



# Stem Cell Technology Conference

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Arnoud van Tulder –Chief Executive Officer

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- Collecting, processing and storing of stem cells at birth, or from adults, for potential use in medical therapies.  
Collected from umbilical cord blood, cord tissue, and adipose (fat) tissue
- Cryo-Save is **not** involved in embryonic stem cells
- Over 185,000 samples stored;  $\pm 50\%$  market share in Europe (30 June '11)
- 300 people, including over 20 medical doctors and over 40 lab technicians
- Processing and storage facilities in Belgium, Germany, France (under validation), Dubai, India, South Africa and North America
- Over 40 countries (Europe, Asia, Africa & North America)

<b>Profitable, cash generative and debt free</b>	<b>1HY 2011 €million</b>
Revenue	21.1
Gross profit	14.2
Gross profit margin	67%
Operating expenses excluding D&A	10.6
<b>EBITDA</b>	<b>3.6</b>
Depreciation and amortization	1.6
<b>Operating profit</b>	<b>2.0</b>
Financial result	(0.3)
<b>Profit before taxation</b>	<b>1.7</b>
Taxation	(0.4)
<b>Profit after taxation</b>	<b>1.3</b>
<b>Basic earnings per share (€cents)</b>	<b>13.9</b>

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- Umbilical cord blood and tissue:
  - Customers pay upfront upon successful storage of sample for initial period of 20 years storage, no annual fee
  - Annual fee introduced in some countries in 2011
- Adipose (fat) tissue Cryo-Lip:
  - Customers pay upfront for processing and storage, plus annual fee for initial period of 5 years storage

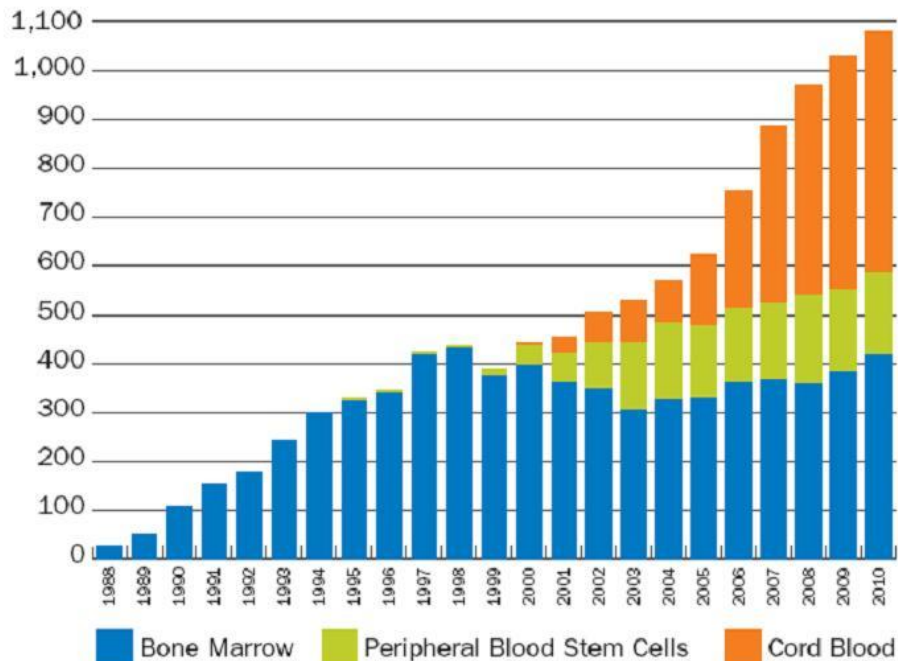
- Historic overview
  - “from a lab with sales partners to a multinational organization with 7 processing and storage facilities in over 40 countries on 4 continents”
  - Founded in 2000
  - IPO November 2007 AIM LSE
    - . Investments in PPE (Belgium, France, India)
    - . Acquisitions
  - NYSE listing October 2009
- Innovation:
  - new processing techniques: dual bag storage, closed bag processing
  - new products: umbilical cord tissue, fat (adipose) tissue
- Competition

# Why store adult stem cells?

- Today: common practice in over 70 blood and blood related diseases, and anecdotal results
- Tomorrow: promising results from clinical trials. Over 3,600 CTs with stem cells.
- Stem cell therapy has the potential to radically change the treatment of human diseases -> regenerative medicine and tissue engineering (repair, replace, regenerate)
- Cord blood banking is an established technology (since 1990's in USA)
- Stem cells derived from umbilical cord offer important advantages:
  - Collection is quick, easy and non-invasive
  - There is no risk for mother or child
  - Stem cells collected at birth are in optimum condition
- Stem cells obtained from adipose tissue:
  - A rich source of stem cell (500 times higher concentration than in bone marrow)
  - Readily available
  - Autologous, adult tissue
  - To be used in advanced medical therapies as well as in regenerative medicine or in plastic surgery

## NMDP Transplants by Cell Source

Pediatric Recipients (Age Younger Than 18 Years)



Source: National Marrow Donor Program FY 2010

- European Commission Framework 7 has funded and launched the HYPERLAB project
  - Cryo-Save cooperates with 7 universities and research institutes
  - Three year project to develop new and improved culture methods, media, and protocols for stem cell cultivation and differentiation
  - Cryo-Save is the only cord blood bank in Europe to take part in these advanced projects, reflecting both its leading market position and its commitment to the development of stem cell research.
- Cryo-Save is founding member of the International Tissue Engineering Research Association (ITERA) Life-Sciences Forum
  - international forum of scientists, headed by Prof. Albert Ramon
  - The next ITERA congress is scheduled for 21 and 22 November 2011
- Involvement in several stem cell research and development projects
  - Prof. Stamm (Germany) for treatment of heart diseases
  - Prof. Surbeck (Switzerland) for treatment of Cerebral Palsy
  - Prof. Ramon (Belgium) for incontinence



- South Eastern Europe and India were the main contributors to organic growth, more than offset by Spain and Hungary
- Organic growth by new services such as the combined service and Cryo-Lip®
- Growth in new geographies (greenfield, partnerships, acquisitions) will materialize in the second half of 2011 as a result of amongst other the launch of the South African joint venture
- Growth by acquisitions via the acquisition of Life R.F., Serbia early 2011 and the late 2010 acquired Tissue Bank Cryo Center Bulgaria
- Cryo-Save will continue to pursue these strategic objectives in the second half of 2011.

- Cryo-Save has a strong strategic position and product portfolio
- The Cryo-Lip<sup>®</sup> service has been introduced in the USA in September 2011
- Cryo-Save will continue to collaborate with new partners or make acquisitions in line with its strategy
- Promising developments in the use of stem cells
- Cryo-Save is confident it will continue to maintain its leadership position as the international family stem cell bank of choice

## ***Cord blood and cord tissue***

- Informing parents by obstetrician or midwife, supported by Cryo-Save website and customer service
- Parents receive collection kit prior to birth
- Sample collected at birth
- Delivery to laboratory via courier within 48 hours

## ***Adipose tissue***

- Informing adults by medical specialist, supported by Cryo-Save website and customer service
- Collection by medical specialist
- Transport, processing and cryopreservation by Cryo-Save



- Receipt of sample at processing and storage facility
- Tested for disease and bacterial contamination
- Samples stored in gas phase of liquid nitrogen
- Samples are split into two halves for dual storage
- Cryo-Save's major differentiation and value proposition
  - Highly trained, experienced and dedicated team
  - Operates multiple storage facilities
  - Dual storage for each sample
  - Fully automated processing of umbilical cord blood (“closed bag system”)



- FDA approves phase III clinical trial for umbilical cord blood expansion (July 2011)
- The European group for Blood and Marrow Transplantation (EBMT) reported on 1,040 patients treated with novel cellular therapies, of which 664 with autologous stem cells. Main indicators were cardiovascular , musculoskeletal and neurological disorders, and autoimmune diseases.
- Men's own stem cells used to rebuild their trachea (March and July 2011)
- Scientists get grant for research to cure premature babies blindness using stem cells (May 2011)
- New heart grown using adult stem cells (April 2011)

- Storing of stem cells from peripheral blood for nuclear workers is revisited (April 2011)
- 5 boys (10 to 14) receive tailor-made urethras grown in a lab from their own cells (March 2011)
- Samples cryopreserved for 23.5 years were validated for recovery and functionality (March 2011)
- Own stem cell transplantation improves end-stage liver disease (Jan 2011)
- Own cord blood stem cells for pediatric traumatic brain injury (Jan 2011)

- To date 25,000 unrelated cord blood transplants
- European private cord blood banks released 36 samples: 12 family-sibling use and 24 autologous
- Two largest USA banks, started 10 years ahead of the European banks, released 369 samples (177 for family-sibling use and 192 for autologous use)
- Clinical trials ([www.clinicaltrials.gov](http://www.clinicaltrials.gov)):
  - over 3,600 CTs with stem cells
  - over 3,300 CTs with hematopoietic stem cells
  - over 200 CTs with stem cells from cord blood
  - almost 200 CTs with mesenchymal stem cells
  - over 30 CTs with stem cells from adipose tissue

Cerebral palsy	Orthopedic applications
Traumatic brain injury	Auto-immune disorders
Stroke	Ophthalmological applications
Spinal cord injuries	Solid tumors
Heart disease	Liver disease
Type 1 Diabetes	Musculo-skeletal and burns



- Revenue up 8% to €21.1 million (1 HY 2010: €19.5 million)
- EBITA up 10% to €2.7 million (1 HY 2010: €2.5 million)
- Operating profit up 6% to €2.0 million (1 HY 2010: €1.9 million)
- Profit before taxation up 7% to €1.7 million (1 HY 2010: €1.6 million)
- Net profit up 2% to €1.3 million (1 HY 2010: €1.3 million)
- Basic earnings per share 13.9 euro cents (1 HY 2010: 13.7 euro cents)
- Net cash from operating activities €1.7 million (1 HY 2010: € 2.0 million)
- Cash position of €3.6 million as at 30 June 2011

# Summary Income Statement

€million	1HY'11	1HY'10	Full year'10
<b>Revenue</b>	<b>21.1</b>	<b>19.5</b>	<b>40.4</b>
Gross profit	14.2	13.4	27.3
Gross profit margin	67%	69%	68%
Opex excluding D&A	10.6	10.2	20.0
<b>EBITDA</b>	<b>3.6</b>	<b>3.2</b>	<b>7.3</b>
Depreciation and amortization	1.6	1.3	2.8
<b>Operating profit</b>	<b>2.0</b>	<b>1.9</b>	<b>4.5</b>
Financial result	(0.3)	(0.3)	(0.6)
<b>Profit before taxation</b>	<b>1.7</b>	<b>1.6</b>	<b>3.9</b>
Taxation	(0.4)	(0.3)	(1.3)
<b>Profit after taxation</b>	<b>1.3</b>	<b>1.3</b>	<b>2.6</b>
<b>Basic earnings per share (€cents)</b>	<b>13.9</b>	<b>13.7</b>	<b>27.6</b>

# Summary Balance Sheet

Period ended	30 June 2011 €million	31 December 2010 €million	Note
Non current assets	55.5	52.2	Acquisition of Life R.F. (€2.3 million) + investments in PP&E (€0.7 million, mainly dual storage location ) + investments in software (€0.2 million)
Current assets	17.5	18.4	
<b>Total assets</b>	<b>73.0</b>	<b>70.6</b>	
<b>Total equity</b>	<b>47.3</b>	<b>46.8</b>	Profit for the period minus dividend
Non-current liabilities	16.1	14.8	Additions to deferred revenue + deferred considerations
Current liabilities	9.6	9.0	
<b>Total liabilities</b>	<b>25.7</b>	<b>23.8</b>	
<b>Total equity and liabilities</b>	<b>73.0</b>	<b>70.6</b>	

## Summary Cash flow statement

Period ended 30 June	2011 €million	2010 €million	Note
Net cash from operations	3.6	3.3	Increased inventory levels, trade receivables and current tax receivables + milestone payment, deferred acquisition payments and corporate income tax payments
Net cash from operating activities	1.7	2.0	
Net cash used in investing activities	(3.1)	(3.1)	Acquisition of Life R.F. (€2.3 million) + investments in PP&E (€0.7 million, mainly dual storage location ) + investments in software (€0.2 million)
Net cash from/(used in) financing activities	(1.0)	(0.5)	share buyback program (€0.5 million) + dividend (€0.4m)
Net increase/(decrease) in cash and cash equivalents	(2.4)	(1.6)	
<b>Cash and cash equivalents at the end of the period</b>	<b>3.6</b>	<b>5.9</b>	

- 19,600 new samples stored in 1 HY 2011, up 6% (1 HY 2010: 18,500); 12,600 new cord blood samples and 7,000 new cord tissue samples
- 184,000 samples stored in total
- Release of sample to treat 6 year old girl with Cerebral Palsy
- 65% of new customers opt for combined storage
- Acquisition of Serbian distributor Life R.F.
- Permission granted in Serbia and Switzerland for combined storage of umbilical cord tissue and stem cells from umbilical cord blood

- Incorporation of Cryo-Save USA, Inc. to commercialize and develop the Cryo-Lip® service in North America, with strategic partner General BioTechnology for processing and storage and Genesis Biosystems for sales and marketing to medical professionals
- JV in South Africa with John Daniel Holdings and Lazon Biotechnologies
- Recent scientific studies have shown that stem cells are able to repair the damage caused by high radiation exposure. Collecting and preserving stem cells of persons at a higher risk of radiation exposure could therefore be a potentially life-saving measure. The Group is now examining the feasibility of offering this alternative to employees of nuclear power plants in Europe.

## Europe

- Permission granted in Serbia and Switzerland for umbilical cord tissue
- Central and South Eastern Europe: continue to grow
- Decreasing volumes in some other European countries (Spain, Hungary). Situation seems to be stabilized though, compared to the second half of 2010.
- Relative market share remained stable
- Continuation of marketing and sales approach through diagnostic centers and private clinics

## Asia

- Main market is India, showing growth.

## Africa

- Joint venture established in South Africa with John Daniel Holdings and Lazon Biotechnologies to form Cryo-Save South Africa

## North America

- Incorporation of Cryo-Save USA, Inc. to commercialize and further develop the Cryo-Lip<sup>®</sup> service in North America, along with strategic partners GBT and GenBio

- Spanish girl recovered from **medulloblastoma** after receiving her own stem cells as part of her treatment. Obtained from her umbilical cord at birth and preserved and stored by Cryo-Save. After surgery and chemotherapy the stem cell transplantation fully rebuilt her immune system. Currently she does not require any medication and lives a normal life.
- Another sample released to Duke University for the treatment of a six year old Portuguese girl with **Cerebral Palsy**. This brain disorder causes many problems, including impaired movement, trembling of the limbs, spasticity, seizures of epilepsy, learning and developmental problems and more. There is no treatment for this disorder and it affects almost half a million people in the USA alone.



## Additional background



- The French oncologist Georges Mathé performed the first bone marrow transplant in 1959
  - on six Yugoslavian nuclear workers whose own marrow had been damaged by irradiation caused by a criticality accident at the Vinča Nuclear Institute.
- Stem cell transplantation was pioneered using bone-marrow-derived stem cells by a team at the Fred Hutchinson Cancer Research Center from the 1950s through the 1970s led by E. Donnall Thomas
  - his work was later recognized with a Nobel Prize in Physiology or Medicine]
- The first physician to perform a successful human bone marrow transplant on a disease other than cancer was Robert A. Good at the University of Minnesota in 1968.
- Finding a matching donor by searching the international registries takes time and often a match is not found.
- In the early 1980's it was discovered that umbilical cord blood (UCB) contained hematopoietic stem cells (HSCs) similar to those in bone marrow and that these cells could be collected, processed and cryopreserved
- The first successful UCB stem cell transplant was performed in France in 1988 for a boy with Fanconi's Anemia. The donor was his sister and her UCB was collected at birth and used in the transplantation. Today, the patient is healthy and cured of the condition
- Over 20 years of umbilical cord blood transplantations have demonstrated that UCB can be obtained with ease and with no risk to mother or child, can be successfully cryopreserved without loss of viability or functionality, allows for greater HLA mismatch without increase in graft-versus-host disease (GVHD), are the most enriched with primitive stem cells and is an effective treatment for numerous blood diseases
- To date, cord blood is the most frequently used source for pediatric application

- To overcome cell dose limitation, research has been extremely active with regard to amplification of stem cells, double cord blood transplants, co-transfusion with other stem cells and the direct route of administering stem cells into the area where they are needed
- Over 20 years of successful umbilical cord blood transplantations have demonstrated that
  - UCB can be obtained with ease and with no risk to mother or child
  - UCB can be successfully cryopreserved without loss of viability and functionality
  - UCB transplantations allow for greater HLA mismatch without increase in graft-versus-host disease (GVHD)
  - UCB transplantations are the most enriched with primitive stem cells
  - UCB transplantation is an effective treatment for numerous diseases
  - UCB is the most frequently used source for pediatric application

- Emerging therapies and regenerative medicine are increasingly focusing on using an autologous source of stem cells to treat previously incurable diseases. As these emerging therapies progress to clinics, samples released from family cord blood banks for illnesses such as Cerebral Palsy, Type 1 Diabetes, traumatic brain injury and other neurological disorders are on the increase.  
Having a banked and viable source of your own stem cells is a real advantage given the current rate of new discoveries and active clinical trials.
- An article published in Bone and Marrow Transplantation in 2008 by Nietfield et al, looking at data from 2001-2003, suggests that the lifetime probability of undergoing a HSCT in the US (both autologous and allogeneic) is as high as 1:200 and will continue to rise as the availability of donors and the applications of HSCT increase. NMDP (National Marrow Donor Program) predicts that there will be an increasing number of cord blood transplants worldwide, possibly as high as 10,000 per year by 2015.
- Regenerative medicine is seen as the next evolution of medical treatment, subdivided into:  
*Cellular Therapy*: transplanting or transfusing cells directly into the body to repair, replace or regenerate damaged tissue and organs that were previously thought to be irreparable;  
*Tissue Engineering*: regeneration of tissue and organs outside the body i.e. taking stem cells and growing tissue or organs in the laboratory or using the cells to coat or contribute to cellular transplantable material and then safely being transplanted back into the body
- Umbilical Cord tissue (UCT), one of the richest sources of mesenchymal stem cells (MSCs), is a source for regenerative medicine

- Storing both UCB and UCT allows maximum recovery of both HSCs and MSCs for any therapeutic applications
- The following diseases are the most promising treatments currently being explored using MSCs: acute myocardial infarction and heart failure; auto-immune disorders including SLE, Crohn's, Type 1 Diabetes, Rheumatoid Arthritis; Type 2 Diabetes; co-transplantation in HSCT; orthopaedic applications (bone and cartilage repair); liver diseases; peripheral artery disease; stroke; spinal cord injury; multiple system atrophy; organ transplant
- Adipose Derived Stem Cells (ADSCs) obtained from the adipose (fat) tissue are also a rich source of MSCs for regenerative medicine. Furthermore, these MSCs are promising with regard to repair a wide range of tissue damages or defects, burns, radiolesions, ulcers and general surgery, and can be used by plastic surgeons for cosmetic applications including anti-aging