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StemCells

& Regenerative Medicine Congress

Top 15 most promising cell therapies

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The future of stem cell therapies is very promising. Clinical attrition is decreasing, manufacturing scale-up strategies are more efficient than ever, and the logistics and supply chain frameworks for this sector are much more effective now than they were a few years ago.

We spoke to approximately 200 representatives from this field, and they were all optimistic about stem cells, and were especially excited about the increase in successful clinical data that they see on the horizon.

We were inspired by these conversations with industry, and decided to share them with you in the format of this report – the top 15 most promising cell therapies. Enjoy!

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Selection criteria

This ranking is based on research conducted with leading biotechs, developing stem cells, cell and gene therapies, as well as with government, universities and research institutions.

The selection criteria included:

- Recent successful clinical data
- Effective capital formation strategies
- Stock history
- Awareness across different markets
- Personal recognition

Did we miss anyone? Let us know – we value your feedback!

Ixmyelocel-T

- Product:
  - Ixmyelocel-T selectively expands mesenchymal cells, monocytes and alternatively activated macrophages, up to several hundred times more than the number found in the patient's bone marrow, while retaining many of the hematopoietic cells collected from only a small sample (50ml) of the patient's bone marrow.

- Indications and development stage:
  - Critical Lim Ischemia – Phase 3 (Fast Track & Special Protocol Assessment)
  - Dilated Cardiomyopathy – Phase 2b (Orphan Designation)

There is enormous therapeutic potential for ixmyelocel-T based on its multicellular composition and the promising results in the treatment of ischemic or damaged tissue demonstrated in preclinical and clinical studies conducted to date.

Prochymal

- Product:
  - Mesenchymal stem cells (MSCs) have the capacity to form a variety of highly specialized cell types including bone, cartilage, muscle, tendon, fat, liver and many others.

- Indications and development stage:
  - GvHD – Phase 3 (FDA Fast Track)
  - Crohn's Disease – Phase 3 (FDA Fast Track)
  - Acute Radiation Syndrome – Phase 3 (FDA Animal Rule)
  - Type 1 Diabetes – Phase 2
  - Acute Myocardial Infarction – Phase 2
  - Pulmonary Disease – Phase 2

Prochymal has been showing consistent and promising data among the different indications, and is also unique because it is the only stem cell therapeutic currently designated by the FDA as both an Orphan Drug and Fast Track product.

ABH001

- Product:
  - ABH001 initiates healing and reduces the wound surface area of selected stalled, chronic cutaneous wounds associated with generalized EB.

- Indications and development stage:
  - Epidermolysis Bullosa (EB) - Phase 3 in US (Fast Track)

Last February, Shire announced the beginning of phase 3 trials for its EB candidate ABH001. This therapy is being recognized for its advanced stage and for being a multi-site, prospective, randomized, open-label, intra-subject controlled trial evaluating the efficacy and safety of ABH001. The therapy will initiate healing and reduce the wound surface area of selected stalled, chronic cutaneous wounds associated with generalized EB.

Cx601

- Product:
  - Cx601: an adipose derived allogeneic stem cell suspension.

- Indications and development stage:
  - Complex perianal fistulas (Crohn's disease) - Phase 3 (Orphan Designation)

With ChondroCelect's increasing sales revenue (+55% over Q1 2012) and new reimbursement agreements in other European markets, TiGenix is in a position where its positive cash flow are supporting the development of Cx601, with an enrolled phase 3 trial. Final results of the trial are expected in H2 2014, and, if positive, will allow the Company to file for marketing authorization with the European Medicines Agency.

Mesenchymal Precursor Cells (MPCs)

- Product:
  - The placement of a precursor cell into the appropriate environment primarily results in the secretion of a number of cytokines or growth factors that then exert an endogenous response, allowing the body to initiate the repair of itself.

- Indications and development stage:
  - Hematologic malignancies – Phase 3

Patients who received hematopoietic cells, from cord blood expanded by Mesoblast's MPCs, showed 100-day patient rates of 80%. The market size for this therapy is pretty big as it can benefit more than 20,000 allogeneic, or unrelated donor, bone marrow transplant procedures currently performed worldwide, apart from so many others patients who cannot find a match.

StemEx

- Product:
  - StemEx is a graft of stem/progenitor cells isolated and expanded from a portion of a single unit of umbilical cord blood (CBU) and transplanted in combination with non-expanded cells from the same unit.

- Indications and development stage:
  - Hematological Malignancies - Phase 3

Phase II/III results show that a StemEx transplant improved survival rate. The analysis of this primary endpoint shows 15.8% 100-day mortality in the StemEx group and 24.5% in a contemporaneous control group that received double cord blood transplant (DCBT) back in 2006-2010. Gamida Cell has a strong partnership with Teva for the development of StemEx and together, they are already sourcing a partner for the commercialization of the therapy.

SPD606 (Lifitegrast)

- Product:
  - SPD606
- Indications and development stage:
  - Dry Eye Disease – Phase 3

Shire is betting hard on the clinical success of its DES candidate. The SARcode acquisition was made in December 2012 and the therapy's phase 3 trials headline data is expected for mid 2014.

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Placental Expanded Cells (PLX-PAD)

Pluristem Therapeutics Inc.

- Product:
  - PLX cells act by secreting therapeutic chemokines, cytokines and growth factors in response to signals produced by inflammatory and ischemic conditions within the body.

- Indications and development stage:
  - Critical Limb Ischemia (IC) – phase II
  - Intermittent Claudication (CLI) – phase II/III

PLX-PAD is a placental-derived mesenchymal-like adherent stromal cell product for patients afflicted with both IC and CLI. Based on encouraging results of two phase I/IIa that indicated PLX-PAD's safety and potentially effective, Pluristem is already enrolling for IC's phase II and CLI's phase II/III trials. Another convincing point of the therapy is that its pre-clinical trial results showed significant improvement in the recovery of white blood cells, red blood cells and platelets in bone marrow deficient animals compared to controlled animals.

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Lenti–D

bluebirdbio™

- Product:
  - Our gene therapy process involves inserting genetic material into the patient's own cells ex vivo, then re-introducing the cells to the patient.
- Indications and development stage:
  - Childhood Cerebral Adrenoleukodystrophy (CCALD) – Phase II/III

Lenti-D is Bluebird's most advanced product candidate. The company has already raised $134 million since 2010 and is planning an IPO expected to raise another $86.2 million. This shows investor confidence in the product. Lenti-D was granted orphan drug designation by both the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) in 2012.

Chondrogen

- Product:
  - Regeneration of the meniscus and prevention of osteoarthritis in the knee.

- Indications:
  - Osteoarthritis (OA) – Phase 2

After the amicable end of a strong and productive partnership with Genzyme, Osiris regained the rights over one of its most promising therapies under development. In phase I/II trials two different dose levels of Chondrogen were evaluated, and the pain sores improved from six months to one year following treatment. This suggests Chondrogen caused a biological modification of OA.

Multistem

- Product:
  - Multistem is a biologic product that is manufactured from human stem cells obtained from adult bone marrow or other nonembryonic tissue sources.

- Indications and development stage:
  - Inflammatory Bowel Disease – Phase 2
  - Ischemic Stroke – Phase 2

MultiStem is Atherys's patented stem cell product. It consists of a special class of human stem cells that have the ability to express a range of therapeutically relevant proteins as well as form multiple cell types. This is why it can serve to treat multiple diseases in cardiovascular, neurological, inflammatory and immune therapeutic areas. The two most advanced MultiStem candidates are for Inflammatory Bowel Disease , which is being developed in partnership with Pfizer, and Ischemic Stroke. As the company prepares to scale-up manufacturing, upcoming trials appear very promising.

Endometrial Regenerative Cell

- Product:
  - The endometrial regenerative cell (ERC), is a “universal donor” stem cell derived from the menstrual blood that possesses the ability to differentiate into nine tissue types, produce large quantities of growth factors, and a large proliferative capacity.

- Indications and development stage:
  - Congestive Heart Failure – Phase 2

MediStem has a double blind, placebo controlled clinical study in patients with end stage heart failure. ERCs were administered via the Medistem’s patent-pending minimally invasive procedure. To date, 14 patients have been treated with no adverse effects demonstrating feasibility of the administration procedure, as well as safety of the cells. Because it is a double blind study, efficacy will not be known until the trial is completed. The potential of this therapy is reinforced by an independently verified and published peer reviewed article by the NIH in 2012. This confirms that ERC possesses a markedly higher expression of genes associated with new blood vessel formation and stem cell potency compared to bone marrow mesenchymal stem cells.

AMR–001

- Product:
  - AMR-001 is an autologous bone marrow derived, CD34 positive selected stem cell product that limits the damage of heart muscle that develops following AMI and, thus, has the potential to limit ventricular remodeling.

- Indications and development stage:
  - Post-AMI preservation of cardiac function – Phase 2

Amorcyte's lead product, AMR-001, for the prevention of major adverse cardiac events following acute myocardial infarction (AMI), has completed Phase I clinical trials. It demonstrated feasibility, safety and biologic activity at a threshold dose. This is the first prospective stem cell trial in AMI ever conducted that has established a significant relationship between dose and effect. The company has now enrolled for a Phase II trial to investigate AMR-001's efficacy in preserving heart function after a heart attack. Given its multiple cardiac applications and successful data so far, AMR-001 could not be disregarded from this ranking.

RGN-259

- Product:
  - A Tβ4-based sterile eye drop that has corneal repair and anti-inflammation properties.
- Indications and development stage:
  - Corneal Healing – Phase 2b

After presenting encouraging data in its phase IIa trial conducted in 2012 in patients with severe dry eye, RegeneRx has proposed to conduct a larger physician-sponsored Phase 2b trial. This confirms prior results that showed statistically significant improvements in patients' dry eye signs and symptoms. This stage requires RegeneRx to manufacture RGN-259 eye drops and advise on certain regulatory and protocol matters. This will prepare the company to effectively develop and commercialize this product for an underserved market.

RGN-137

REGENERX

- Product:
  - A topical gel formulation of the peptide Tβ4 that affects multiple dermal healing pathways, such as apoptosis, angiogenesis, collagen deposition, and inflammation to accelerate dermal healing.

- Indications and development stage:
  - Epidemolysis Bullosa – Phase 2

Probably RegeneRx's most advanced candidate, this novel treatment to accelerate dermal healing has recently completed Phase 2 trials. Data is encouraging, showing utility of Tβ4 for other indications like Pressure and Venous stasis ulcers. Clinical trials have already been enrolled. The company has received $675,000 in grants from the FDA to support this clinical trial.

We'd love to hear your views on all of this…

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Want to hear more about the therapies in this report?

At this year's Stem Cells & Regenerative Medicine Congress, more than half of the companies listed in this report will be represented.

Participants will discus:

- How to keep the cell therapy industry moving forward
- How to overcome the current and predicted challenges in translating promising studies into the clinic
- How to deliver these therapies to patients

Can you afford to miss it?

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