

The stem cell therapy market picking the winners

Stem cells. The combination of these simple words conjures up a variety of emotions, from miracle cure to moral outrage. President Obama's Executive Order in March 2009 freed up federal dollars for some limited research on human embryonic stem cells, but the debate rages on. Rising above these controversies, the adult stem cell space is being hailed as the next multi-billion dollar market.

Adult derived stem cells (such as mesenchymal stem cells) have been studied in the clinic for a number of years and are now arguably ripe for commercialisation, but large pharmaceutical companies have only recently woken up to the prospect that a wonder drug to treat symptoms is not what we want. We want a cure. Instead of drugs for life following heart failure or other currently incurable diseases, we could have stem cell therapies that repair the tissues so that drugs are not needed.

At the beginning of 2009, Geron Inc. was the first biotechnology company to get approval from the regulators to commence Phase I studies, which meant it could start injecting living cells, as cell therapy, into the damaged spines of people suffering total paralysis from the chest down. Although it is still some 10 years away from commercialising a spinal cord treatment, the company was courted by GE Healthcare, who announced an alliance in July 2009.

With Pfizer announcing that it will invest up to \$100 million in regenerative research, what can we expect from big pharma in the stem cell therapeutic arena? Some claim that within the next five years, it's quite possible that physicians could come into routine possession of a remarkable new set of tools. The tool kit is autologous stem cells, derived from the patients themselves or

from adult stem cells, amplified in culture, and infused back into the patient according to a precise protocol. But the development of these new therapies, in the US at least, has been thwarted by the regulators. The FDA contends that if one cultures stem cells at all, regardless of the use of those cells, then it amounts to a prescription drug. Cynics are already arguing that regulators could be working to protect the interest of big pharma, whose \$60 billion drug and device care market is threatened by a \$6 billion stem care market. The opportunity-cost in terms of morbidity and mortality claimed by the supporters of autologous stem cells while the regulators procrastinate could be catastrophic, if accurate. Equally, the consumer may be less likely to attend a regenerative medical clinic if the products and procedures are not tried, tested and regulated for safety and efficacy. Maybe this is why so many clinics have emerged, yet so few, if any, products are truly regulated, reimbursed and marketed. Nevertheless, over 200 clinical trials are now registered.

The frontrunner in the adult stem cell space is Osiris Therapeutics, with its principal biologic drug candidate, Prochymal. The drug is in Phase III clinical trials for three indications, including acute and steroid refractory Graft versus Host Disease (GvHD), Crohn's disease



and for the repair of gastrointestinal injury resulting from radiation exposure, and is the only stem cell therapeutic granted both Orphan Drug and Fast Track status by the FDA. So the cynics could be silenced if the product is successful and approved. It is also much closer to market than embryonic stem cells. Osiris Therapeutics recently signed a partnership with Genzyme Corporation to develop two late-stage adult stem cell therapies, creating yet another alliance in this space.

One could argue that such a promising commercial market for adult stem cells is spurning other entrepreneurial companies such as Neostem Inc., who claim to be the first to provide adult stem cell collection and storage services to the general adult population, keeping them safe in case of future therapeutic need. After all, adult stem cells have been in use for at least 40 years, treating blood cancers through bone marrow transplant. So why not keep them in storage for wound healing, bone reconstruction treatments, lupus, multiple sclerosis, scleroderma, cancers, diabetes, heart disease, and so on?

However, the jury is still out as to whether this is a good business model as there are still several fundamental limitations. Adult stem cells are often present in only minute quantities, making them difficult to isolate, purify and scale up to an effective dose. Additionally, adult stem cells may contain more DNA abnormalities caused by sunlight, toxins, and errors in making more DNA copies during the course of a lifetime. But despite these limitations, adult stem cell therapy still presents itself as the near-term multi-billion dollar market with potential regulated products.

So, who would pay for the treatment? Currently, it is a treatment of last resort for those who can drum up the money. When the efficacy is shown in clinical trials, no doubt the health economics will define how it could be reimbursed, but managing the health

economics is hugely different from managing the risk to back or invest in emerging and nascent stem cell therapy companies. At the moment, there are only a limited number of stocks which are either pure plays or semi-pure plays in the stem cell industry, and crucially they are often grouped together with no distinction between adult or embryonic. Additionally, it's important to note that, while Obama's lifted ban on federally-funded embryonic stem cell research has helped to focus attention on the whole subject of stem cell-based therapies, it also includes iPSCs (induced Pluripotent Stem Cells derived from a skin biopsy), a whole new area of opportunities that pharma companies are seizing for drug discovery. Investors should heed the differences. Robin Young, a medical industry analyst from RRY Publications, estimates that gross sales of adult cellular therapies will be well over \$100 million in the US half way through 2009. Some analysts suggest that stem cell therapy revenues could grow to \$8.2 billion by 2018.

So with the promise of such a big market, how do you pick the winners and manage your investment risk? Should it be stem cell-based therapies manufactured, bottled and stacked in hospital freezers, or a tool kit derived from the patients' cells themselves, amplified in culture and ready to be infused back into them? Understanding the whole process and where the weak links are in either of the two approaches will minimise the risk.

The debate will continue to rage on and the combination of the two words will fuel mixed emotions for a while yet. But just like IVF, organ transplant or the first antibody-based therapeutic, when shown to save and improve lives and cure illnesses safely and at reasonable cost, the debate will turn to who pays and who is going to make money out of it.

Elizabeth.Hill@CambridgeConsultants.com

