SNAPSHOT OF STEM CELL AND REGENERATIVE MEDICINE COMPANIES IN AUSTRALIA

8th Edition

2022

INDEX

ABOUT THIS SNAPSHOT

This is the eighth version of the snapshot, which highlights key regenerative medicine companies, largely compiled from information that was publicly available. The information contained within this Snapshot is up-to-date and relevant as of 26th October 2022. The publication was launched online, in conjunction with the Centre for Commercialization of Regenerative Medicine Australia and distributed at AusBiotech 2022 on 26th October 2022.

FOREWORD

The NSW Stem Cell Network defines its goal by networking and interconnecting stakeholders for the purpose of exchanging and sharing information. By organising workshops and seminars, we provide opportunities for scientists, clinicians, and those in industry, government, community, and higher education to connect. This enables collaborative research and fosters the development of commercial initiatives, thereby creating a path to improved patient care.

In May this year, The NSW Stem Cell Network held a one-day workshop on "Parkinson's Disease and Regenerative Medicine" (program and speakers can be found on The NSW Stem Cell Network website).

Speakers and delegates from around Australia and the UK gathered at the Brain and Mind Centre, University of Sydney, to learn about advancements in our understanding of the pathophysiology of Parkinson's Disease (PD) and treatment developments including those in the field of regenerative medicine.

PD is a progressive, degenerative neurological condition that is caused by the loss of dopamine-releasing neurons in the brain. Over time, patients experience tremor, rigidity and dyskinesia as a result of motor pathways being affected. PD affects ~100,000 people in Australia and 10 million globally, and while it is most commonly diagnosed in patients over the age of 65, up to ~20% of patients are diagnosed before the age of 50.

Currently, there is no cure for PD and treatment options are concentrated on symptomatic improvement with dopamine replacement; the goal of treatment is to prolong inevitable disease progression.

Those who attended the workshop learnt about progress being made in several areas, including reparative dopamine therapy. This therapy aims to regulate dopamine release by targeting the site of dopamine loss in the brain and releasing dopamine in the affected areas by gene therapy.

Voyager Therapeutics, a USA based company, is currently undertaking clinical trials that aim to preplace dopamine cells in affected brain areas through enhanced neurogenesis. While the trial shows promising results, gene therapy for enhanced neurogenesis may not be a feasible treatment option.

Living Cell Technologies, an Australasian biotechnology company based in Australia and New Zealand, is embarking on its third PD clinical trial using porcine choroid plexus tissue encapsulated in alginate, collectively known as NTCELL. The tissue produces multiple growth factors that promote neuronal growth and repair of PD-affected cells. Results are promising, with Phase 2 studies showing safety and advising the optimal number of capsules to implant.

Recently, the Australian drug development company Pharmaxis Ltd announced a clinical drug trial in collaboration with Professor Roger Barker from The University of Cambridge and Addenbrooke's Hospital, UK, and Professor Simon Lewis of Cognitive Neuroscience Brain & Mind Centre, The University of Sydney. Pharmaxis develops drugs to inhibit inflammatory diseases; in the context of PD, the aim of this international trial is to target inflammation in the brain to slow down or even stop the development of neuronal cell death in high-risk patients, and ultimately delay and reduce associated symptoms seen in patients with PD.

Professors Barker and Lewis were both speakers at The NSW Stem Cell Network PD workshop.

Researchers from the John Curtin School of Medical Research, in collaboration with Professor Clare Parish from the Florey Institute, are researching the use of hydrogels to support the growth, proliferation and transplantation of adult stem cell-derived neurons for the treatment of PD in animal models. The stem cells are grown on the hydrogels in vitro. When shaken the gel turns into liquid which is then injected into the brain. Once inside the brain, the gel turns back into its solid form to support the cells to release growth factor GDNF to promote the survival of many types of neurons, including those that secrete dopamine. Animal trials have shown positive results in improving PD -associated movement pathologies. The aim is to start human trials in about 5 years. The hydrogel technology is cost-effective and is easy to manufacture.

Professor Peter Silburn from the Queensland Brain Institute discussed deep brain stimulation – a neurosurgical procedure that uses implanted electrodes and electrical stimulation within specific areas of the brain to regulate abnormal impulses. The procedure can result in abolition of symptoms for a finite period, but eventually they recur.The treatment is being used earlier on in the course of PD, whereas previously it was used late in PD when oral medication ceased being useful.

Concluding the workshop, speakers were invited to participate in a panel discussion. While various PD treatments were discussed throughout the workshop, the general consensus from the panel was, in order to move forward, early diagnosis of PD was crucial. For example, identifying early signs of PD, such as rapid eye movement sleep behaviour disorder, as well as relevant biomarkers, may help diagnose and target at-risk patients. Diagnosis well before any symptoms become apparent, would enable early treatment and intervention. This might result to slow down or prevent the progression of PD.

The Australian Government is committed to the development of Australian-based treatments for PD. In 2019, the Federal Government provided funding in the form of a $30 million Medical Research Future Fund, which helped to establish the Australian Parkinson's Mission. The Australian Parkinson's Mission is a 5-year research program combining clinical trials and biomarker technology with genomics research to target disease pathophysiology, disease treatment and prevention, and to develop a framework for precision medicine. This Australian-led clinical trial has eight trial sites around Australia, including The Brain and Mind Centre's PD Research Clinic, and involves the following Foundations and Institutes: The Garvan Institute of Medical Research, Shake It Up Australia Foundation, The University of Sydney, The Cure Parkinson's Trust (UK), Michael J Fox Foundation (USA) and Parkinson's Australia.

The NSW Stem Cell Network is pleased to see that our not-for-profit organisation continues to enable collaborative research and commercial initiatives to create a path to improved patient care. We thank our sponsors, because without their support we would not be able to provide this important service.

This 8th edition of the SnapShot lists Stem Cell and Regenerative Medicine Companies in Australia and their contact details, as well as highlighting some of the leading companies in our country.

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Prof Bernie Tuch
Director
NSW Stem Cell Network

Dr Margret Schuller
Board Member
NSW Stem Cell Network

Dr Rachel Shparberg
Deputy Director
NSW Stem Cell Network

Professor Tuch is a practising endocrinologist, Executive Chairman of the biotechnology company Living Cell Technologies Ltd, and a Director of Sydney Cell Therapy Foundation Pty Ltd.

Dr Margret Schuller has over 25 years of experience in the life science industry.

Dr Rachel Shparberg did her PhD in the stem cell field and now is a medical writer.

For more information, please contact:
Deb Rooz
Manager, NSW Stem Cell Network
Phone: (02) 9552 9982
Email: stemcellmanager@stemcellnetwork.org.au

BUILDING UP TOWARDS THE CCRM GLOBAL NETWORK

It is common to hear the reflection that a country, any country, ought to do more translation and commercialisation of their innovation. Even countries that are the most innovative and adapt at commercialising their ideas are not resting on their laurels. The American Government is constantly commissioning white papers, opinion pieces, other studies and institutes to plant the flag on the next generation infrastructure investments and cultivate new skills to enrich the workforce, all to best harness the genius of humanity.

Countless papers and comments have been made about Australia's less-than-commendable performance translating medical science into therapeutics or medical devices. But Australia is not alone, as each country is its worst critic. The Centre for Commercialization Medicine (CCRM) was established in 2011 as part of Canada's Centres of Excellence Program to help commercialise Canadian innovations in regenerative medicine and not lose them to its Southern neighbour in Boston. Ten years on, CCRM has over 180 employees, incubated 12 companies supported over 12 patent families. It has helped raise over CAD770million into the sector and is constantly expanding. Its success has resulted in it being consistently approached by biotechnology companies and researchers from many countries around the world.

Noticing that the challenges faced by Canada were not unique, a blueprint was conceptualised that depicted a network of CCRM hubs across the globe to help commercialise local technologies and grow local markets (Figure 1).

Figure 1: Conceptual overview of the CCRM Global Network

2022

CCRM Australia was established to provide access to a de-risked commercialisation model that made better use of existing local infrastructure and incorporated existing skills and capabilities. Moreover, by identifying the local bottlenecks and gaps, CCRM Australia could work with existing partners to help overcome these bottlenecks and help grow Australia's regenerative medicine sector.

To date, CCRM Australia has assisted over 90 companies in 2021 from 16 different countries in various activities that include capital raising, setting up clinical trials, and searching for local collaborators in research and clinical settings. CCRM Australia has also experimented with new training and development formats targeted at the Master and Doctoral levels to provide exposure to commercialisation activities.

Alongside Australia, CCRM Hubs in the Netherlands and Norway are also developing, and new hubs are potentially emerging in the US, Israel and Korea. While each hub operates independently, it is expected that each hub would provide a specialised service back to the Global Network as a contribution, which can be shared and leveraged for network effects. In 2018, CCRM Australia envisioned a unique business unit called BioNano, which would offer state-of-the-art biomaterial and nanofabrication facilities and be supported by a consortium of local partners with expertise in fabrication. This business unit will develop enabling technologies that support characterisation, validation and testing platforms. In the initial stage, BioNano will focus on four key enabling technologies: lab-on-a-chip devices, biomaterials, bio-delivery devices and biosensors; each will be useful in the sourcing, delivery and biocompatible of regenerative medicine therapies. Regardless whether the BioNano-type business unit does become CCRM Australia's contribution to the CCRM Global Network, it is imperative now that plans and actions need to be made to build up CCRM Australia's local capabilities and capacities.

As such, CCRM Australia is in the process of developing its next 5 Year Strategic Plan; to shape our ability to service the Australian industry and meet the local needs of our biotechnology companies and researchers but also to engage on the world stage and 'Internationalise' Australia's regenerative medicine technologies.

Silvio Tiziani
Chief Executive Officer
Centre for Commercialization of Regenerative Medicine Australia

AUSTRALIAN-BASED COMPANIES

Cynata Therapeutics Ltd is a clinical stage company developing a proprietary therapeutic stem cell platform technology, Cymerus™, which arose from the University of Wisconsin-Madison, a world leader in stem cell research. Cymerus addresses a critical shortcoming in existing methods of production of allogeneic mesenchymal stem cells (MSCs) for therapeutic use: the ability to achieve consistent economic manufacture at commercial scale without reliance upon multiple donors. There is extensive interest in the development of MSCs as therapeutic agents, in light of their ability to secrete bioactive molecules such as cytokines, chemokines, and growth factors, in addition to their immunosuppressive and immunoregulatory properties. There are currently over 1000 clinical trials of MSCs, covering an extremely wide range of therapeutic indications, including haematological, cardiovascular, orthopaedic, gastrointestinal and autoimmune disorders, among others. However, there are very major limitations in conventional methods of MSC production including the dependence upon multiple donors, the variability between donors, the relative scarcity of MSCs in adult tissue, and the low proliferative capacity of adult stem cells compared to pluripotent stem cells. Cynata believes that the Cymerus technology addresses these issues, uniquely placing Cynata to capitalise on the flourishing field of stem cell therapeutics. The Company has been covered in highly favourable equity research analyses published by Baillieu Holst, BBY, SeeThru Equity, H.C. Wainwright, Shaw & Partners and MST Access. Cynata's first therapeutic product CYP-001 has shown highly promising efficacy in a Phase 1 clinical trial in acute graft-versus-host disease (aGvHD). This has enabled the Company to initiate multiple further clinical trials. Cynata has a strategic partnership with FUJIFILM, a major participant in the regenerative medicine sector and the third largest shareholder in Cynata, behind Fidelity and BioScience Managers, with around 6% of the shares.

PRODUCT PIPELINE

Cynata is the world leader in developing iPSC-derived cell therapy products. Following excellent results in a Phase 1 clinical study in a GvHD, the Company filed an IND application with the US FDA and secured clearance of that IND in 2022, enabling trial start-up activities to commence on a potential Phase 2 clinical trial in aGvHD. A phase 3 clinical trial commenced in 2020 in osteoarthritis in association with the University of Sydney while a clinical trial in diabetic foot ulcers commenced in 2021. A clinical trial in patients with severe respiratory complications, such as have been seen in COVID-19, patients, commenced in 2020. However this trial concluded in 2022 due to ongoing recruitment challenges.The Phase 1 clinical trial results in aGvHD, which have been the subject of a front-page article in Nature Medicine, provide a sound foundation for further development in numerous other indications, such as those in which MSCs from other sources have previously been investigated. Cynata has also reported clear efficacy in pre-clinical proof-of-concept studies with its Cymerus MSC products in models of cytokine release syndrome (CRS), CLI, diabetic wounds, myocardial infarction, asthma, idiopathic pulmonary fibrosis, sepsis, acute respiratory distress syndrome (ARDS) and in GvHD. Cynata is pursuing a vigorous partnering agenda in order to fully exploit its outstanding cell therapy platform.

LATEST NEWS

Active recruitment has continued in the osteoarthritis and diabetic foot ulcer trials. The long-standing relationship with FUJIFILM was strengthened with the establishment of a new strategic partnership involving manufacturing services to ensure long term supply of Cynata's proprietary Cymerus MSC products. Cynata has successfully achieved IND clearance from the US FDA for a proposed Phase 2 clinical trial in aGvHD. Additionally, the Company's intellectual property portfolio has advanced with the grant of patents in multiple jurisdictions, including the USA.

CEO: Dr Ross Macdonald
Established in Australia in 2011
ABN: 98 104 037 372
Status: PUBLIC (ASX:CYP)
www.cynata.com

CONTACT
Dr Ross Macdonald
P: +61 3 7067 6940

Mesoblast is using its proprietary technology platform to develop and commercialize innovative allogeneic cellular medicines to treat complex diseases resistant to conventional standard of care and where inflammation plays a central role.

The Company's portfolio of Phase 3 product candidates comprises RYONCIL™ (remestemcel-L) for steroid-refractory acute graft versus host disease (acute GVHD), remestemcel-L for the treatment of moderate to severe acute respiratory distress syndrome (ARDS) due to COVID-19 infection, REVASCOR® for advanced chronic heart failure and MPC-06-ID for chronic low back pain due to degenerative disc disease. Mesoblast also has a promising emerging pipeline of product candidates and next generation technologies.

Innovative technology platform enables scalable manufacturing
Mesoblast's novel allogeneic product candidates are based on rare (approximately 1:100,000 in bone marrow) mesenchymal lineage cells that respond to tissue damage, secreting mediators that promote tissue repair and modulate immune responses.

Mesenchymal lineage cells are collected from the bone marrow of healthy adult donors and proprietary processes are utilized to expand them to a uniform, well characterized, and highly reproducible cell population. This enables manufacturing at industrial scale for commercial purposes. Another key feature of Mesoblast's cells is they can be administered to patients without the need for donor–recipient matching or recipient immune suppression.

Mesoblast has proprietary technology that facilitates the increase in yields necessary for the long-term commercial supply of its product candidates, and next generation manufacturing processes using xeno-free technologies and three-dimensional bioreactors to reduce labour, drive down cost of goods and improve manufacturing efficiencies.

Robust Intellectual Property Estate
Mesoblast has an extensive patent portfolio with over 1,100 patents and patent applications across 82 patent families, and patent terms extending through 2040. These patents cover composition of matter, manufacturing, and therapeutic applications of mesenchymal lineage cells, and provide strong commercial protection for our products in all major markets, including the United States, Europe, Japan and China. Licensing agreements with JCR, Grünenthal, Tasly and Takeda highlight the strength of Mesoblast's extensive intellectual property portfolio covering mesenchymal lineage cells.

Mesoblast will continue to use its patents to prosecute its commercial rights as they relate to its core strategic product portfolio. When consistent with the Company's strategic objectives, it may consider providing third parties with commercial access to its patent portfolio.

Evidence-based Science and Translational Medicine
Mesoblast's approach to product development is to ensure rigorous scientific investigations are performed with well-characterized cell populations in order to understand mechanisms of action for each potential indication. Extensive preclinical translational studies guide clinical trials that are structured to meet stringent safety and efficacy criteria set by international regulatory agencies. All trials are conducted under the continuing review of independent Data Safety Monitoring Boards comprised of independent medical experts and statisticians. These safeguards are intended to ensure the integrity and reproducibility of results, and to ensure that outcomes observed are scientifically reliable.

Global Operations
Mesoblast has locations in Australia, the United States and Singapore and is listed on the Australian Securities Exchange (MSB) and on the Nasdaq (MESO).

Chief Executive: Dr. Silviu Itescu
Established in Australia 2004
ABN: 68 109 431 870
Status: Public

www.mesoblast.com
info@mesoblast.com

Orthocell Ltd (ASX:OCC) is a regenerative medicine company dedicated to improving the lives of patients suffering musculoskeletal conditions by developing products that restore patient mobility, function and performance. Orthocell's two lead technologies are CelGro™, a collagen medical device that augments bone, nerve and tendon injury, and OrthoATI™, a world-leading cellular therapy for the treatment of chronic tendon injury. Both products are manufactured at Orthocell's quality controlled (GMP) and ISO 13485 certified facility in Perth, Western Australia.

CelGro™ Platform
The CelGro™ Platform of collagen medical devices can be used in multiple clinical indications. CelGro™ has distinct advantages over existing tissue repair scaffolds, particularly with respect to its mechanical strength, ease of use, and the quality of tissue repair.

Striate+™ for dental bone and tissue repair
Striate+ is a market-leading resorbable collagen medical device used in guided bone and tissue regeneration procedures and the first CelGro™ Platform product to receive regulatory approval in Australia, Europe and the US. Clinical studies demonstrated that Striate+ supported transition from two-stage to single-stage dental implant procedures, reducing the treatment time by several months. This is of significant interest to patients and clinicians due to potential improvements in efficiency and efficacy of treatment options to replace missing teeth. In June, 2022 Orthocell entered into an exclusive agreement with BioHorizons Implant Systems Inc, one of the largest dental implant companies in the world, covering patent and trademark licenses and distribution and supply of Striate+™. In consideration of the license granted, Orthocell received in cash AU $21,461,686 million, net of fees. Orthocell is working closely with BioHorizons on US market entry, with first orders dispatched and a market launch planned for 4Q CY 2022.

Remplir™ for nerve regeneration
In March 2022, Orthocell achieved Australian market approval for its Remplir™ peripheral nerve repair device, the second CelGro™ Platform product, for introduction into the Australian nerve repair and regeneration market. Clinical trial results have been extremely encouraging, with 24 month post-treatment data showing 85% (23 of 27) of nerve repairs resulted in functional recovery of target muscles closest to the repair site. These results further support that nerve reconstruction with Remplir™ following injury to the spinal cord, brachial plexus and other peripheral arm/hand nerves consistently restores arm and hand function. In September 2022, Orthocell appointed Device Technologies as its exclusive distributor of Remplir™ in the Australian market. Device Technologies has established relationships with leading plastic reconstructive and orthopaedic surgeons and an experienced sales team throughout Australian and New Zealand. Orthocell is expecting inclusion on the Australian Prosthesis List in November 2022 and is working with Device Technologies to expand the Key Opinion Leader network using Remplir™ in peripheral nerve repair procedures. Orthocell believe this product has significant potential to disrupt the US nerve repair market and is working with US regulatory advisers to confirm the most appropriate US regulatory pathway, potential for inclusion in expedited programs and what this will mean for reimbursement value for the product.

OrthoATI™ for treatment of chronic tendon injuries
OrthoATI™ (Autologous Tenocyte Implantation) is a world-leading cell therapy developed to treat chronic degenerative tendon injuries. OrthoATI™ uses the patient's own tendon-derived cells to stimulate healing of damaged tendons that have failed to respond to treatment, addressing a significant unmet clinical need. Over 900 patients have been treated with OrthoATI™ in Australia, New Zealand and Hong Kong under restricted access regulatory authorisation and in clinical trials for tendon regeneration in the elbow, shoulder and hip. Results from the recent Phase 2a multi-centre randomised controlled trial (RCT) of rotator cuff tendon repair demonstrated that OrthoATI™ is significantly more effective than steroid injection for treatment of rotator cuff tendinopathy with intrasubstance tendon tear. In light of the study results, Orthocell is progressing its US commercialisation plan, including investigations into technology scale-up, FDA engagement and commercial preparation activities to initiate a Phase 2b RCT that will support an FDA regulatory submission.

CEO: Paul Anderson
Established in Australia in 2006
ABN: 57 118 897 135
Status: Public
www.orthocell.com

CONTACT
Paul Anderson
P: +61 411 861 626
paul.anderson@orthocell.com.au

CLINICAL TRIALS IN AUSTRALIA

CLINICAL TRIALS

In September 2021, the Regenerative Medicines Catalyst Programme released an up-to-date and extensive overview of Australia's Regenerative Medicine Clinical Trials Database, which can be viewed here. Read more about the report here.

COMPANY DIRECTORY

DIRECTORY

Company	Contact	Website
Avita	N/A	www.avitamedical.com
Cartherics	+61 3 8572 2500	www.cartherics.com
Cell Care	1800 071 075 (Toll Free)	www.cellcare.com.au
Cell Therapies Pty. Ltd.	+61 3 8559 7310 admin@celltherapies.com.au	www.celltherapies.com.au
Clinical Stem Cells	N/A	www.clinicalstemcells.com
Cryosite	N/A	www.cryosite.com
CSL	N/A	www.csl.com.au
Cynata Therapeutics	+61 3 7067 6940 ross.macdonald@cynata.com	www.cynata.com
Eppendorf	+61 2 9889 5000 info@eppendorf.com.au	www.eppendorf.com
In Vitro Technologies	1300 552 003 daina.elliott@invitro.com.au	www.invitro.com.au
Inventia Life Science	1800 849 128 jeremy.dobrowolski@inventia.life	www.inventia.life
Living Cell Technologies	+61 2 8999 0970 info@lctglobal.com	www.lctglobal.com

DIRECTORY

Company	Contact	Website
LONZA	1300 657 508 bioscience.australia@lonza.com	www.lonzaboiscience.com.au
Magellan	info@magellanstemcells.com.au	www.magellanstemcells.com.au
Melbourne Stem Cell Centre	N/A	www.melbournestemcellcentre.com
Mesoblast	+61 3 9639 6036 info@mesoblast.com	www.mesoblast.com
Miltenyi Biotec	+61 2 8877 7400	www.miltenyi.com
Orthocell	+61 411 861 626 paul.anderson@orthocell.com.au	www.orthocell.com
Regeneus	1300 995 098	www.regeneus.com.au
Scientifix Pty. Ltd.	nikki@scientifix.com	www.scientifix.com.au
STEMCELL Technologies	1800 060 350 cyndy.nauer@stemcell.com	www.stemcell.com
Terumo BCT	0408 244 342 shane.torok@terumobct.com	www.terumobct.com
Tessara Therapeutics	christos.p@tessaratx.com	www.tessaratherapeutics.com
Thermofisher	N/A	www.thermofisher.com.au