Snapshot of Stem Cell and Regenerative Medicine Companies in Australia

2018

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About the NSW Stem Cell Network

The NSW Stem Cell Network is a professional community with an interest in all forms of stem cells.

The Network strategy is to work with the scientific, health and medical research communities, the higher education sector and business to promote growth and innovation to achieve positive outcomes for the people of NSW. Our work encompasses science, medicine, ethics, law, business and public awareness of stem cells.

Objectives of the NSW Stem Cell Network

The Network, since its establishment in 2002, has worked towards:

- Facilitating communication among members to promote the use of stem cells within an ethical framework
- Acting as a source of information on stem cells for the community
- Promoting the development of resources to support the use of stem cells within New South Wales
- Enhancing the R&D and/or commercialisation potential of stem cells within New South Wales

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About AusBiotech

AusBiotech is Australia's biotechnology organisation, working on behalf of members for more than 30 years to provide representation and services to promote the global growth of Australian biotechnology. It represents over 3,000 members in the life sciences, including therapeutics, medical technology (devices and diagnostics), food technology and agricultural, environmental and industrial sectors. AusBiotech is dedicated to the development, growth and prosperity of the Australian biotechnology industry, by providing initiatives to drive sustainability and growth, outreach and access to markets, and representation and support for members nationally and around the world. It facilitates sustainability and growth of the industry through its critical mass and united all-of-industry approach.

Through AusBiotech, members have access and outreach to industry and government networks, which builds strong business relationships. Members are invited to an extensive state and national events program as-well-as the opportunity to take part in regular international biotechnology missions and be represented at international trade fairs and conferences. AusBiotech represents and supports individual biotech companies, special interest groups and the Australian biotechnology industry as a whole. AusBiotech represents its members by providing expertise as industry advocates and committee members on all biotech steering committees; as well as providing industry submissions to policy review panels at both government and corporate levels. The organisation also has substantial experience in administering government grant and funding programs on a state and national level.

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About this Snapshot

This is the fourth version of the snapshot, the first version being created in 2015 with the assistance of our former manager Rachel Shparberg. A list of companies was formulated, largely compiled from information that was publicly available. A questionnaire was sent out to relevant company representatives, and the information was compiled into the Snapshot. The information contained within this Snapshot is up to date and relevant as of October 2018.

A draft was circulated back to the company representatives for approval before its publication and launched at AusBiotech National Conference (31st October—2nd November Brisbane, Australia) by Lorraine Chiroiu (CEO, AusBiotech).

The fourth edition of the Snapshot includes a more comprehensive list of regenerative medicine companies and contains details of current clinical trials run by cell therapy companies in Australia (page 20).

Disclaimer:

The information contained in the Snapshot of Stem Cell and Regenerative Medicine Companies in Australia: October 2018 is intended solely for general information. This publication must not be relied upon as a substitute for medical, investment or other professional advice. You are encouraged to speak with the relevant contacts provided in the Snapshot for further information. This Snapshot should not be read as reflecting the policies of the NSW Stem Cell Network, its Executive, officers or members. Nor does the Snapshot represent an endorsement of the processes, procedures and technologies described therein. The NSW Stem Cell Network does not accept any liability arising in any way from information contained in this publication, including by reason of negligence for errors or omissions in the information. Only companies that have agreed to be published in the Snapshot were included and, any liability resides with them.

Foreword

Great progress has been made since the first attempts to treat diseases using stem cells or regenerative medical approaches over the past 50 years, with blood disorders being the lead disease treated. In Australia, there are more than 150 people with acute leukaemia treated annually with haemopoietic stem cells. In this Century, the use of stem cells for other disorders is being contemplated and trialled. These include multiple sclerosis, diabetes, macular degeneration, spinal cord lesions and cancer. Despite the innovative advances in this field, the full potential of cell therapies is yet to be realised.

The NSW Stem Cell Network has nurtured the stem cell and regenerative medicine communities for the past 15 years to grow and advance research and development in these areas. The Network has over 500 members around Australia including clinicians, researchers, policy developers, members of Government, lawyers, ethicists, students, patients and companies, who are all passionate advocates working together for the growth of the stem cell industry. With this report, our intention is to elevate stem cell and regenerative medical business in Australia to the next level.

In the snapshot, we profile current regenerative medicine and stem cell companies, some of whom are licensed by the TGA, and are carrying out controlled clinical trials registered with an appropriate entity. Details of Australian clinical trials run by such companies can be found on page 20 of this document.

The growing number of stem cell and regenerative medicine trials registered in Australia and worldwide reflect recent efforts to expand the use of cell therapies to a broader range of conditions. However, maximal research and development potential can only be achieved with the provision of substantial support from government bodies and the private sector.

Research and development with stem cells and in regenerative medicine is particularly flourishing in countries where there is plenty of investment from both Government and the private sector. In the US, Singapore, Israel and Canada, there is a solid business model for progressing innovative stem cell research. Meanwhile, changes in regenerative medicine regulations in Japan have attracted great international interest for the Japanese market, especially due to accelerated commercialisation opportunities.

In Australia, commercialisation of stem cell and regenerative medicine opportunities has been an enormous challenge over the past decade for a number of reasons. The perception of being a risky investment, lack of strong Government funding and the small pool of specialist people with skills in this area that sit on company boards and mentor the growth of the industry, are just a few of the hurdles.

A number of companies have chosen to seek investment from overseas organisations to assist their growth in Australia, whilst others have secured a foot of their business overseas to create a channel for investment. Some companies are desperately seeking partnerships with pharmaceutical companies, with minimal success.

The companies progressing with autologous stem cell products already on the market for patients with sports or other injuries have come up against other challenges relating to a relatively unregulated marketplace including scrutiny from Government regulatory bodies. Indeed in July, the Therapeutic Goods Administration changed the regulations for carrying out autologous cell interventions in Australia, tightening advertising requirements and insisting that trials be conducted through hospitals which will oversee them.

According to a number of industry experts, there is a need for stem cell and regenerative medicine organisations including companies to come together under one banner with a united voice. Indeed, the Centre for Commercialisation of Regenerative Medicine was recently created for this purpose, and is attempting to emulate a very successful entity of a similar nature in Canada.

It was pleasing to see a recent announcement be the CEO of the NSW Government Office of Health and Medical Research, Professor Tony Penna, of $5 million dollars for a number of cell and gene therapy projects. On a more

commercial basis, the NSW Government Department of Industry has recently invested matching funds for a diabetes cell therapy in Australia, partnering with the Israel Innovation Authority, which is supporting the collaborative Israel company involved.

The Regulations

In pursuing the goal of developing stem cell and regenerative medicine, there is the need to obtain regulatory approval for both development of the product, and for conducting clinical trials to test safety and efficacy.

The Therapeutics Goods Administration (TGA) provides guidance and advice concerning all of the above, with the regulatory framework being that for biologicals. It is advantageous for discussions to be held with relevant officers of the TGA prior to proceeding with clinical trials, to help circumvent problems that might otherwise arise.

The conducting of clinical trials with stem cell and regenerative medicine requires approval from a duly constituted Human Research Ethics Committee. This will require reasonable pre-clinical evidence that they might work in humans, and that the cells are well characterised, and free of microbiological contamination. Good Clinical Practice is needed.

In addition, before the Trial can proceed, acknowledgement by the TGA that the Trial is being conducted (Clinical Trial Notification), or a more thorough assessment of it by the TGA (Clinical Trial Exemption), is needed. If the use of the stem cells or the regenerative medicine approach has been approved by the Regulatory Body of another country, especially the Food and Drug Administration of the USA, the TGA has indicated its own regulatory requirements for a trial in Australia will be low.

Registration of stem cell or regenerative medicine product as a treatment for a medical condition requires them to have been tested in several phases, initially for safety (phase 1), then efficacy in a relatively small study (phase 2), and finally at multiple sites in a larger cohort of people (phase 3). Evidence that the therapy will work usually requires it to be tested against a control group, to determine the placebo effect, which can be quite large. Registration of the product occurs after phase 3 trials.

Sometimes, stem cells will be placed in a device before being used. This might be a scaffold to allow the stem cells to attach and proliferate more readily, or an immunoisolation system to protect them from the recipients' immune system. Approval for the use of such devises also comes under the biologics framework.

The NSW Stem Cell Network has committed to continuing to compile a list of stem cell and regenerative medicine companies as a step forward to drive the development of the industry in Australia, hopefully providing insight around where Australia is at right now. Combining this information with the Snapshot of Regenerative Medicine research in Australia published in 2014 by the National Stem Cell Foundation of Australia we believe will create a solid landscape of stem cells R & D in our country.

Professor Bernie Tuch	**Dr Daniella Goldberg**	**Tamara Treleaven**
NSW Stem Cell Network	NSW Stem Cell Network	NSW Stem Cell Network
Director	Executive	Manager

Professor Tuch is an endocrinologist, non-executive Director of the biotechnology company Living Cell Technologies Ltd, and a Director of Sydney Cell Therapy Foundation Pty Ltd. Dr Goldberg is a PR and Marketing Consultant at Bio-link Australia Pty Ltd; Tamara Treleaven is the Manager of the NSW Stem Cell Network.

Commercialisation Opportunities

While stem cells hold incredible potential and opportunities, it is a field that also presents many challenges. Being a bespoke technology customised for each patient, the clinical development program is expensive and economies of scale are smaller. Attracting investors has sometimes been difficult due to the risks outweighing the benefits, and the high cost of producing the product. Cost issues are compounded by the reliance on materials from other industries.

Othon Gervasio, Acting Medical Director at Novartis Oncology Australia/New Zealand, said that the field of cell-based therapies is a growing area in the treatment of cancer patients, and innovative thinking for further development and access to therapies is warranted. The path for funding requires a multi-stakeholder approach to find sustainable solutions and there is also greater education needs for patients and all those involved in the delivery of such therapies.

Paul Anderson, Managing Director of Orthocell commented that the challenges are ongoing on a daily basis: "There are no risk-free avenues available, work out what you can and can't control. Companies need to ask is there a genuine market need? How internationally transferable is it? Will it cost more to make than sell? Can we protect IP? Do we have the money? Can we raise it? Investors need to understand your business. There's a lot of peripheral noise in the stem cell space, we need to show who's doing it properly."

One recent success story is biotech company Mesoblast, a global leader in cellular medicines. Mesoblast has three Phase III trials targeting acute graft versus host disease, advanced heart failure and chronic low back pain due to disc degeneration, the latter two representing blockbuster ($1 billion plus p.a.) markets. Its licensee in Japan, JCR Pharmaceutical, received full approval for the first allogeneic cell-based product in Japan based on Mesoblast's mesenchymal lineage cell technology. Mesoblast believes it is well positioned to have the first industrially manufactured allogeneic cell-based product approved in the United States.

Rhenu Bhuller of Frost and Sullivan commented: "The global regenerative medicine market is expected to rise at a compound annual growth rate (CAGR) of 22.4% to nearly $67.50 billion in 2020. Cell-based immuno-therapies and stem cell developments are significantly driving the market, representing over 60% of the total market. The overall cell therapy market is growing rapidly at CAGR of 20.2% between 2015 and 2020, with over 500 companies globally involved in product development in this space. The stem cell-based segment is the largest with over 500 clinical studies currently ongoing globally. Cardiology, oncology, and neurology have the strongest pipelines of stem cell therapies, accounting for 56.1% of the overall ongoing studies in this area. Oncology is the most popular segment for cell therapy collaborations and deals, holding 29.2% of all the deals made in 2015. Of these oncology funds, a growing percentage is for immuno- and combination therapies. Cardiovascular and neurology are the other major market segments that are receiving a lot of attention, especially in the field of stem cells.

Interest and investment are high in this area and this growth is a result of the increasing regulatory support regarding stem cell research, advancements in regenerative medicine and stem cell therapies as well as the standardisation of clinical environments which are encouraging the introduction of new technology and products. With an increasing number of products reaching late phase clinical trials, the need for increased large-scale manufacturing capacity is growing and we do see the need to further develop process engineering capabilities, automated systems, logistics capabilities, and a plan to reduce the cost of goods sold to bring these products closer to the consumer and commercialisation.

Japan and South Korea are the frontrunners and set to dominate the Asia Pacific stem cell market in the coming years while China and Australia are increasingly developing in the area as well with companies like

Avita, Mesoblast, Orthocell and Regeneus. Australia is continuing to develop critical infrastructure needed for regenerative medicine research and there have been some achievements such as the success of companies like Mesoblast and Cell Therapies. Australia is also starting to gain ground and the Australian Regenerative Medicine Institute is one of the leading centres for regenerative medicine and stem cell research in the region. We are also seeing investments from Japanese companies like Fujifilm into Australian research companies" wrote Ms Bhuller.

Dr Tim Oldham, former Chief Executive Officer, Cell Therapies Pty Ltd, writing in the September 2015 edition of Australasian Biotechnology, stated: “A whole new manufacturing and supply industry must be created if thousands of patients are to benefit from these breakthrough therapies. Traditional pharmaceuticals are inert, largely temperature stable and can be manufactured centrally in batches of thousands or millions of doses to sit on a pharmacy shelf until needed. Cellular therapies are patient specific, living products that are inherently fragile, have very short shelf-lives unless stored in liquid nitrogen and are highly variable. A clinical prescription initiates and just-in-time, time critical production process with each batch producing a single product for one patient. Today these processes are very manual and very expensive.”

“An advanced manufacturing eco-system is developing around these new therapies. Cell Therapies already collaborates with Invetech Ltd in Melbourne for process automation, the CRC for Cell Therapy Manufacturing in Adelaide for cost reducing processes and Peter Mac for optimising cell collection by apheresis. Australia has a genuine opportunity to be more than a local manufacturing hub – it can also become an advanced manufacturing leader in this field.”

Australia faces the challenge of needing a regulatory approach that enables Australian companies to be part of this exciting medical frontier, but also addresses the safety and quality concerns. Structural weaknesses in regulation in some other countries have seen some patients travel overseas to access “stem cell therapies” the safety and efficacy have yet to be established . To realise the clinical promise of stem cells, companies must address the challenges of how to reduce risk, how to increase cost-effectiveness and eventually how to deal with explosive demand.

R & D Tax Incentive and other tax reform

The 2011 introduction of the R&D Tax Incentive was a momentous point for Australian innovation. The Incentive is actively attracting companies from around the world to bring their R&D to Australia and supporting medical R&D via small innovation companies. Start-up innovation companies, especially biotechnology companies trading in loss, are the biggest beneficiaries from the Tax Incentive’s 43.5% refundable component. The legislation also benefits large innovative companies by reducing the cost of conducting eligible R&D activities in Australia, making Australia a more competitive location for conducting biomedical and pharmaceutical R&D and clinical trials.

At the time of going to print, legislation had entered the Australian Parliament to make changes to the R&DTI and conditions may have changed when you read this information.

Lorraine Chiroiu, CEO, AusBiotech

Investment offers a series of state-based, national and international investor events as a platform to showcase Australian biotech companies to potential partners and investors. The annual Australia Biotech Invest and Asia Biotech Invest are the keystone events. More details can be found at

http://ausbiotechinvestment.com.au/

Stem Cell and Regenerative Medicine Companies

The future of cancer treatment – combining stem cells and immunotherapy

Melbourne based Cartherics Pty Ltd leads an AU$2.987 million Department of Industry, Innovation and Science Co-operative Research Centre project in partnership with the Hudson Institute of Medical Research, Monash University, Mesoblast Ltd and Cell Therapies Pty Ltd.

The company uses its expertise in successful research, development, relevant trials and commercialisation of clinical products and medical services to:

- Create a new class of cancer treatments beyond surgery, chemotherapy and radiation.
- Supercharge a patient's own immune system, helping it eliminate cancer.
- Develop accessible '**off-the-shelf' immunotherapies** to fight aggressive forms of cancers like relapsed ovarian and gastric cancers.

The company maintains a strong research base at the Hudson Institute for Medical Research and Monash University and its affiliated clinical institutes of Monash Health. It is closely aligned with leading cancer research groups and has excellent connections to leading companies in cell therapy, regenerative medicine and oncology therapeutics.

OUR SCIENCE

Cartherics is harnessing the body's immune system to target and kill cancer by arming T-cells with 'seek and destroy' capacity. Cartherics is developing key cancer-killing technologies:

- **CAR (Chimeric antigen receptor):** Engineered molecules that recognise cancer cells and activate killer T-cells.
- **TCR (T-cell receptor):** Naturally occurring molecules on a T-cell which are engineered to better recognise and kill cancer cells.

Cartherics has filed provisional patent applications on its technologies. It is creating a portfolio of state-of-the-art intellectual property to support the commercialisation of affordable, effective CAR-T technology.

Transforming cancer from a fatal disease to a manageable condition.

CEO/President: Emeritus Professor Alan Trounson

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Cell Therapies is the premiere GMP contract manufacturer for supply and distribution of cellular therapies around the world. We provide the essential deployment infrastructure for the safe, reliable and scalable delivery of cellular therapies for clinical trials and therapeutic use.

Cell Therapies is one of the most experienced contract manufacturers of global cellular therapy products. For over 15 years, Cell Therapies has been providing the essential deployment infrastructure for the safe, reliable and scalable delivery of cellular therapies into clinical trials and for therapeutic around the world. Playing a pivotal role in the cellular therapy value chain, we are poised to deliver critical capability to, and capture significant value from, a sector now delivering transformative health outcomes.

Cell Therapies has a 10 clean room cell processing facility at our home in the Peter MacCallum Cancer Institute, where these facilities are available on a fee-for-service basis to some of the world's leading cellular therapies companies. This facility has been licensed by Australia's Therapeutic Goods Administration for the processing of CAR T-cell products for clinical supply. This TGA license ensures clients are confident that their therapeutic products made by Cell Therapies meets regulatory standards for clinical trials within Australia.

Globally, we have successfully helped develop products and processes that are compliant with international regulatory and cGMP requirements and have successfully integrated with worldwide manufacturing networks. Cell Therapies has expanded its deployment network with a strategic alliance with PharmaBio in Japan. We have also added an apheresis site management service line to provide control over this critical starting material across differing geographies.

PIPELINE

Cell Therapies has broad experience manufacturing and delivering a wide range of cellular therapy products and tissue types, using an extensive array of cell processing techniques. Our expertise is deepest in autologous processing of gene-modified immunotherapies (eg CAR T-cell products), gene therapies, cell-based immunotherapies (eg DC vaccines), haematopoietic stem cells, regenerative medicine and apheresis.

LATEST NEWS

Clinical manufacturing at Cell Therapies is ongoing for a clinical trial of CAR T-cells targeting the Lewis Y antigen (a specific receptor appearing in certain cancers) in patients with Lewis Y-expressing solid tumours, including lung cancer. The trial opened in November 2016 and recruitment has been exceptional. Cell Therapies was awarded 1 of only 9 Global Innovation Linkages grants by the Australian Government for clinical translation of a novel cell tracking and imaging agent for use in cellular therapies. This development work is progressing rapidly and will be in patients by early 2019. Cell Therapies was also part of a collaboration, led by Cartherics Pty Ltd, that was awarded a CRC-P grant for the development of an "off-the-shelf" T-cell product for treatment of different cancers in clinical trials.

Chief Executive Officer: Dawn Driscoll, PhD MBA

Established in Australia in 2003

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Status: Private

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Cynata Therapeutics Ltd is a Phase 2 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

There has been 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 800 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 may address all of these issues, and the Company's activities in relation to the Cymerus™ technology are aimed at achieving that. This uniquely places 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 and Shaw & Partners. In early 2017 the Company announced a strategic alliance with FUJIFILM, a major participant in the regenerative medicine sector. Fujifilm is the second largest shareholder in Cynata behind Fidelity with around 8% of the shares.

PIPELINE

Cynata is the world leader in developing iPSC-derived cell therapy products. Following excellent results in a Phase 1 clinical study, the Company will soon commence several Phase 2 programs, one in **graft-versus-host disease (GvHD)** and another in **critical limb ischemia (CLI)**. The Phase 1 GvHD study results 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 is pursuing a vigorous partnering agenda in order to fully exploit its outstanding cell therapy platform.

LATEST NEWS

Cynata has successfully completed a Phase 1 clinical trial with its first Cymerus therapeutic MSC product, CYP-001, in acute steroid resistant (GvHD). The study met all endpoints, demonstrating an excellent safety profile and a very clear indication of efficacy in this challenging condition. Cynata will now proceed to a Phase 2 trial in GvHD. In addition, the Company will also progress a Phase 2 program for its second MSC product, CYP-002, in critical limb ischemia (CLI). 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 and in GvHD.

CEO: Dr Ross Macdonald

Established in Australia in 2011

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Status: PUBLIC (ASX:CYP)

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Mesoblast leading the way to commercialisation of off-the-shelf cellular medicines

Mesoblast's leading portfolio of allogeneic cellular medicines is based on its disruptive cellular technology platform, proprietary manufacturing processes and multiple Phase 3 assets.

The Company's Phase 3 trials are evaluating Mesoblast's product candidates for the treatment of steroid refractory acute graft versus host disease (aGVHD), chronic heart failure, and chronic low back pain due to degenerative disc disease.

Two allogeneic products using Mesoblast's patented mesenchymal stem cell technology have been approved in Japan and Europe, with both licensees the first to receive full regulatory approval for an allogeneic cellular medicine in these major markets.

Mesoblast's goal is for MSC-100-IV (remestemcel-L) to be the first commercially manufactured allogeneic stem cell product in the United States. Remestemcel-L has successfully met the primary endpoint of Day 28 improved overall response rate and associated survival benefit at Day 100 and Day 180 in a Phase 3 trial in 55 children with aGVHD. Preparations for a Biologics License Application (BLA) filing are underway.

Mesoblast's intellectual property portfolio encompasses approximately 800 patents or patent applications across 69 patent families, which the Company believes will provide substantial competitive advantages for the commercial development of its cell-based therapies in major markets including the United States, Europe, Japan and China.

Mesoblast's cellular technology platform enables allogeneic 'off the shelf' product candidates with batch to batch consistency and reproducibility. The inherent technical properties of Mesoblast's mesenchymal lineage cells allow for scalable culture expansion for purposes of producing anticipated commercial quantities. Proprietary media formulations, advances in development of 3D bioreactor technology and automation are intended to deliver step-changes in yield and COGS reductions.

This robust pipeline of late-stage cellular medicines for serious and life-threatening conditions, recognition by the FDA of their importance, a burgeoning portfolio of earlier stage therapy candidates and a very comprehensive IP portfolio puts Mesoblast in a very strong position going forward.

LATEST NEWS

End of study safety, efficacy and key clinical outcomes from a Phase 2b trial presentation evaluating Mesoblast's product candidate MPC-150-IM in 159 end-stage heart failure patients implanted with a left ventricular assist device will be presented by independent investigators as a late-breaking presentation at the upcoming 2018 Scientific Sessions of the American Heart Association.

CEO: Professor Silviu Itescu

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Orthocell is a regenerative medicine company committed to improving the lives of patients suffering from serious musculoskeletal conditions by developing innovative products that restore patient mobility, function and performance. Orthocell is a publicly traded company listed on the Australian Securities Exchange (ASX:OCC). Orthocell's two lead products are CelGro®, the superior collagen medical device for bone and soft tissue reconstruction and Ortho-ATI®, the world leading cell therapy for treatment of chronic tendon injury. Orthocell's technologies have now been de-risked; its target markets are large and growing; its products and procedures are regarded by key opinion leaders as being superior to existing therapies.

LEAD PRODUCTS

CelGro® is approved for use in Europe (CE Mark) in a variety of dental bone and soft tissue regeneration procedures and has demonstrated superior clinical performance for dental bone defect repair when compared to the market leading product. Orthocell is focussed on market entry of CelGro® in Europe and is preparing for first approval in the US and Australia. CelGro® is a platform technology enabling Orthocell to accelerate the products use in other indications including bone, tendon, nerve and cartilage repair procedures in key markets.

Orthocell's Ortho-ATI® is a first in class cell therapy for treatment of chronic tendon injuries. The unique treatment uses each patient's own tendon-derived cells to stimulate tendon regeneration and is delivered via ultrasound guided injection under local anaesthetic. Orthocell is delighted to be undertaking its research collaboration with Johnson and Johnson, designed to assess the safety and effectiveness of Ortho-ATI® in the treatment of rotator cuff tendinopathy and tear. Orthocell is focussed on completing this study and driving the technology into the US, the world's largest health care market.

LATEST NEWS

Orthocell has achieved key development and marketing approval milestones for both CelGro® and Ortho-ATI®:

EU regulatory approval (CE Mark) – On 9 November 2017, OCC announced receipt of European regulatory approval (CE Mark) for CelGro® to be used for a range of dental bone and soft tissue applications. This marks a significant milestone for the Company as it enables commercial rollout in the significant dental bone and soft tissue regeneration market, validates the platform technology, and provides a strong foundation for expansion into target jurisdictions such as the US, Australia and China.

Appointment of Key Opinion Leaders, distributors and first product use and sales – OCC achieved significant commercial progress in the EU leading to first product use and sales of CelGro® within 6 months of receiving CE Mark)for dental bone and soft tissue repair.

Superior clinical data –OCC announced the completion of a clinical study using CelGro® for treatment of dental bone defects. Results demonstrated that CelGro® guides superior quality bone formation when treating bone defects and results in up to 26% better quality newly formed bone when compared to the market leading comparative product.

Ortho-ATI® research collaboration - Enrolment of patients began for the Company's lead clinical trial of Ortho-ATI®, undertaken in collaboration with DePuy Synthes Products, Inc., part of the Johnson & Johnson Medical Device Companies. The objective of the study is to assess the safety and effectiveness of Ortho-ATI® compared to corticosteroid injection in the treatment of rotator cuff tendinopathy and tear, and to demonstrate the cost effectiveness of Ortho-ATI® as a minimally invasive injectable treatment for resistant tendon injuries of the elbow.

CEO: Paul Anderson

Established in Australia in 2006

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Status: Public

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Regeneus Ltd is an ASX-listed clinical stage regenerative medicine company developing a portfolio of novel cellular therapies for the human and animal health markets

Regeneus' clinical focus is on osteoarthritis (OA) and other musculoskeletal disorders, oncology, dermatology and chronic pain.

The company's product pipeline is underpinned by proprietary stem cell and immunotherapy technologies comprising:

- Allogeneic off-the-shelf adipose-derived mesenchymal stem cells (MSCs) for OA and other inflammatory conditions and pain (**Progenza** for humans and **CryoShot** for dogs and horses)
- Allogeneic off-the-shelf secretions from adipose-derived MSCs for inflammatory skin conditions and pain (**Sygenus**)
- Cancer immunotherapy that uses the patient's tumour cells and a bacterial adjuvant for immune recognition (**RGSH4K** for humans and **Kvax** for animals)

MSCs are the body's natural healing and repair cells and respond to the local disease environment and secrete a diverse variety of bioactive factors including cytokines and growth factors that are responsible for reducing inflammation, promoting tissue repair and reducing scarring.

PIPELINE

The company has completed its Phase 1 human STEP trial using Progenza to treat OA which delivered positive results showing Progenza to be safe and well tolerated by patients providing clinically meaningful pain relief and disease modification. The results have been published in the Journal of Translational Medicine. The company has completed recruitment for the Phase I Safety Study (ACTIVATE) of RGSH4K, the Company's cancer vaccine immunotherapy. The results show that all dose levels of RGSH4K were safe and well tolerated and showed encouraging signs of immune stimulation and anti-tumour activity in patients from each cohort. Sygenus has delivered positive results across a number of preclinical studies including pain, acne and age spots.

LATEST NEWS

Regeneus is leveraging off the manufacturing licence agreement and JV with AGC which has led to advanced stages of discussion and due diligence with potential licensees for the clinical development and commercialization of Progenza in Japan. Progenza has been granted patent coverage in United States and Japan and we anticipate receiving allowance of the grant of the patent in Europe in FY19. Our patent coverage for Progenza in key markets will open up further licensing opportunities in FY19. The company continues to explore licensing opportunities for the other products in its portfolio.

CEO: John Martin

Established in Sydney, Australia in 2007

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Status: Public (ASX: RGS)

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Scientifix Pty Ltd represents Takara Bio; a company with over 15 years' experience providing stem cell derived products and services for the drug discovery, toxicity testing and regenerative medicine industries. Takara Bio leverages long-standing experience in stem cell handling and scale up, and is able to provide tools and service support for every stage of their customers' stem cell research.

Specifically, the company possesses broad expertise in the following:

- Human pluripotent stem cells generation and culture, including hiPSC and hESC, and related media
- Gene editing in stem cells using CRISPR/Cas9 systems, viral vectors, gesicles and electroporation
- Directed stem cell differentiation and cell lines, including cardiomyocytes, hepatocytes, definitive endoderm cells, beta cells and neural differentiation
- Stem cell monitoring and characterisation of pluripotency, engraftment, and differentiation using antibodies, molecular markers, HLA typing and pluripotency check-kits
- Custom iPS cell-based service requests:

◊ Clinical-grade hES cell line generation
◊ Sourcing of patient- or disease-specific fibroblasts or PBMCs for later reprogramming into iPSC cells
◊ Footprint-free reprogramming of your samples or sourced samples using Sendai virus technology
◊ Generating Master Cell Bank from iPS or ES cells
◊ Directed differentiation of your patient- or disease-specific iPS or ES cell lines into hepatocytes or definitive endoderm cells

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In Vitro Technologies are the premier supplier for cell biology and immunology research throughout Australia and New Zealand. Partnering with world-class providers, In Vitro provides a premium portfolio of products, resources and applications support for stem cell research and therapeutic development.

Cells	Mouse eSCs, Human eSCs, Human iPSCs, NPCs and MSCs
Expansion	Extra Cellular Matrices (ECMs), Shaking Incubators, Bioreactors and Stem Cell Media
Differentiation	Cytokines, Growth Factors and GMP Proteins
Verification	Antibodies, Verification Kits and Flow Cytometry
Investigation	Real-Time Cell Analysis, Flow Cytometry, Cell Metabolism Analysis, IHC and RNA ISH
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Accelerate discovery into stem cell research through high quality, reproducible data and publish high impact papers.

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PreproTech operates in Australia via a distributor*

Mr. Offir Manor | General Manager, PeproTech Asia
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Supporting life science research since 1988, **PeproTech** has a long record of being a trusted manufacturer of high quality cytokine products for the life-science and cell therapy markets.

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With over 2,000 products, PeproTech has developed and refined innovative production and purification protocols to ensure the quality, reliability and consistency of its products. Our mission is to provide the highest quality products and premium support and customer service that address the needs and requirements of today's scientific community and the growing landscape of cellular therapy oriented companies. We pride ourselves on being a trusted partner within the basic and applied scientific research community.

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- ELISA kits
- Stem Cell Culture Media and Kits
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- Antibodies and Reagents for Flow cytometry

*PeproTech is distributed in Australia by LONZA and in New Zealand directly with an Office in Australia managed by Margret Schuller

***Table 1*. Details of clinical trials run by cell therapy companies listed in the Snapshot ***

Company	Study identifier	Study title	Phase	Comparator	Ethics approval
Cynata	CYP-GvHD-P1-01	An Open-Label Phase 1 Study to Investigate the Safety and Efficacy of CYP-001 for the Treatment of Adults With Steroid-Resistant Acute Graft Versus Host Disease	1	N/A	No details available
Magellan Stem Cells	ACTRN12617001095358	Evaluation of the safety and tolerability of allogeneic adipose-derived mesenchymal stem cells administered by intra-articular injection to patients with symptomatic osteoarthritis of the knee	1	N/A	Approved
Magellan Stem Cells	ACTRN12617000638336	Evaluation of adipose derived mesenchymal stem cells for the treatment of arthritis	1	N/A	Approved
Magellan Stem Cells	ACTRN12617000636358	Evaluation of adipose-derived mesenchymal stem cells for the treatment of chronic lower back discogenic pain - a prospective, case series pilot study	1	N/A	Approved
Magellan Stem Cells	ACTRN12615000260527	The evaluation of autologous adipose derived mesenchymal stem cells as treatment for symptomatic hip osteoarthritis on pain, function and cartilage volume in osteoarthritis patients.	N/A	N/A	Approved
Magellan Stem Cells	ACTRN12615000258550	The evaluation of autologous adipose derived mesenchymal stem cells as treatment for symptomatic knee osteoarthritis on pain, function and cartilage volume in osteoarthritis patients	N/A	N/A	Approved
Magellan Stem Cells	ACTRN12615000257561	The evaluation of autologous adipose derived mesenchymal stem cells in combination with arthroscopic microfracture as treatment for symptomatic hip osteoarthritis on pain, function and cartilage volume in osteoarthritis patients	N/A	N/A	Not yet submitted
Mesoblast	NCT02032004	The Purpose of This Study is to Evaluate the Efficacy and Safety of Allogeneic Mesenchymal Precursor Cells (CEP-41750) for the Treatment of Chronic Heart Failure	3	Sham comparator: control treatment	No details available
Mesoblast	NCT02362646	Safety & efficacy of intramyocardial injection of mesenchymal precursor cells on myocardial function in LVAD recipients	2	Sham comparator: control solution	No details available

* Clinical trial registries (clinicaltrials.gov, anzctr.org.au) were accessed BEFORE 18/10/2018. This is not an exhaustive list of studies. *HREC:* Human Ethics Research Committee; *MPC(s):* mesenchymal progenitor cell(s); *MSC (s)*: mesenchymal stem cell(s); *N/A:* not applicable.

***Table 1* (Continued). Details of clinical trials run by cell therapy companies listed in the Snapshot ***

Company	Study identifier	Study title	Phase	Comparator	Ethics approval
Mesoblast	NCT01781390	Safety study of allogeneic mesenchymal precursor cell infusion in myoCardial infarction (AMICI)	2	Placebo	No details available
Mesoblast	NCT02412735	Safety and efficacy study of Rexlemestrocel-L in subjects with chronic discogenic lumbar back pain (MSB-DR003)	3	Placebo	No details available
Mesoblast	NCT02336230	A Prospective Study of Remestemcel-L, Ex-vivo Cultured Adult Human Mesenchymal Stromal Cells, for the Treatment of Pediatric patients Who Have Failed to Respond to Steroid Treatment for Acute GVHD	3	N/A	No details available
Mesoblast	NCT01854567	P3 Study of Umbilical Cord Blood Cells Expanded with MPCs for Transplantation in patients with Hematologic Malignancies	3	Active comparator: Control	No details available
Mesoblast	NCT01851070	A Multi-center Study a Single IV Infusion of Allogeneic MPCs in patients with Rheumatoid Arthritis and Incomplete Response to at Least One TNF Alpha Inhibitor	2	Placebo	No details available
Mesoblast	NCT01843387	Safety and Efficacy of Mesenchymal Precursor Cells in Diabetic Nephropathy	1/2	Placebo	No details available
Mesoblast	NCT00482092	Evaluation of PROCHYMAL® Adult Human Stem Cells for Treatment-resistant Moderate-to-severe Crohn's Disease	3	Placebo	No details available
Orthocell	ACTRN12615000027516	Single-centre, open-label, pilot study of Celgro(tm) collagen membrane for guided bone regeneration around exposed dental implants in patients undergoing dental implant surgery	N/A	Uncontrolled	Approved
Orthocell	ACTRN12614000532606	Repair of Symptomatic Ear Drum Perforations: A Pilot Study using Celgro Trademark Type I/III Collagen Bioscaffold	1/2	Uncontrolled	Approved

* Clinical trial registries (clinicaltrials.gov, anzctr.org.au) were accessed BEFORE 18/10/2018. This is not an exhaustive list of studies. *HREC:* Human Ethics Research Committee; *MPC(s):* mesenchymal progenitor cell(s); *MSC (s)*: mesenchymal stem cell(s); *N/A:* not applicable.

Company directory

Company	Contact	Profile
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Clinical Stem Cells	www.clinicalstemcells.com	N/A
Cryosite	www.cryosite.com	N/A
CSL	www.csl.com.au	N/A
Cynata Therapeutics	www.cynata.com P: +61 (0) 412 119 343 E: ross.macdonald@cynata.com	**Page 12**
Eppendorf	www.eppendorf.com	N/A
In Vitro Technologies	www.Invitro.com.au P: 1300 552 003 E: daina.elliott@invitro.com.au	**Page 18**
Living Cell Technologies	www.lctglobal.com	N/A
Magellan	www.magellanstemcells.com.au	N/A

Company directory

Company	Contact	Profile
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STEMCELL Technologies	www.stemcell.com E: cyndy.nauer@stemcell.com P: 1800 060 350	**N/A**

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Thermofisher	www.thermofisher.com.au	N/A