



BioPreservation Today[®]

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19TH ISCT ANNUAL MEETING
AUCKLAND, NEW ZEALAND

FEATURE ARTICLE

WHAT'S UP DOWN UNDER

Cell Therapies in Australia

ALLIANCE FOR REGENERATIVE MEDICINE

2012 Perspective

IN THIS ISSUE

3

EDITOR'S CORNER

Mike Rice, Chairman and CEO, BioLife Solutions, Inc.

4

WHAT'S UP DOWN UNDER Cell Therapies in Australia

By Dawn Driscoll

10

ALLIANCE FOR REGENERATIVE MEDICINE 2012 Perspective

Robert Margolin, VP, Communications, Alliance for Regenerative Medicine
Lee Buckler, Managing Director, Cell Therapy Group



REFLECTION OF THE SKY
TOWER COMPLETED IN 1997
1,076 FEET

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WEB RESOURCES

www.aabb.org | American Association of Blood Banks

www.celltherapy.org | International Society for Cellular Therapy

www.asbmt.org | American Society for Blood and Marrow Transplantation

www.ishrs.org | International Society of Hair Restoration Surgery

www.alliancerm.org | Alliance for Regenerative Medicine

www.bestcollaborative.org | BEST Collaborative

www.regenerativemedicinefoundation.org | Regenerative Medicine Foundation

www.phacilitate.co.uk/pages/cgtherapy/index.html | Phacilitate

UPCOMING EVENTS

19th ISCT Annual Meeting
April 22-25, 2013
Auckland, New Zealand

**World Stem Cells &
Regenerative Medicine**
May 21-23, 2013
London, UK

**11th Annual International
Cord Blood Symposium**
June 6-8, 2013
San Francisco, CA

**Stem Cells USA &
Regenerative Medicine
Conference**
September 30 - October 1, 2013
Cambridge, MA





EDITOR'S CORNER

Mike Rice, Chairman & CEO, BioLife Solutions, Inc.

Greetings from Down Under and the 19th ISCT Annual Meeting,

Readers of BioPreservation Today® (BPT), we welcome you to Auckland for what I'm sure will be another highly valuable scientific and business meeting of the International Society for Cellular Therapy. Our field is advancing daily with innovation and scientific rigor that bring hope for new and improved cell and tissue based products and therapies to millions around the world suffering from life-impacting and life-threatening diseases and disorders. We're proud to again be a bronze level corporate sponsor of this key event in the field of regenerative medicine.

Please join us from 12:30PM – 1:30PM on April 23rd for a corporate tutorial presented by Aby J. Mathew, Ph.D., our Senior Vice President and Chief Technology Officer, on the topic: Roadmap for Cell/Tissue Stability Gap Analysis and Clinical Qualification of Biopreservation Excipients/Ancillary Reagents. The abstract of this presentation follows:

Cellular therapies and regenerative medicine utilize cell and tissue products sourced from blood, bone marrow, and various tissues. The clinical and commercial success of these products is potentially impacted by stability limitations, which include transport of the source material and biopreservation of the final cell or tissue product (either frozen or non-frozen). Traditional home-brew reagent cocktails (including serum) utilized for biopreservation are an area of risk within a GMP clinical manufacturing process. This discussion will address how to identify gaps within system stability, and how to qualify methods of biopreservation reagent optimization. Topics include best practices in optimizing biopreservation workflow, including transportation and storage of source material and final dose, intermediate manufacturing process hold steps, and evaluation, selection, and qualification of ancillary and excipient reagents. Case studies of clinical applications in a range of cellular therapies utilizing HypoThermosol® for non-frozen products and CryoStor® for cryopreserved products will be discussed.

For those readers attending the meeting in Auckland, you will note several oral abstracts and poster presentations citing the use of our clinical grade biopreservation media products.

In this issue of BPT, Dawn Driscoll, Ph.D., managing director of DCi Biotech, an Australian and US based cell therapy commercialization consultancy, provides an excellent overview of cell therapy innovations in Australia.

Also in this issue, Robert Margolin, VP, Communications for the Alliance for Regenerative Medicine, and Lee Buckler, Managing Director at the Cell Therapy Group, provide a state of the industry overview of approved products and therapies.

Thank you for your continued interest in BioLife products. I hope you enjoy this issue of BioPreservation Today. We look forward to seeing you at our exhibit in spaces 22 & 23 and corporate tutorial on April 23rd.

Best regards,

Mike



WHAT'S UP DOWN UNDER? CELL THERAPIES IN AUSTRALIA

By Dawn Driscoll

With input from Marian Sturm, Cecilia Prêle, Flavia Kuhn,
David Toner, Tom Loudovaris, Tony Mason, and Stewart Hay

Development and commercialization of cell therapies is racing ahead globally with notable progress being driven via groundbreaking activities in Australia. While many are familiar with the advances that companies such as Mesoblast (www.mesoblast.com) and Invetech (<http://www.invetech.com.au/markets/life-sciences/cell-therapy/>) have made with innovative clinical therapies and technologies, this article focuses on several lesser known and hot off the presses cell therapy activities in Australia.

Australia has a flexible approach to clinical development of advanced biologicals such as cell therapies and regenerative medicines, as mapped out in the Therapeutics Goods Administration's Regulatory Framework for Biologicals <http://www.tga.gov.au/industry/biologicals-framework.htm>. This provides for entry into early stage clinical trials without full GMP licensure, but with an appropriate ethical review for the safety of patients. Novel and very promising developments are taking place in Australia under this framework, across hospital-based groups, academic consortia, global corporations, and academia-government-industry partnerships. We present several of Australia's latest cell therapy ventures below.

Cell & Tissue Therapies, Western Australia (CTTWA)

CTTWA at the Royal Perth Hospital in Perth Australia has been blazing ahead on multiple cell therapy and regenerative medicine fronts under the direction of Clinical Professor Richard Herrmann and Dr Marian Sturm. The group's exciting progress with a Crohn's disease trial was recently highlighted in a TV news story which can be seen on <https://www.facebook.com/photo.php?v=10152765286875424&set=vb.135107816501387&type=2&theater>.

CTTWA was developed following recognition by RPH of the advantages in integrating all current cellular and tissue manufacturing into a single facility, enabling the demands of new emerging cellular and tissue therapies and increased regulatory requirements to be met. CTTWA was

constructed, qualified and commissioned in 2006, with clinical manufacturing commencing in December 2006 with TGA approval (Licence No. 44165). The facility consists of five clean rooms, specified as ISO class 7, with rooms outfitted with biological safety cabinets and multiple incubators for cell expansion.

CTTWA currently manufactures human heart valves, skin, haemopoietic stem cells, serum eyedrops and other cells and tissue for the WA Health Service. CTTWA also manufactures biotherapeutic products for local, national and international clinical trials. The facility has extensive experience in the manufacture of culture expanded products.

CTTWA is actively involved in advancing research and development of potential new cell and tissue therapies, with a strong interest in mesenchymal stromal cells and the development of bio-scaffolds. It currently has six clinical trials underway using CTTWA manufactured allogeneic MSC for both immune disorders and tissue repair. The first trial of MSC in steroid refractory GVHD has progressed to a randomised Phase II trial for naïve GVHD. The Phase II study in biologic refractory Crohn's disease has shown a high clinical response rate to treatment and will be presented at the ISCT Auckland meeting .

Preliminary outcomes for other studies in organ transplantation are also encouraging. CTTWA is available to support approved public and commercial therapeutic manufacturing. For further information, contact details Dr. Marian Sturm at marian.sturm@health.wa.gov.au

“THE AIM OF THE CENTRE FOR CELL THERAPY AND REGENERATIVE MEDICINE IS TO PROMOTE RESEARCH IN THE AREA OF STEM CELL THERAPY AND REGENERATIVE MEDICINE”

Centre for Cell Therapy and Regenerative Medicine at the University of Western Australia

The Centre for Cell Therapy and Regenerative Medicine is a newly established research at the University of Western Australia. The vision of the Centre, ‘New Ideas leading to new Medicines’, is supported by a common research strategy across many areas of medicine. Disease areas include: cancer, asthma, chronic lung diseases, diabetes, heart disease, rheumatoid arthritis, osteoarthritis, osteoporosis, fibrosis, macular degeneration, muscle degeneration and neurodegenerative disease such as Parkinson’s and Alzheimer’s. In addition, researchers within the Centre for Cell Therapy and Regenerative Medicine are investigating strategies to replace damaged tissue following acute trauma. The aim of the Centre for Cell Therapy and Regenerative Medicine is to promote research in the area of stem cell therapy and regenerative medicine and to translate discoveries into novel therapies and improve health outcomes for patients.

The Centre is a broad, collaborative research network, which currently links more than 50 researchers across Western Australia with international scientists at leading Universities and research institutes, including University College London, UK and Helmholtz Zentrum, Munich,

Germany. The Centre is directed by Winthrop Professor Geoffrey Laurent, an internationally recognised researcher who until recently led a world leading research and training centre at University College London, UK. Professor Laurent is supported by the Centre’s Deputy and Clinical Directors, Winthrop Professors George Yeoh and Fiona Wood. Professor Yeoh is a world expert in liver stem cell biology, particularly in relation to cancer. Professor Wood is a leading surgeon with an international reputation for the clinical use of cell therapy approaches for skin repair. For more information on the Centre for Cell Therapy and Regenerative Medicine or to be added to the Centre’s mailing list please email cecilia.prele@uwa.edu.au



Participants of the CCTRM Inaugural meeting held on 20th June 2012

The Cooperative Research Centre for Cell Therapy Manufacturing

In a world first, the newly established Cooperative Research Centre for Cell Therapy Manufacturing will bring together, under one roof, the spectrum of skills and facilities required to turn a promising cell into a viable cell therapy. The Centre’s vision is to provide new treatments and develop new materials-based manufacturing technologies to increase the accessibility, affordability and efficacy of cell therapies. With a total of \$59M in cash and in-kind resources, including a \$20M grant from the Government of Australia, the Centre will develop smart material interventions to facilitate the cost-effective manufacture and rapid translation of cell therapies into clinical practice.

Based at the University of South Australia, the Centre's national and international partners include research providers, manufacturers, hospitals and charities. Underpinning this partnership is a newly established cGMP manufacturing facility at UniSA's Mawson Lakes campus, designed to deliver cell-based therapeutics for the Centre's first-in-man clinical trials.

The Centre's research activities will be managed through two integrated research programs. Program 1 (Materials and Bioprocessing) will develop new materials and surfaces to enable the cost-effective isolation, expansion and delivery of therapeutic cells, while Program 2 (Clinical Translation) will validate these innovations through preclinical testing and clinical trials of novel cell populations and delivery devices. Initially the Centre's research will focus on mesenchymal stem cells, endothelial progenitor cells, T-regulatory cells and pancreatic islets. Potential clinical applications for these cells include diabetes, chronic wound repair and autoimmune disorders.

The Centre will also train a new generation of highly skilled graduates, including PhD students with entrepreneurial skills to support Australia's expanding cell therapy industry.

For further information please contact: Flavia Kuhn (Flavia.Kuhn@unisa.edu.au)

Therapeutic Innovations Australia

Therapeutic Innovation Australia (TIA) is an Australian not-for-profit company which supports translational health researchers through providing world class commercial expertise and through enabling access to state of the art equipment and facilities. TIA is specifically funded to implement the Australian Governments' 'Translating Health Discovery into Clinical Application' project. This includes cell therapies.

One of the most recent efforts of TIA is the development of the National Regulatory Repository (NRR). Dr Stewart Hay of TIA comments, "For novel therapeutics to reach the clinic the investigator must satisfy the safety and efficacy requirements



*Photo courtesy of the University of South Australia
Image: University of South Australia's Mawson Institute Cell Therapy Laboratory*

of the regulator. Much of the documentation used to meet these regulatory standards, particularly those that relate to facility or process compliance, is reproducible. Furthermore, this process of compliance is both time consuming and expensive with a full system often taking well over 12 months and \$300,000 to create.

In an effort to reduce the cost and time burden of creating documents to meet this requirement TIA has established the National Regulatory Repository (NRR). This resource provides open licence documentation which can be used to support efforts to comply with regulators such as the Therapeutic Goods Administration. The NRR seeks to bring greater efficiency to the process of compliance by ensuring that a) there is no needless duplication of effort and b) by facilitating a unified response to meeting the requirements of the regulator."

Documents can be viewed on:

http://www.therapeuticinnovation.com.au/Infrastructure/National_Regulatory_Repository.aspx

Victorian Consortium for Cell-based Therapies

The Monash Institute of Medical Research and St Vincent's Institute, together with 21 other public sector partners and 13 Industry partners, have recently come together to form the Victorian Consortium for Cell-based Therapies (VCCT) with the aim of sharing knowledge and developing shared infrastructure to accelerate the delivery of cell therapies to improve patient outcomes. This Consortium has used \$2M of funding obtained from the Federal Government Education Investment Fund to purchase two new BioSpherix GMP Isolator Units for cell processing in Victoria, one to be based at the new Monash Health Translation Precinct, currently under construction at the Monash Medical Centre, and one on the St Vincent's Hospital campus. The BioSpherix Isolators were chosen because they had advantages over other Isolators that were evaluated, namely more flexibility to accommodate the diverse needs of the VCCT members. The Isolator Units have been designed for future expansion and customization, including the addition of independent "dockable"

incubators to increase flexibility and multiplicity of use.

The St Vincent's Isolator Unit (see picture) is comprised of 9 linked modules that can be individually updated as required, or replaced to accommodate new equipment or procedures. It has a module that was customized to incorporate a water-cooled GMP centrifuge, so the products do not leave the Isolator containment during centrifugation steps. There is also a module that incorporates a microscope so cells can be visualized in the same environmental conditions in which they are cultured. Another module is refrigerated so processing can occur at 4°C to 8°C for cells or tissues that are temperature sensitive. Alternatively, the temperature can be set at up to 37°C in another Isolator module when metabolic or digestive processes are used or evaluated. In addition to temperature control, the levels of oxygen, nitrogen and carbon dioxide are adjustable and can be set to optimize processing or culturing requirements for particular tissues or cells. Three independent incubators are available to culture three different cell types or the same cells under three different conditions. The Monash Isolator Unit is similar in construction with 8 linked modules, including GMP centrifugation and microscopy capacity, and temperature and gas controlled environments. Both Units will be housed in Class D facilities.

The first product to be manufactured using the Isolator at St Vincent's will be human islets for transplantation. Since 2005, islet cell processing has been successfully undertaken in a conventional Class A/B environment of a clean room at the Peter MacCallum Cancer Centre. The move to Isolators in 2013 is expected to improve the overall process further by reducing costs and processing times, as well as providing a more comfortable environment for operators.

The Monash Isolator Unit will initially be used to isolate human Amnion Epithelial Cells for a clinical trial of the treatment of Broncho Pulmonary Dysplasia in premature infants. Isolation and expansion of human endometrial stem cells for incorporation into novel matrices for use in the

treatment of Pelvic Organ Prolapse will also be undertaken in this Unit, while isolation and expansion of bone marrow derived Mesenchymal Stromal Cells within the Isolator is planned for a Multiple Sclerosis clinical trial in late 2013.

Both Monash Institute of Medical Research and St Vincent's Institute have been working closely with the Australian Red Cross Blood Service under the auspices of a separate Therapeutic Innovations Australia agreement to develop the required quality control systems necessary to operate the two facilities to GMP standards. The facilities are expected to be operational by the end of June 2013.

For further information about the Isolators and access to the facilities via the VCCT, please contact Graham Jenkin at Monash Institute of Medical Research (Graham.Jenkin@monash.edu) or Tony Mason at St Vincent's Institute (tmason@svi.edu.au).



The St Vincent's Isolator Unit.

Verigen Australia Pty Ltd.

While the autologous cellular product Carticel® is well known as the first and only FDA-approved cell therapy product that can be used to repair articular cartilage injuries in the knee of adults, it is less well known that there is also a gleaming production facility in Australia that is manufacturing a next generation of this product.

Verigen Australia Pty Ltd ABN 15 085 385 637 ("Verigen") is a wholly subsidiary of Genzyme, a Sanofi Company and manufacturer of the MACI® (matrix- induced autologous chondrocyte implant) at its state-of-the-art facility in Perth suburb of Malaga, Western Australia. The MACI implant is an innovative third (3) generation autologous chondrocyte implantation product for treating

chondral and osteochondral defects in the knee. It offers effective treatment by culturing a patient's (autologous) own cartilage cells and implanting these cells in the damaged area of the knee joint using a dissolvable collagen matrix scaffold delivery system.

Verigen is one of three global operational sites within Genzyme's Cell Therapy and Regenerative Medicine business unit and we supply product within Australia and throughout the Asia Pacific region. Our mission is to transform disease through regenerative medicine and we aim to be recognised as a global leader in cell-based therapies and regenerative medicine by providing innovative solutions for unmet medical needs. As a subsidiary of Genzyme, a Sanofi Company, Verigen has links in all of the major markets of the world and is well placed to be the business partner of choice for new cell therapy products.

As one of the world's leading biotechnology companies, Genzyme is dedicated to making a major positive impact on the lives of people with serious diseases. With many established products and services helping patients in approximately 100 countries, Genzyme is a leader in the effort to develop and apply the most advanced technologies in the life sciences business sector.

Sanofi is committed to treating and preventing human disease through the discovery, development, manufacture and sale of innovative pharmaceutical products aimed at satisfying unmet medical needs. One of the four largest pharmaceutical companies in the world, Sanofi has core strengths in the field of healthcare, is the world leader for human vaccine production and commercialisation of major biological products, and has a worldwide presence with a strong long-established presence in emerging markets.



Verigen Australia GMP facility in Malaga, Western Australia

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Dawn Driscoll, PhD MBA, is the managing director of DCi Biotech Inc, a cell therapy commercialization consultancy, with offices in the US and Australia. For more information on DCi's comprehensive business services, please see www.dci-biotech.com or contact DCi directly at info@dci-biotech.com

ALLIANCE FOR REGENERATIVE MEDICINE 2012 PERSPECTIVE

Robert Margolin, VP, Communications, Alliance for Regenerative Medicine
Lee Buckler, Managing Director, Cell Therapy Group



Arguably the most prominent segment of the regenerative medicine industry, the cell therapy sector, is currently engaged in over 1,900 clinical trials around the world. This includes more than 300 clinical trials being sponsored by approximately 250 companies developing commercial products for almost every imaginable disease or condition.

In addition to the products commercially available and in development, cells have been used as a standard of care for decades in the medical practice of hematology and oncology.

In fact, stem cell transplants have been a staple of cancer treatment since it was first introduced in the late 1960s. Stem cell transplantation continues to be routinely used in, and investigated for, an increasingly diverse and growing list of (now over 70) malignant and non-malignant diseases. Over one million stem cell transplants have been performed globally to date.

Cells are Today's Biotech Products

Living cells are incorporated into today's regenerative medicines to achieve a variety of positive effects:

- To replace damaged or diseased cells and/or tissue
- To stimulate an endogenous response that promotes the body's own healing such as an immune response or regeneration in diseased tissue
- To deliver genetic or molecular therapies to targets

There are approximately 40 cell therapy products commercially distributed in regulated markets.¹

While no cell therapy products were approved by any regulatory agency from 2002 to 2008. In the past five years there have been 12 approvals in the United States (six), Europe (one), Canada (one), New Zealand (one), and South Korea (three).

All of the cell therapy products commercially available are for skin, wound, bone or cartilage repair with the exception of Dendreon's Provenge, approved by the FDA in 2010 for late-stage prostate cancer. The first of these products, Apligraf, was brought to market in 1998. Collectively, these top 20 cell therapy products are estimated to have treated over 500,000 patients through the end of 2011, and approximately 140,000 patients in 2012 alone. Research conducted by ARM valued the top 20 cell therapy products based on revenue generation to total the following amounts beginning in 2010:

\$460 million <i>(2010 estimated)</i>	\$730 million <i>(2011 estimated)</i>	\$900 million <i>(2012 estimated)</i>
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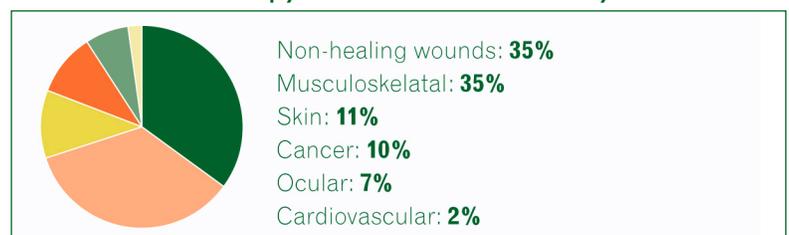
Cells are Tomorrow's Future Therapies in Development Today

A variety of cell types including primary cells, progenitor cells, tissue-specific stem cells (adult stem cells), embryonic stem cell and now reprogrammed cells (induced pluripotent stem cells) are in various stages of development. They are being tested for almost every imaginable human condition ranging from large-scale indications like chronic heart failure, cancer and diabetes to orphan indications for which there are few available treatments.

This pipeline of cell-based therapies represents a maturation of the science surrounding such products and therapeutics. As such, these next-generation products carry with them enhanced expectations of efficacy and commercial viability.

Compared to the first generation of cell therapies, the products currently in clinical development must be better characterized

Over 40 Cell Therapy Products Commercially Available



and understood mechanistically. This in turn often requires advanced culturing techniques which may involve genetic engineering and also more targeted and effective delivery techniques. Additionally, these products often require significantly more sophisticated and scalable manufacturing technologies while also being subject to the requirements of a regulatory framework that has evolved considerably since the first products were approved.

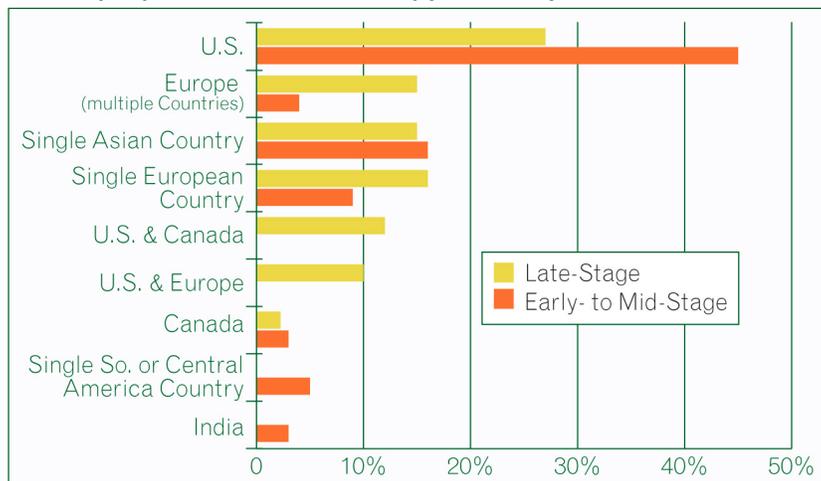
At the same time that these therapies are targeting more complex indications and involving more sophisticated technologies, there is also concurrent pressure to significantly lower the cost of goods to improve commercial viability and support applications for reimbursement.

“THIS PIPELINE OF CELL-BASED THERAPIES REPRESENTS A MATURATION OF THE SCIENCE SURROUNDING SUCH PRODUCTS AND THERAPEUTICS”

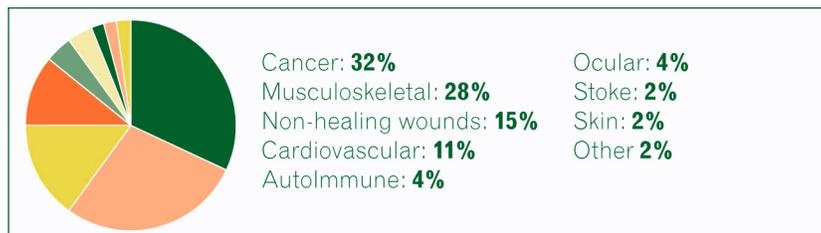
Ongoing Industry-Sponsored Cell Therapy Trials by Phase

54 Late-Stage 43 companies	209 Mid-Stage 114 companies	63 Early-Stage 49 companies
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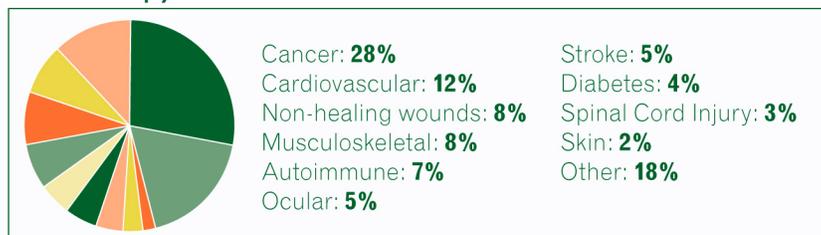
Industry-Sponsored Cell Therapy Trials by Location



Currently in Late-Stage Industry-Sponsored Cell Therapy Trials (Phase 2/3, 3, pivotal)



Currently in Early- to Mid-Stage Industry-Sponsored Cell Therapy Trials (Phase 1, 1/2, 2)



¹ For the purposes of this report, we have restricted this data to countries with formal regulatory frameworks for this type of product, thus excluding cell therapy treatments provided in unregulated markets.

THANK YOU FOR YOUR BUSINESS AND SUPPORT



BIO LIFE SOLUTIONS CUSTOMER SERVICE TEAM

BioLife Solutions develops and markets patented hypothermic storage/transport and cryopreservation media products for cells, tissues, and organs. BioLife's proprietary HypoThermosol[®], CryoStor[®], and BloodStor[®] platform of biopreservation media products are marketed to academic research institutions, hospitals, and commercial companies involved in cell therapy, tissue engineering, cord blood banking, drug discovery, and toxicology testing. BioLife products are serum-free and protein-free, fully defined, and formulated to reduce preservation-induced, delayed-onset cell damage and death. BioLife's enabling technology provides research and clinical organizations significant improvement in post-preservation cell and tissue viability and function.