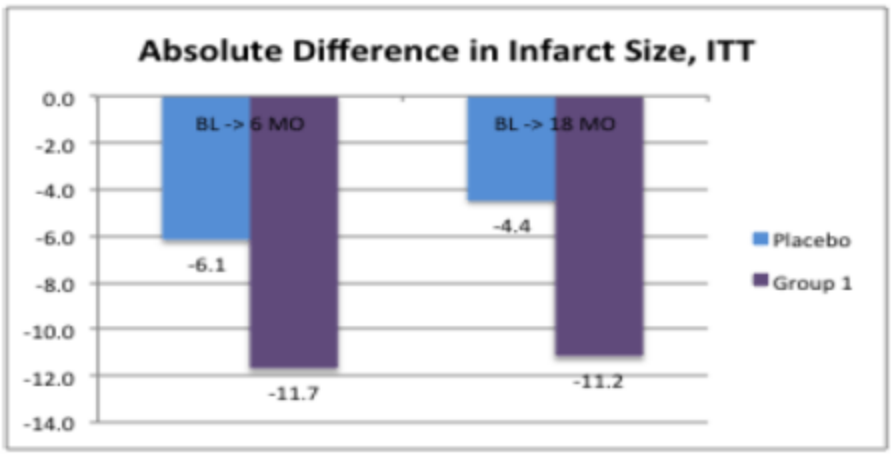
There is solid preclinical data showing efficacy of ADRC in myocardial infarction. In a porcine model, after induction of infarct, the cells were introduced in the infarct-related artery. The study concluded that the introduction of adipose-derived cells at the time of vessel reperfusion is feasible and improves ventricular function[6].

We believe that, mechanistically, the introduction of cells following the initial acute ischemic insult allows the cells to ameliorate the inflammatory response and subsequent fibrotic scarring, as well as promote the process of neo-angiogenesis through the SDF-1 gradient where an ischemic condition exists or is developing.

At both 6 months and 18 months in the APOLLO trial, treated patients showed a significant difference in infarct size. Infarct size correlates well with survival and adverse events. The results also showed through in ventricular arrhythmias.

[6] *International Journal of Cardiology*, ICJA 11698, "*The effect of freshly isolated autologous tissue resident stromal cells on cardiac function and perfusion following acute myocardial infarction.*[6]"

Exhibit 14. Differences in Infarct Size in the APOLLO Trial



Source: Cytori

In addition, the trial also showed an improvement as measured by SPECT, an improvement in blood flow into the heart muscle (perfusion defect), and a reduction in scar formation (infarct size).

Next Step: ADVANCE (a PIII registration quality study along the "notified body" pathway). This is a prospective, randomized, double-blind, European heart attack trial in up to 216 patients in up to 35 sites in the G5, Canada, Netherlands, and Poland. The accepted primary endpoint with regulators is reduction in infarct size, which has been shown to directly correlate with mortality benefit.

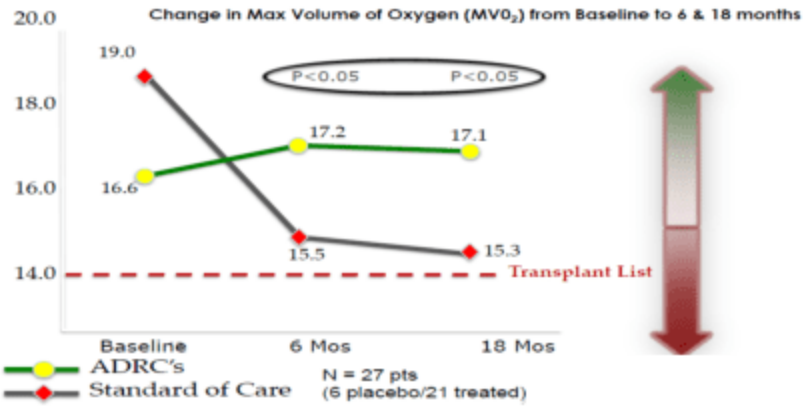
Chronic myocardial ischemia (CMI). Cytori completed the "PRECISE" trial in patients with CMI, a severe form of coronary artery disease. Primary six-month outcomes and longer-term 18-month data demonstrated safety and sustained improvement in cardiac functional capacity (MVO_2). Based on this data, in 2011 Cytori applied for approval in Europe to expand the Celution CE Mark (currently approved for general processing, breast reconstruction, and other soft tissue claims) to include patients with no-option chronic myocardial ischemia (CMI). A regulatory decision is expected this year.

In the United States, however, Cytori has enrolled the first patient in the U.S. FDA "Pilot" Phase II trial ATHENA. Our channel checks have been very positive and show that enrollment is strong. Given the small size of the trial (N=45), we believe the trial can be completed very quickly. Guidance is for approximately 2H-2013, but we believe Cytori may be able to do better, based on the interest in the trial and the high demand. Our understanding is that, on conclusion of the ATHENA pilot study, Cytori will need one modestly powered phase III trial provided that it has an acceptable endpoint with FDA and a p-value to be approved. This could put Cytori neck to neck with Mesoblast for having the first approved product in CVD.

Data from Phase I CMI Trial: A few key points. MVO_2 as a primary endpoint has been shown to correlate with survival[7,8]. These data validate that MVO_2 is a widely accepted measure for cardiac function in CMI patients.

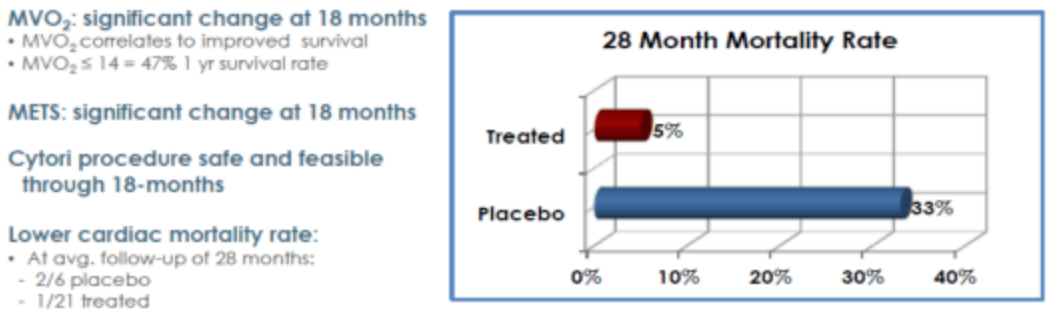
Exhibit 15. Improvement in MVO_2 in the treated group versus a deterioration in the control group.

[7]Mancini et al, "Value of Peak Exercise Oxygen Consumption for Optimal Timing of Cardiac Transplantation in Ambulatory Patients with Heart Failure" Circulation (1991) 83 (3)
[8]Mancini et. al. Peak $V0_2$, A simple yet Enduring Standard" Circulation (2000) 101:1080-1082.



Source: Cytori

Exhibit 16. Correlation of survival (treated vs. control)



Source: Cytori

Local autologous processing is when patient samples are processed on site at the hospital and then immediately delivered back to the patient. This is the Cytori process, in which patients undergo a modest liposuction and then cells are processed and returned. We estimate the COGS of this process to be a minimal $250-$500 per unit. We estimate the process time to be approximately one hour. We also note that adipose tissue appears to represent a more robust source of cells that are protected from the age factors (cell senescence)[9].

[9] Emerson C. Perin, MD, PhD and James T. Willerson, MD "Buying New Soul,"

Stroke: an unmet medical need and a blockbuster opportunity. The leading cause of serious disabilities and the third leading cause of mortality in both the United States and across the world is stroke. Approximately 800,000 people are victims of stroke annually in United States, as well as 15 million globally. The majority of these strokes (~85%) are ischemic strokes. According to Athersys, the economic impact of both direct and indirect costs of stroke on the United States is estimated at ~$73 billion annually (based on 2009 data). There is no argument that stroke represents a tremendous unmet need. With an aging population, the clinical need and commercial opportunity is expected to increase dramatically between 2010 and 2030 (and beyond).

A stroke occurs when blood flow to the brain is interrupted. This can occur due to either ischemia (lack of blood flow) caused by blockage (thrombosis, embolism) or a hemorrhage (rupture of blood vessel in the brain). Loss of blood in brain results in cell death, causing neurological deficit, which are usually unilateral (affecting one side of the body) and trigger the inability to move one or more limbs, understand, speak, or see on one side of the visual field.

Signs and symptoms. Stroke symptoms typically start suddenly and depend on the area of the brain affected. However, the first signs are typically sudden onset of facial weakness, arm drift, and abnormal speech. Usually, symptoms affect only one side of the body, depending on the part of the brain affected. The defect in the brain is usually the opposite side of the body.

Pathophysiology. The loss of blood supply to part of the brain results in ischemic stroke. This can either happen due to the narrowing of blood vessels (atherosclerosis) leading to a reduction of blood flow, formation of clots in the vessel, or by release of small atherosclerotic plaques (emboli) that lodge in and obstruct the brain's blood vessel. Depending on length of time, blood/oxygen deprivation of the brain could lead to irreversible injury and tissue death (infarction).

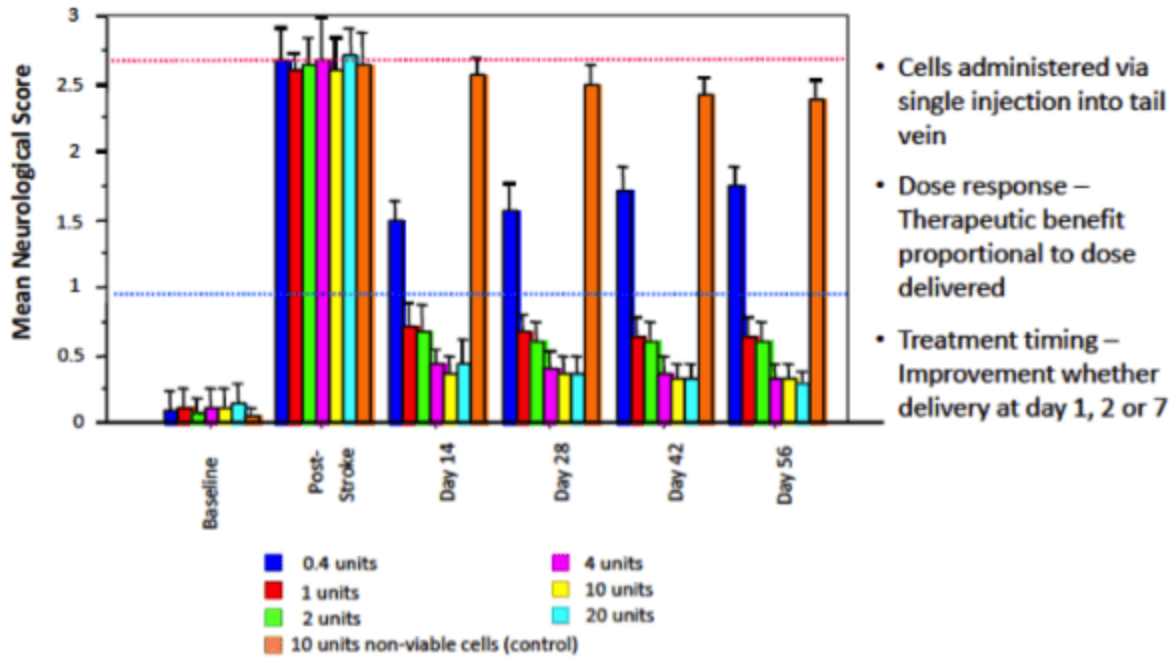
This concept is similar to what happens when we engage in an intense workout—our muscles are deprived of oxygen and resort to using anaerobic metabolism (without oxygen) for an energy source. This form of energy leads to fewer ATPs compared to aerobic metabolism, as well as the generation of lactic acid, an irritant that causes disruption in acidity of the microenvironment. Oxygen deprivation leads to a shorter amount of intense activity and lack of clearance of lactic acid leads to muscle pain.

The brain uses the most energy of any organ in the body and accounts for approximately 20% of the body's energy expenditures. Oxygen is the main supply for this energy; hence, upon oxygen deprivation due to inclusion, the brain uses less efficient anaerobic metabolism, leading to increased lactic acid accumulation and the inability to maintain microenvironment, resulting in cell death.

Treatment. The only approved viable therapy today is recombinant tissue plasminogen activator (rtPA). It has limitations, as it must be administered within three to four hours of the initial ischemic stroke. If administered after this time, it can cause or exacerbate cerebral bleeding (i.e. hemorrhage), resulting in a worsening of damage, or even death. As such, it is only actually used on ~5% to 8% of treatable patients.

Athersys' lead program is MultiStem, a patented and proprietary, non-embryonic stem cell product candidate that is produced by obtaining a special class of stem cells from healthy, consenting donors' bone marrow. Using cells obtained from a healthy consenting donor, millions of doses of MultiStem may be manufactured and stored in frozen form until needed. In contrast to traditional bone marrow transplants, MultiStem is administered like type-O blood, without tissue matching or immune suppressive drugs (i.e., an "off-the-shelf" product). In early trials, it has shown utility for treating a range of diseases and, as such, may have the potential for widespread application in the field of regenerative medicine, particularly in the cardiovascular, neurological, inflammatory, and immune disease areas.

Exhibit 17. Animals' neurological function increases with delivery of MultiStem day 2 post-stroke



Source: Athersys and Mays et al. (2010)[10]

Preclinical data. One area where Athersys shines is the quality of the science. In preclinical studies conducted to date, MultiStem has been well tolerated and has not required immunosuppression. MultiStem has also demonstrated impressive activity in rodent models of ischemic stroke. In a rat middle cerebral artery occlusion (MCAo) model of ischemic stroke, animals received IV delivery of 400,000 to 20 million MultiStem one day, two days, and seven days post-occlusion[10]. The extent of neurological deficit post experimentally induced stroke was evaluated according to the Bederson Composite Score. Administration of a single dose of MultiStem one week after an experimentally induced stroke led to substantial and durable therapeutic benefits across nearly all measures of neurological function, including mobility, strength, and fine motor skills. Interestingly, if delivered before or simultaneously, there was no effect[10]. The hypothesis is that the cells act on an inflammatory response—so if there is nothing to act on, the cells do nothing. In addition, Athersys was able to statistically show that treatment with MultiStem leads to expression of immunomodulatory proteins in brain cells, thus supporting its hypothesis that the therapeutic benefit is derived through reduction of inflammation and immune system modulation at the ischemic site, as well as the protection and rescue of injured neurons.

Athersys believes that, beyond the initial ischemic event, a host of secondary events cascade through the body. These include maturing T-cells that migrate to the damaged areas of the body (in this case, the brain). This effect has been shown in multiple animal models, where a dramatic reduction in spleen size is seen in mice post stroke or other acute neurological injury, while splenectomy reduces infarct size (although this creates a state of permanent immune depletion). As a consequence, the inflammation results in the loss of healthy tissue that might have otherwise been saved (e.g. due to cellular apoptosis). It also creates scar tissue, which effectively walls off the area of the stroke. It becomes impossible then for neurons (which have retracted) to penetrate this wall. The inflammatory response and the role of the spleen is a key part of the disease mechanism. In fact, the acute over-production of inflammatory immune cells often leaves patients vulnerable to infection, which is a major post-stroke complication. The administration of MultiStem appears to play a significant role in preserving spleen function, by both downregulating the

[10] Mays et al., Development of an allogeneic adherent stem cell therapy for treatment of ischemic stroke. JESTM (2010), 3(1):34-36

initial inflammatory response and allowing the spleen to later fight infection-related complications that may have occurred as a result of the initial trauma or traumatic brain injury (aka: car accident, explosion) that caused the event. Since inflammatory cells mobilize over several days, there is a longer therapeutic window for Athersys. Furthermore, Athersys and its collaborators have shown that MultiStem induces an escalation in reparative cell populations, such as regulatory T cells and M2 macrophages.

How might MultiStem work? According to data, MultiStem expresses proteins and other factors involved in tissue repair and immune system regulation and acts through multiple mechanisms, such as **protecting damaged or injured cells, reducing inflammation, and promoting new blood vessel formation** in areas of ischemic injury.

Clinical trials: Phase II. Athersys has already completed other clinical trials using MultiStem, showing a clean and consistent safety profile. In addition to its other clinical programs, Athersys is conducting a placebo-controlled trial for ischemic stroke that will involve ~140 patients. The trial began in 4Q11 and is currently in multiple active U.S. sites (a total of 25 are planned). The trial (based on DSMB findings) is now focusing on the high-dose group. Entry criteria for patients is those who have suffered an ischemic stroke [who have suffered a moderate to moderately severe stroke, as defined by a National Institutes of Health Stroke Scale (NIHSS) score of 8 to 20], within the prior one to two days. Patients will receive MultiStem intravenously versus the control (placebo). We also note that, unlike its peers, Athersys is able to deliver a very large dose (> 1 billion cells) because of the efficiency, scalability, and cost effectiveness of the MultiStem production process. In addition to the ability to treat acute stroke patients in a simple manner (i.v. administration) and within a clinically practical time frame, we believe the manufacturing advantage is a major differentiator in the competitive landscape. The study is double blinded (blind to both doctors and patients).

In summary: cardiovascular and related indications. We believe the application of cell therapy in heart disease may represent one of the greatest opportunities in medicine and a way to preserve life and create economic value. There are now multiple late-stage trials underway. These include trials from Baxter, Mesoblast, and Cytori. All of them are in or about to start their pivotal march towards the finish line.

- Athersys: Allogeneic. A phase I trial of MultiStem is completed, and the company is ready to start a phase II trial (based on funding). The cells in the phase I study were delivered via catheter directly into the damaged region of the heart following percutaneous coronary intervention in patients post AMI. The data showed encouraging improvements in all metrics.

- Capricor: Allogeneic. The ALLSTAR Phase I/II trial is in myocardial infarction. Capricor believes the barrier to entry with allogeneic stem cells is lower, with headway made by Mesoblast and others showing that these cells are immunologically inert. The Phase I trial will enroll 42 patients with expectation of a larger 260-patient Phase II trial in the second half of the year.

- Mesoblast: Allogeneic. A phase III trial (n=1,700) is expected this year in CHF. In a phase II trial, Revascor delivered via coronary artery infusion using a standard catheter, after angioplasty and/or stent implantation following a heart attack. Revascor consists of allogeneic mesenchymal precursor cells, which secrete trophic factors that promote healing. Mesoblast believes these cells are much more potent than MSCs found later in the lineage, such as CD34+ cells. The trial data showed no deaths in the treated arm out to three years and was significant (P values) between the active and control arms.

- Osiris: Allogeneic. A phase II trial of Prochymal for the repair of heart tissue following a heart attack. Prochymal is an allogeneic, bone-marrow-derived mesenchymal stem cell population. We note that prochymal was approved in Canada in May 2012or GvHD. Currently, Osiris does not appear to be focused on cardiology.

- Baxter: Autologous. We understand that Baxter is in a large phase III trial in CMI. Baxter uses GCSF to mobilize stem cells into the peripheral blood, where they are then sent to the factory for processing and enrichment for CD34+ content. Cost of goods is high and, as such, we are concerned that if an equivalent but cheaper product (Cytori or Mesoblast product) works, it has the potential to make the Baxter product obsolete.

- Cardio3 Biosciences: Autologous. The CHART-1 trial is a phase III trial to treat CHF in Europe. The company expects to obtain IND approval by mid-2014 for the phase III trial in the United States.

- Cytori: Autologous: The "ADVANCE" trial is now enrolling. It is an EU pivotal trial, investigating the Celution System for AMI. In addition, the company has begun enrollment in the ATHENA trial. ATHENA will investigate the use of the Celution System to treat chronic myocardial ischemia (CMI).

- NeoStem: Autologous: A phase II trial in AMI. Cells are harvested at days 4-6, if patients' ejection fraction has not recovered; 300cc of marrow are collected, processed, and enriched for CD34+ cells. Like Baxter, the cost of goods is high, and the harvest of cells (>300 cc bone marrow) may be problematic for many patients. As such, we are concerned that if an equivalent but cheaper product (Cytori or Mesoblast product) works (and less invasive), it has the potential to make the Baxter product obsolete.

DISCLOSURES

To receive full disclosures for the companies under Maxim Group coverage that are mentioned in this report, please send your request to: Maxim Group c/o Todd Klein, 405 Lexington Avenue, 2nd Floor, New York, NY 10174

I, **Jason Kolbert**, attest that the views expressed in this industry research report accurately reflect my personal views about the subject security and issuer. Furthermore, no part of my compensation was, is, or will be directly or indirectly related to the specific recommendation or views expressed in this research report.

The research analyst(s) primarily responsible for the preparation of this research report have received compensation based upon various factors, including the firm's total revenues, a portion of which is generated by investment banking activities.

DISCLAIMERS

Some companies that Maxim Group LLC follows are emerging growth companies whose securities typically involve a higher degree of risk and more volatility than the securities of more established companies. The securities discussed in Maxim Group LLC research reports may not be suitable for some investors. Investors must make their own determination as to the appropriateness of an investment in any securities referred to herein, based on their specific investment objectives, financial status and risk tolerance.

This communication is neither an offer to sell nor a solicitation of an offer to buy any securities mentioned herein. This publication is confidential for the information of the addressee only and may not be reproduced in whole or in part, copies circulated, or disclosed to another party, without the prior written consent of Maxim Group, LLC ("Maxim").

Information and opinions presented in this report have been obtained or derived from sources believed by Maxim to be reliable, but Maxim makes no representation as to their accuracy or completeness. The aforementioned sentence does not apply to the disclosures required by NASD Rule 2711. Maxim accepts no liability for loss arising from the use of the material presented in this report, except that this exclusion of liability does not apply to the extent that such liability arises under specific statutes or regulations applicable to Maxim. This report is not to be relied upon in substitution for the exercise of independent judgment. Maxim may have issued, and may in the future issue, other reports that are inconsistent with, and reach different conclusions from, the information presented in this report. Those reports reflect the different assumptions, views and analytical methods of the analysts who prepared them and Maxim is under no obligation to ensure that such other reports are brought to the attention of any recipient of this report.

Past performance should not be taken as an indication or guarantee of future performance, and no representation or warranty, express or implied, is made regarding future performance. Information, opinions and estimates contained in this report reflect a judgment at its original date of publication by Maxim and are subject to change without notice. The price, value of and income from any of the securities mentioned in this report can fall as well as rise. The value of securities is subject to exchange rate fluctuation that may have a positive or adverse effect on the price or income of such securities. Investors in securities such as ADRs, the values of which are influenced by currency volatility, effectively assume this risk. Securities recommended, offered or sold by Maxim: (1) are not insured by the Federal Deposit Insurance Company; (2) are not deposits or other obligations of any insured depository institution; and 3) are subject to investment risks, including the possible loss of principal invested. Indeed, in the case of some investments, the potential losses may exceed the amount of initial investment and, in such circumstances, you may be required to pay more money to support these losses.

ADDITIONAL INFORMATION IS AVAILABLE UPON REQUEST