

## On the Front “Lines:” The Quest for Stem Cell Products

Since the first pluripotent (multiple potential) stem cells were isolated from a human embryo in 1995, the promise of stem cell technology has been a hotly discussed topic. Stem cells have the remarkable ability to divide, without limit, into many different types of cells. Consequently, stem cells could be used, at least in theory, to repair tissue or replace damaged cells that cannot be replenished on their own. Proponents argue that stem cells could have a host of applications, from generating neurons to rebuilding damaged heart tissue, and that they could one day provide cures for diseases such as Parkinson’s disease, diabetes, cystic fibrosis, and multiple sclerosis.

From an investor’s perspective, many of these applications are wishful thinking today, but in decades ahead, hold the promise of becoming actual products. Along the way, companies will need to resolve numerous issues, including product regulation, production facilities, reimbursement, patentability, and optimal business models for product development and dissemination.

A variety of cell therapy products have their origin in adult or embryonic human stem cells. Many are related to the formation, regeneration, or repair of injured, malfunctioning, or missing tissue. Other possibilities for future products are different forms of tissue engineering, some of which could have cosmetic as opposed to medical applications. Potential stem cell products can be classified into three broad categories:

- *Transplantation:* Two future uses of stem cell technology include introducing stem cells into a heart after a heart attack to regenerate new muscle cells and blood vessels, or forming new beta cells in the pancreas to create insulin-secreting capacity in diabetic patients. The timeline for taking these products from development to the market is, at a minimum, five to ten years, given their newness to both the companies that develop them and the authorities that regulate them. Several companies are currently exploring these kinds of products, including StemCells Inc., Geron Corp., Osiris Therapeutics Inc., and ES Cell International.

- *Neurogenesis/pharmaceutical approaches:* Products within closer reach include those using neurogenesis or other pharmaceutical approaches to producing new cells. While these techniques harness the power of stem cells, they do not involve transplanting stem cells, relying instead on small molecules or recombinant proteins to trigger new tissue regeneration in diseased tissue. For this method to work, some adult and functional stem cells must still be present in the diseased tissue. Companies such as Sweden’s NeuroNova AB are already planning for clinical trials on different indications using neurogenesis.

- *Screening:* Another application in this group of products is developing and commercializing methods to isolate stem cells with favorable properties, for example, bone marrow transplants. Cellerant Therapeutics Inc. is already in the clinical development stage of this application. Viacell Inc. has developed products to preserve already isolated stem cells for future use. Other companies on the market with stem cell screening products include Cellartis AB, VistaGen Therapeutics Inc., and StemCell Sciences Ltd.

From Singapore to Sweden and Sweden to Scotland, companies are making progress in developing techniques to improve this science. Singapore-based ES Cell International is a provider of products and technologies derived from human embryonic stem cells. Sweden’s NeuroNova AB is using stem and progenitor cells to develop novel drug therapies for Parkinson’s disease, Alzheimer’s disease, stroke, and depression. Cellartis AB, also from Sweden, is providing stem cells to clients through a patented transportation method to protect the delicate cells. Stem Cell Sciences of Scotland has centers in the UK, Australia, and Japan, and is focused on technologies to grow, differentiate, select and purify embryonic stem cells. In the United States, the San Francisco Bay area is home to many stem cell companies, including VistaGen, Geron, and StemCells. Osiris Therapeutics of Maryland has just received FDA clearance to begin the first clinical trial for adult-derived stem cells in humans

to determine their effectiveness in treating injured tissue for knee surgery patients.

Since some forms of stem cell research involve using human embryos, the field has generated ethical and religious controversy. The regulatory and legal response to these issues has been different in the United States and EU—with potential consequences for the evolution of their respective sectors.

In August 2001, the Bush Administration limited U.S. federal government funding of human embryonic stem cell research to cell “lines” in existence at the time. The number of viable lines turned out to be far fewer than originally anticipated, and in 2004, several U.S. states stepped into the breach by setting aside funds for stem cell research.

Many European countries, on the other hand, have long had clearer regulations on stem cell research. Sweden has had laws governing research on fertilized eggs since 1991, and the legal framework is uniform across universities and companies. The permissiveness of the regulatory environment differs across member states—Germany, for instance, has stronger restrictions on embryonic stem cell research. The European Parliament recently announced that it will apply the “subsidiarity principle” in connection with embryonic stem cell research, which means that the EU will not directly fund such research because of restrictions in some member states.

The uncertain regulatory environment in the United States increases risk for investors in this sector. The restrictions placed by the Bush Administration have led to forecasts that other regions will take the lead in developing products from stem cell research, and it is no coincidence that some of the top companies in this sector are located in Europe and Asia. However, the recent funding initiatives in California and other U.S. states have changed the game, and 2005 should see heightened competition for leading scientists on both sides of the pond. The battle “lines” have been drawn, and things are starting to get interesting. ■