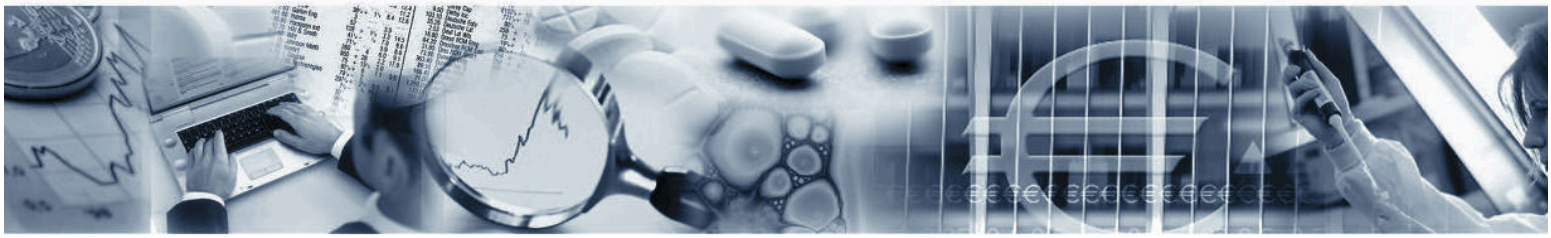


Research Note

Cynata Therapeutics Ltd

Emerging Industry Leader in Regenerative Medicine

Chief Research Analyst

Marcel Wijma MSc

+1 (917) 460 6185 (US)

+31 (6) 1848 4204 (NL)

m.wijma@leeuwenhoeck.com

http://www.leeuwenhoeck.com

Date: 1 June 2017

Name:	**Cynata Therapeutics**
Country:	**Australia**
Price:	**AUD 0.57**
ISIN Code:	**AU000000CYP7**
Reuters Code:	**CYP.AX**
Market Cap (AUD m):	**51.6**
EV (AUD m):	**40.0**
Cash & cash eq. (AUD m):	**11.6**
Shares outstanding (m):	**90.0**
Volume:	**190,846**
Free float:	**91%**
52-week Range:	**0.26-0.81**

AUD million	2014/15A	2015/16A	2016/17E
Total Revenues	0.375	1.247	3.000
Net (Loss)/Profit	(3.712)	(4.939)	(4.000)
Net (loss)/profit ps (cents)	(6.12)	(6.82)	(4.42)
R&D costs	1.920	4.155	4.000
Cash increase/(decrease)	(0.424)	0.208	5.121
Cash and marketable sec.	4.704	4.879	11.000

Executive Summary

- Cynata Therapeutics Limited (ASX: CYP) is a clinical stage Australian stem cell and regenerative medicine company that is developing a therapeutic stem cell platform technology, Cymerus™, originating from the University of Wisconsin-Madison. The proprietary Cymerus™ technology addresses a critical shortcoming in existing methods of production of mesenchymal stem cells (MSCs) for therapeutic use, which is the ability to achieve batch-to-batch consistency and economic manufacture at commercial scale.

- Japanese multinational Fujifilm (major shareholder with ~9%), has an exclusive worldwide option to a license to market and sell its lead product CYP-001 for graft-versus-host disease (GvHD). Earlier this month, Cynata announced the commencement of a world-first Phase I trial with a first patient with GvHD treated. A total of 16 patients are expected to participate in the phase 1 trial and participating patients will receive two infusions of CYP-001, with a week between doses. The potential GvHD peak annual sales are estimated to be USD 300 million.

- The market for regenerative medicine, particularly stem cell therapy is growing rapidly. Even though the majority of people still perceive regenerative medicine as something of the future, it is actually here and now. The global market for stem cells has been estimated at USD 12 billion in 2016 and is projected to reach USD 26.6 billion by 2021, at a CAGR of 13.7% during the forecast period 2016 to 2021.

- The Company's current cash position is AUD 11.6 million which should be sufficient to carry out the further development of its pipeline beyond 2018. Beginning of this year, Cynata raised AUD 10 million including an equity stake of 9% that Fujifilm took as part

of the partnership in GvHD. The funds will be used to continue to develop its Cymerus therapeutic MSC products in its key target areas of GvHD, cardiovascular disease, oncology (glioblastoma) and respiratory disease.

- **Based on NPV based valuation, we believe that Cynata Therapeutics is substantially undervalued at the current share price of AUD 0.57. Using our valuation model and taking into account the future revenues from its Cymerus™ platform, the company's current total value should be AUD 150-175 million, or AUD 1.67-1.95 per share. This represents a substantial upside from the current share price.**

Company Profile & Technology Platform

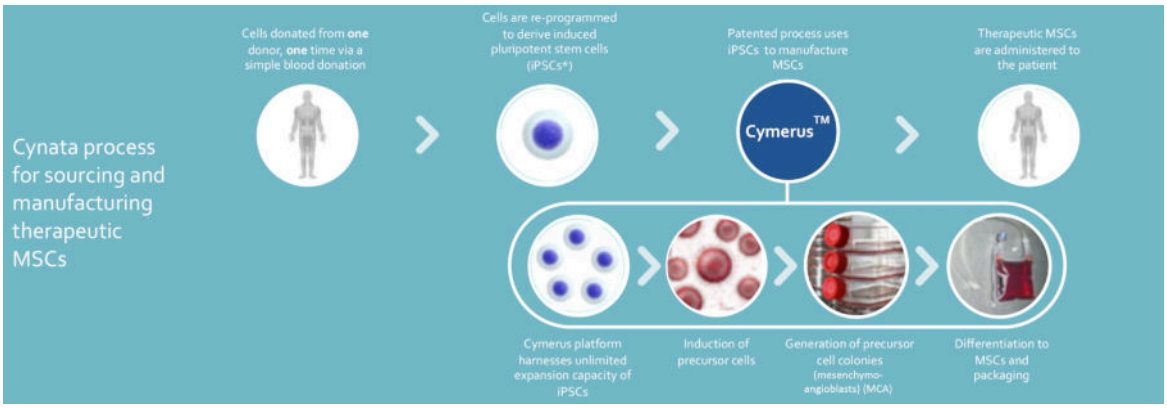
Cynata Therapeutics Limited is a clinical stage Australian stem cell and regenerative medicine company that is developing a therapeutic stem cell platform technology, Cymerus™, using discoveries made at the University of Wisconsin-Madison (UWM). The Cymerus™ technology addresses a critical shortcoming in existing methods of production of mesenchymal stem cells (MSCs) for therapeutic use, which is the ability to achieve economic manufacture at commercial scale. Stem cells, and particularly mesenchymal stem cells (MSCs, also known as mesenchymal stromal cells), are the subject of widespread research and use in 650+ clinical trials around the world.

Cymerus Technology Platform

Limitations in conventional methods of MSC production include the dependence upon 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. The numbers of adult stem cells in the tissue sources commonly used are very small. For example in one study, only 0.001-0.01% of cells isolated from bone marrow were MSCs with a typical bone marrow donation yielding around 20,000 MSCs. Similarly, from 1g of adipose tissue, only 5,000 MSCs can be isolated. This scarcity means the isolated cells have to be expanded (ie multiplied) in culture to provide sufficient numbers of cells for a single dose (typically around 100-200 million cells). This raises a significant challenge to commercial development of adult stem cell-based therapies, in the limited expandability in culture of such cells. Thus, it has been suggested that attempts to maximise the number of potential treatment "doses" from a donor through expansion in culture could compromise the quality of the product and the clinical outcome. This is one of the major reasons why doses per donor in many clinical studies are limited to the range of about 5-10 and why

recommendations are often to undertake only limited expansion prior to clinical use. This problem substantially limits the commercial application of the therapeutic MSC products.

Cynata believes that the Cymerus™ technology may address all of these issues, and the Company's development of the Cymerus™ technology is aimed at achieving that. The Cymerus™ technology utilises induced pluripotent stem cells (iPSC) and a recently identified precursor cell, known as a mesenchymoangioblast (MCA), to achieve economic manufacture with batch-to-batch consistency of MSC cell therapy products, at commercial scale.



Business Strategy and Partnerships

Cynata aims to develop the Cymerus™ technology into an "off-the-shelf" stem cell platform for therapeutic product use, with a pharmaceutical business model and economies of scale. If development continues to be successful, this will create a new standard in the fast growing arena of stem cell therapeutics. The company's strategy for commercialising specific Cymerus™ therapeutic products and technology will be through the formation of development and commercialisation partnerships. Cynata already has formed several collaborative partnerships that form part of the company's strong commercialisation and R&D platforms. A vigorous partner engagement program will likely see the Company form additional revenue-yielding partnerships in the near term.

Apceth

In May 2016, Cynata entered into a partnership with German private company apceth & Co., GmbH. It is a clinical stage biopharmaceutical company and a contract development & manufacturing organization (CDMO) for complex cell-based and gene therapy products. apceth's modular platform technology is based on genetically modified MSCs. Its lead program Agenmestencel is a first-in-man, genetically modified MSC product for the treatment of cancer. In addition, apceth develops new cell therapy candidates for the treatment of lung diseases and for immunomodulation. The agreement provides for an immediate upfront cash payment to Cynata, followed by a series of success-based milestone payments. Royalties on product sales will be also payable to Cynata. Given the substantial unmet medical needs that this relationship seeks to address, the agreement has the potential for substantial revenues to Cynata. In March 2017, apceth completed its evaluation of Cynata's Cymerus™ platform. It demonstrated the necessary characteristics required for use with apceth's own technology. However, apceth has undertaken a strategic review of its core areas and these have shifted to non malignant indications. It has therefore returned the license rights in oncology to Cynata but retained an option to non-exclusive rights to several other disease target areas.

Fujifilm Corporation

Beginning of 2017, Cynata signed a license option agreement with Fujifilm Corporation of Japan for the development and commercialization of certain Cynata technology, including Cynata's lead product CYP-001. Fuji has taken an equity stake in Cynata which now equates to around 9%. Under the agreement, Fujifilm has an option to an exclusive worldwide licence to market and sell Cynata's lead product CYP-001 as a treatment of GvHD. The potential future upfront and milestone payments are in excess of AUD 60 million. Cynata will also have the right to double digit royalties on future net sales of CYP-001. Fujifilm has successfully transformed its business strategy by

expanding away from traditional photographic film and toward new priority business fields – significantly in regenerative medicine. Fujifilm is making a major strategic commitment and investments into the area, encouraged by supportive dedicated regulations and policies in Japan. Earlier in 2015, Fujifilm acquired US firm Cellular Dynamics International (CDI) for the sum of USD 307 million. CDI manufactures and modifies human cells for ongoing research and development of therapies. CDI emerged from the same founders behind Cynata and they know the technology very well, so there is a logical fit between CDI, Fujifilm and Cynata. Fujifilm recognized that Cynata's technology was the missing piece in the puzzle to making viable stem cell treatments

Aging population and the rise in chronic degenerative diseases dictate the need for novel therapies to regenerate the damaged tissue. Stem cell technologies have a potential to significantly improve management of medical conditions associated with tissue damage, diseases which include such commercially important targets such as stroke, osteoarthritis, heart attack and asthma. Stem cell therapies are rapidly developing. Recently, significant effort has been made to translate pluripotent stem cell technologies into the clinic. Within several years we will see more clinical trials with stem cell therapies. In 2014, the Japanese government approved the law that provide rapid approval process for human stem cell-based therapies allowing such products to now come to market at the end of Phase II clinical trials. This law will facilitate swift translation of novel stem cell technologies into the clinic.

Pipeline: Strong Platform in Regenerative Medicine

Cynata's proprietary Cymerus Technology Platform can be used for the development of products for various indications. Potentially any of the indications being pursued in the more than 650 clinical trials being undertaken around the world with MSCs could be available to Cynata's Cymerus products. In the past quarter, the company commenced a Phase I clinical trial with CYP-001 in GvHD. This study is a world first in using an iPSC-derived allogeneic MSC product; Cynata's advance has received considerable global attention from the industry. Furthermore, the company also started to investigate the use of Cymerus MSCs as a treatment for acute respiratory distress syndrome (ARDS). The study evaluates the effectiveness of Cymerus MSCs in sheep with ARDS. A successful evaluation would lead to a potential clinical study.

The company also received positive preliminary data from its preclinical heart attack study. The results indicated that Cymerus MSCs have the potential to restore cardiac function and reduce scare size after a heart attack. A final report is due later in 2017. Compelling results have also been described in an asthma model where Cynata's MSCs demonstrated significant beneficial effects on all three key components of asthma: airway hyper-responsiveness, inflammation and airway remodeling. The scale and nature of these beneficial effects had not been seen with equivalent doses of human bone marrow-derived MSCs, or other stem cells, in the same model. Cynata has also published data on the utility of its Cymerus MSCs in an animal model of critical limb ischaemia (CLI), a circulatory condition that frequently occurs in diabetes patients.

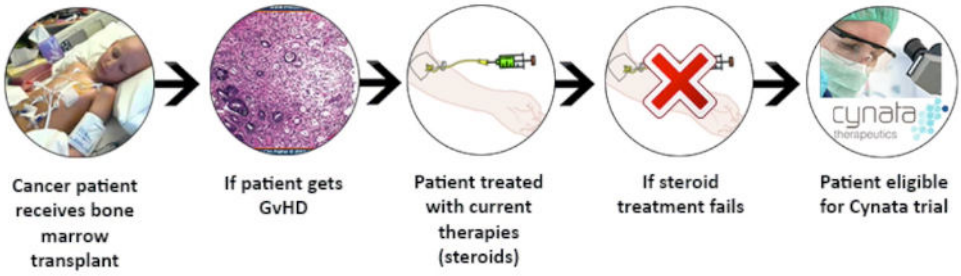
Therapeutic Area	Indication	Preclinical	Phase 1	Comments
Immunological Disorders	Graft versus host disease			World first trial
	Organ transplant rejection			
Pulmonary Disorders	Pulmonary fibrosis			
	Asthma			Compelling pre-clinical data
Circulatory Disorders	Critical limb ischaemia			Compelling pre-clinical data
	Myocardial Infarction (heart attack)			Compelling pre-clinical data
Cancer	Glioblastoma (brain tumour)			

Source: Cynata Therapeutics Ltd

CYP-001 in GvHD

In May 2017, Cynata commenced patient treatment in a world-first Phase I clinical trial to investigate the safety and efficacy of CYP-001 for the treatment of adult patients with steroid resistant acute GvHD. Patients that will be enrolled in the trial have undergone an allogeneic haematopoietic stem cell transplant (HSCT) to treat a haematological disorder and subsequently have been diagnosed with steroid resistant Grade II-IV GvHD. The first eight patients will be enrolled in Cohort A and receive two infusions of CYP-001 at a dose of 1 million cells per kilogram bodyweight, up to a maximum dose of 100 million cells. There will be one week between the two infusions. The next eight patients will be enrolled into Cohort B and receive two infusions of CYP-001 at a dose of 2 million cells/kg up to a maximum dose of 200 million cells. Efficacy will be assessed on the basis of response to treatment as determined by change in GvHD grade as well as overall survival at 28 and 100 days after the administration of the first dose. The trial has been

opened for recruitment at several major transplant centres in the UK and Australia with the first patient treated at one of the UK centres.



The start of the trial is a very important milestone for the company as it is the first time ever that a patient has been treated with an allogeneic induced pluripotent stem cell (iPSC)-derived therapeutic MSC product. CYP-001 is manufactured in a scalable process using Cynata's proprietary Cymerus platform with iPSCs as the starting material. The iPSCs are sourced from CDI, part of Fujifilm. The iPSCs were derived from a single blood donation using a non-viral and non-integrating episomal reprogramming method without any genomic modification. Thanks to the Cymerus process there is no need to source multiple donors that would bring about variability in products derived from multiple donations.

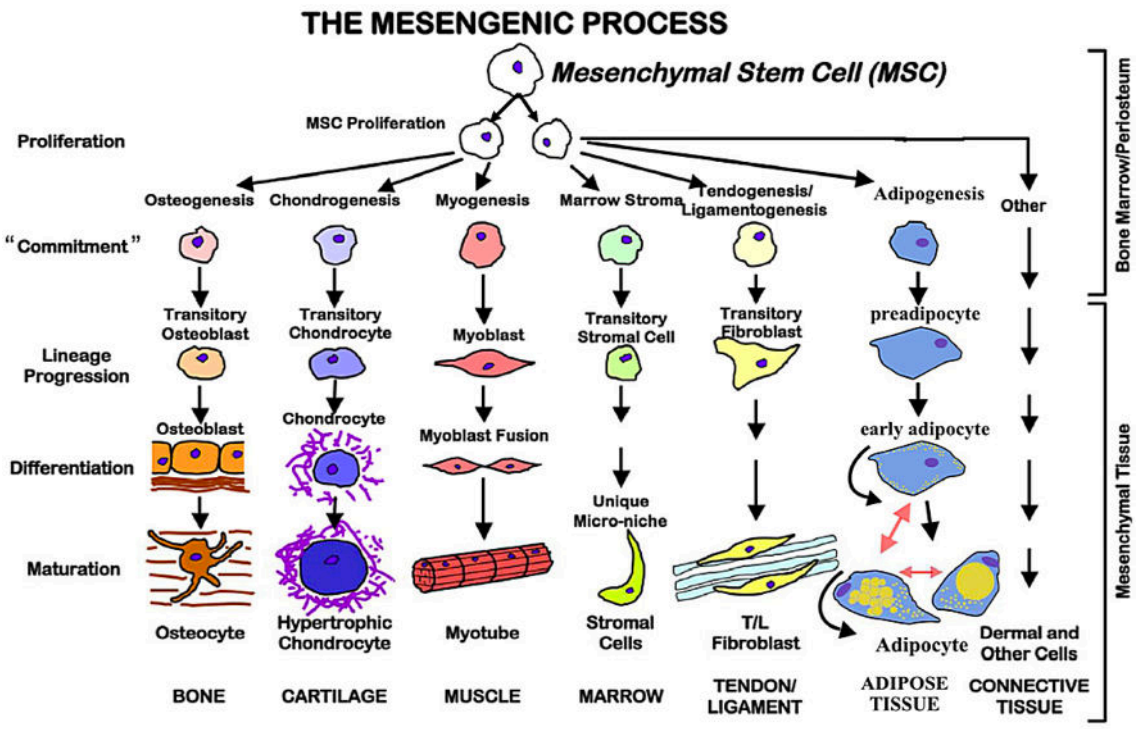
GvHD is the attack of a transplant donor's immune system (graft) against the recipient's body (the host), after an allogeneic HSCT. Typically, the onset of acute GVHD is 21–28 days after transplantation, but may be considerably later if lower dose conditioning is used. The organs most commonly affected are the skin, liver, and gastrointestinal tract. Immunosuppression with corticosteroids is the primary preferred form of therapy in acute GVHD. A response was seen in 55% in one large series of 443 patients but a durable response was maintained in only 35%. The prognosis for patients refractory to corticosteroid therapy is poor, with approximately 30% alive at one year. An MSC-based product was approved in Japan in 2016 for the treatment of acute GvHD; the product is marketed by JCR Pharma as "Temcell".

Regenerative Medicine: The New Holy Grail?

Regenerative medicine represents a new paradigm in human health with the potential to resolve unmet medical needs by addressing the underlying causes of disease. The emerging field of regenerative medicine is unique in its aim to augment, repair, replace or regenerate organs and tissue that have been damaged by disease, injury or even the natural ageing process. This rapidly evolving, interdisciplinary field is transforming healthcare by translating fundamental science into a variety of regenerative technologies including biologics, chemical compounds, materials and devices. It differs from other fields of medicine in the array of disciplines it brings together and in its ability to create or harness the body's innate healing capacity.

The use of Stem Cell Technology in Regenerative Medicine

Ever since their discovery, stem cells have been a focal point in regenerative medicine. In 1963, Canadian scientists Ernest McCulloch and James Till discovered a self-renewing cell found in the bone marrow of mice. The late 60's brought about the discovery of mesenchymal stem cells in bone marrow by Friedenstein. It was not until 1978 that similar cells were found in human umbilical cord blood and named hematopoietic stem cells. The most potent stem cells, still capable of differentiating into cell types of all three embryonic germ layers, are embryonic stem cells, which are referred to as pluripotent. However, the ongoing intense ethical and political debate restricts their use. An alternative source is provided by adult, bone marrow-derived mesenchymal stem cells (MSCs), present within the bone marrow stroma and in certain other tissues. These bone marrow-derived stromal cells have already demonstrated efficacy in multiple examples of cellular therapies, some of which have sought to exploit their differentiation and immunomodulatory capacity as shown in Figure 1 below.



Source: Texas Cell Institute

There are many different types of stem cell, and they vary in their abilities to reproduce themselves and differentiate. However, they can be broadly categorised into two major groupings being pluripotent and adult stem cells. The characteristics of these two groups of stem cells are described further below:

- Pluripotent Stem Cells: Pluripotent stem cells are the most versatile cells of all, having the ability to reproduce themselves indefinitely, and also differentiate into any other type of cell in the body. There are two main types of pluripotent stem cell, being embryonic stem cells (ESC), and induced pluripotent stem cells (iPSC).

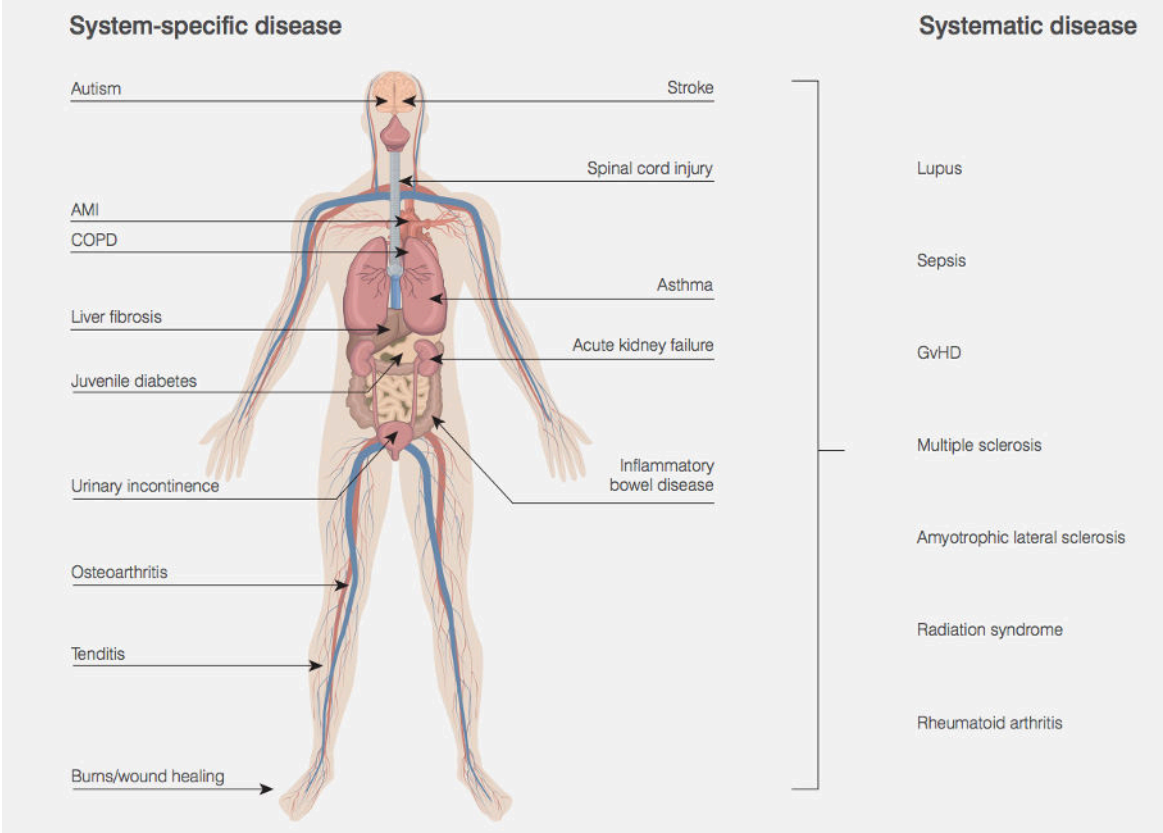
- Adult Stem Cells: Apart from embryonic and re-programmed sources described above,

stem cells can also be isolated from adult tissue (and also from tissues in infants and children). Such stem cells are typically called "adult stem cells"; "somatically derived MSCs" or "adult MSCs" are examples of adult stem cells.

Mesenchymoangioblasts (MCAs) are a newly identified and extremely important class of early clonal mesoendodermal precursor cells, meaning that they are the common precursor for both MSCs and endothelial cells

The retrieval of stem cells from the bone marrow, however, is highly invasive and provides only low numbers of stem cells. And that is exactly what the enormous added value is of Cynata's Cymerus technology. Cynata's Cymerus™ technology which incorporates MCA-derived MSCs has the potential to address these issues, and in addition, has the possibility of being able to derive multiple cell therapeutics platforms.

The range of diseases in which stem cells are being studied is illustrated in the graph below. MSCs have the ability to modulate a recipient's immune response, probably doing so by secreting bioactive molecules that regulate the local immune response. Consequently, they have been tested as therapies for diseases where an ability to temper an inappropriate immune response might be helpful. One example is GvHD.



Range of potential uses for MSCs

Analyst: Marcel Wijma MSc
Marcel Wijma, Chief Research Officer and managing partner, has a longstanding history in financial biotech research. After selling Van Leeuwenhoeck Research (VLR) to SNS Securities in 2006, he established an award winning analyst team in biotech/life sciences at SNS Securities. In 2009, Marcel was awarded by Financial Times/Starmine as being one of the Top-3 biotech analysts in Europe. Later that year, Marcel purchased VLR from SNS Securities after which the company was reconstituted. At VLR, he leads the professional VLR research organisation, which is augmented by selected external financial researchers with a specialisation in Life Sciences. Mr. Wijma has a Masters degree in Financial Economics from Erasmus University in Rotterdam.