Translating breakthrough research into transformative treatments

Annual report **2014**

Celyad

we care · we cure

Celyad in brief - **Key figures**

CLINICAL PROGRAMS IN CARDIOVASCULAR DISEASE AND ONCOLOGY

Cardiovascular Disease

BEGAN OUR **First Phase III** CLINICAL TRIAL OF C-CURE® AS A TREATMENT FOR ISCHEMIC HEART FAILURE IN EUROPE AND ISRAEL, OR **CHART-1**.
CHART-1 EVALUATING PATIENTS IN 16 COUNTRIES, ALL PATIENTS ENROLLED, CURRENTLY IN FOLLOW-UP PHASE.
SECOND PHASE III CLINICAL TRIAL OF C-CURE AS A TREATMENT FOR ISCHEMIC HEART FAILURE, CHART-2, TO COMMENCE IN THE UNITED STATES FOLLOWING FDA CLEARANCE TO BEGIN THE TRIAL.

240 **PATIENTS** FOR EACH TRIAL.

Oncology

CHIMERIC ANTIGEN RECEPTOR, OR **CAR T-cell** **THERAPY**, ONE OF THE MOST PROMISING CELL THERAPIES FOR CANCER TREATMENT TODAY.
PHASE I CLINICAL TRIAL FOR NKG2D – CAR T-CELL THERAPY APPROVED BY FDA.

Finance & Corporate

82 **EMPLOYEES** AS OF MARCH 26, 2015.

€30 **MILLION IN CASH** AND TERM DEPOSITS AT YEAR END 2014.

ADDITIONAL **€32** **MILLION RAISED** IN MARCH 2015.

OPERATING BURN RATE (EBITDA) LIMITED TO €15 MILLION IN 2014.

MORE THAN 2 YEARS OF CASH AS OF MARCH 2015 BASED ON CURRENT PRECLINICAL AND CLINICAL PROGRAMS AND CURRENT OPERATING BURN RATE.

A new identity to better embody our corporate vision and mission

After the acquisition of OnCyte, LLC and its oncology portfolio, it became clear that the name "Cardio3 BioSciences" was no longer wholly connected to the activities and therapeutic areas covered by the Company.

The new name "Celyad" was very carefully chosen – short, easy to remember, and distinctive at the same time, Celyad fully anchors the company into the broader cell therapy sector.

"The name Celyad represents a direct connection with the core focus of the Company: cell therapies, and the suffix -yad refers to the connection with humanity - 'Yad' meaning the hand in Arabic and Hebrew."

DR. CHRISTIAN HOMSY, CEO

CARDIO 3 BIOSCIENCES

We care. We cure.

becomes

Celyad

we care · we cure

The new, circular logo is a reference to the core focus of the company: engineering cells. The four objects fanning out from the centre circle represent Celyad's pillars of innovation. Their precision aims to highlight the technical expertise and commitment to quality that are central to the Company's mission of discovering, developing and manufacturing engineered cells. The four colours in the logo emphasize the resolve to drive positive change in cell therapy and the human approach that are the foundation of the Company's business.

"We believe that the name change better aligns our identity with our core activities and overall unified objective of identifying and translating innovative cell therapies into therapeutics, not only in cardiology, but now also in oncology and potentially in other areas in the future."

DR. CHRISTIAN HOMSY, CEO

2014, strengthening the Company's lead program

The momentum built over 2014 has seen our Company reach significant milestones in its lead program C-Cure® -an autologous cell therapy for the treatment of patients with ischemic heart failure. The completion of the enrolment of patients into the Phase III clinical trial in Europe and Israel, CHART-1, was reached by mid-March 2015. A significant achievement for our research, production, and clinical teams: in two years, they have made it possible to translate a therapy into a reality for hundreds of patients.

Not only did our lead program register significant progress, but our acquisition of a CAR T-cell portfolio in early 2015 heralds the first major step in our strategy to leverage our unique expertise in cell therapies and drug development to expand beyond the cardiovascular disease arena. With the objective to move into at least five later stage trials in 2016, in various solid tumors and blood cancers, we believe our immuno-oncology portfolio will be a tremendous spring board for our future expansion into innovative cell therapies.

"Overall, 2014 was an exciting and successful year for Celyad, but more importantly, it set the stage for potentially even greater accomplishments in the years to come."

DR. CHRISTIAN HOMSY, CEO

Interview with Christian Homsy, Chief Executive Officer, **and Michel Lussier,** Chairman of the Board of Directors

"2014 was a crucial year during which we consolidated the fundamentals of our business. In 2014, we sowed the seeds, and in 2015, we need to cultivate our crops so that we can reap the harvest from 2016 onwards."

DR CHRISTIAN HOMSY, CEO

How do you view the past year? What were the highlights?

Christian Homsy : In 2014 we consolidated on the significant progress we made in 2013 to build and lay the groundwork for the future–progress that is now unlocking very substantial opportunities.

Our IPO enabled us to speed up the pace at which we are proceeding with the clinical program for C-Cure®, our lead product candidate. We plan to commence our second Phase III clinical trial of C-Cure® as a treatment for ischemic heart failure, CHART-2, in the United States following FDA clearance to begin the trial. In addition, the European Medicines Agency (EMA) issued a certificate of quality data for C-Cure®. This Advanced Therapy Medicinal Products, or ATMP, certification recognizes that the data generated for C-Cure® in its development programs to date meet the standards imposed by the EMA. This is in keeping with our proactive approach to advance on the regulatory front with the goal of obtaining marketing authorization for C-Cure®.

Finally, Celyad began to lay the foundations for its expansion strategy from mid-2014 onwards, giving rise to acquisitions at the end of the year.

Michel Lussier : We ended 2014 in great shape from both a financial and organizational point of view. We successfully realized our 2013 vision, and we hope to see its full potential materialize over the next few years.

C-Cure® is now running a Phase III trial in Europe and Israel. What does that mean for the Company?

CH : C-Cure® is the first product candidate emerging from Celyad's pipeline. Today, we have proven our ability to bring a product candidate discovered in 2007 through to a Phase III clinical trial, within a very limited timescale. We achieved this through the hard work and perseverance of an entire team, and with the unwavering support of our investors. Discovery was not our role – that we leave to our academic partners, the Mayo Foundation for Medical Education and Research, or the Mayo Clinic in this case. Our role is to develop product candidates from proof of concept through to marketing. We successfully completed this development, and the fact that it is now in a Phase III clinical trial is proof of this. But that is not an end in itself; the final stage is, of course, to secure regulatory approval and then market the product.

What makes Celyad a unique business?

ML : In my view, Celyad has been a unique business from day one. Unique because it has developed an autologous cell therapy used to treat ischemic heart failure, and managed to bring it through Phase II and now onto Phase III clinical development. Unique because very early on in its development it joined forces with one of the leading academic research organization – the Mayo Clinic. Unique because it is one of the first companies to have developed expertise in cell production at various development stages. That has been a tremendous financial, human and technological achievement. However, having its own production capacity is now one of Celyad's major strengths.

Today, we are demonstrating once again what makes our company unique by harnessing the experience we have gained from the development of C-Cure® to tackle the challenges posed by cancer.

But I think what makes Celyad even more unique is our high-performance, close-knit team at every level of the organization. Our team is supported by a Board of Directors that has been remarkably stable from the outset and has always given us its backing, as has our core group of investors.

Did you encounter any stumbling blocks in 2014?

CH : When it comes to investing in innovative technologies, difficulties are the rule rather than the exception. We have a very great ability to reinvent ourselves and to face up to challenges. And this is where the team dimension is so crucial: the value of the business is first and foremost the value of its men and women.

What challenges lie ahead in 2015?

ML : Our main challenge will be to manage our growth. In 2015, Celyad needs to spread its wings to continue its ascent. Today more than ever, we need to keep our feet on the ground while reaching for the stars! We have very clearly defined operational goals to carry out clinical trials, pursue our geographical expansion in the United States and Asia, and move into immuno-oncology. We also need to focus on the big picture and continue running the business while keeping an eye on what will happen in six months, in the next year, in the next two years, and so on.

CH : We need to continue to "put our actions into words and our words into action". The business needs to keep delivering on its promises in cardiovascular disease, immuno-oncology and medical devices. And we have the scope to create tremendous value during 2015. If we meet these challenges–and our past demonstrates that our team can do just that–our group will look very different by the end of 2015 to how it looked in late 2014. We will have scaled up and achieved a far higher level of security than ever before.

And what is the rationale for geographical expansion?

ML : Building a solid platform for Celyad in the United States is one of the priorities for the coming year. We will continue to pursue growth in Europe, and our expansion in the United States will feed into this growth. Naturally, we do not intend to quit our European positions, but during 2015 we will work to help our operations to take off very quickly in the United States, and this will enable us to capitalize on the country's tremendous potential in terms of markets, access to capital and local technological skills.

And Asia?

CH : Asia is definitely a key region for expansion, whether in Japan, China or other markets. We are fortunate to have a major investor based in Hong Kong – Medisun International Limited – which provided €25 million in financing in June 2014. Expansion in Asia can be a harder task, and having a local partner there is a clear advantage. The current strategy is still primarily focused on Europe and the United States.

What is the benefit of moving into oncology?

CH : We are guided by the principle of "helping the body repair itself", rather than taking palliative action with external drugs. To secure the Company's future, we need to know which assets we can truly rely on. The first of these is Celyad's unique know-how in autologous, as well as allogeneic cell therapies. We have learnt how to manufacture these cells while protecting all their characteristics, and we have the requisite production infrastructure with a laboratory in Belgium and, shortly, with another facility in Rochester, Minnesota (United States). We can thus draw on the significant internal expertise we have acquired in the course of our development work. That also ties in with the technological aspect of our diversification. Moreover, immuno-oncology is a field with massive potential. The idea of using our immune defenses to fight cancer, in the same way as we use them to fight certain infections, is immensely appealing. The technology we have bought allows us to mobilize these defenses and, with a single product candidate, we believe will help the body defend itself against cancers. If we manage to demonstrate the safety of our approach over the next few months, we will be able to set about tackling additional cancers. Cancer is the second leading cause of death in the United States after cardiovascular diseases, according to the U.S. Centers for Disease Control and Prevention. Cancer accounts for nearly one out of every four deaths in the United States, according to the American Cancer Society Therapies of this kind could transform medicine – and that's what we are looking to do!

What will the acquisition of CorQuest Medical Inc. add to Celyad?

CH : To make sure that our therapies are effective against heart failure, we must take a holistic approach to the condition. The addition of CorQuest Medical, Inc., or CorQuest, during 2014 will help us to do just that. The medical device we received in the CorQuest acquisition gives us a unique ability to treat a condition from various angles by injecting cells to rebuild the heart and/or by addressing mitral valve diseases secondary to heart failure. The same will hold true in immuno-oncology.

How do you see the future for Celyad?

ML : The future will bring extraordinary advances for patients by "giving them the power" with the development of personalized diagnostic tools and also unique, targeted therapies, in a break with the approaches of the past. Cell therapy focuses on the patient's own resources and uses them for his/her own good. We hope, too, that the side effects will be considerably reduced and, crucially, the therapeutic benefit all the greater. We will continue to be guided by our "We care, we cure" mantra. Our goal is to be involved in developing this personalized medicine and to be able to offer patients more than palliative treatments.

"Building a solid platform for Celyad in the United States is one of the priorities for the coming year. We will continue to pursue growth in Europe, and our expansion in the United States will feed into this growth."

MICHEL LUSSIER , CHAIRMAN OF THE BOARD

And for medicine at large? What technological advances may have an impact on our society?

ML : In certain leading academic research institutions, such as the Mayo Clinic, personalized medicine is already a reality. The patient is treated based on a full examination and a review of his/her genetic profile, with the therapy tailored accordingly. Medicine will increasingly move in this direction.

In addition, we have merely scratched the surface in terms of the potential for each of the technologies we have developed. There is very substantial demand in heart failure. Over time, and if clinical trials are successful, we should be able to increase the number of patients who will benefit. In oncology, too, we believe that our approach can provide a therapeutic solution for numerous cancers. Of course, we will need to demonstrate all these applications one by one. Today, the only limiting factor for Celyad is the time it will take to complete these clinical trials.

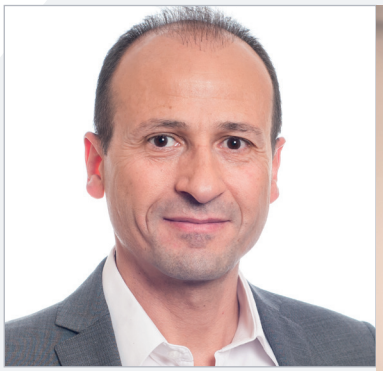
CH : No longer will medicine be confined to the approaches of the past. Research is shifting towards therapies that will be extremely targeted. We are fortunate to be contributing to this movement, along with other businesses that will be joining us in this adventure.

ML : From the outset, we have been fortunate to have the confidence and support from investors and the authorities. Today, in Belgium and around the world, we are no longer ploughing a lone furrow in the biotechnology and cell therapies sector–and that's great news.

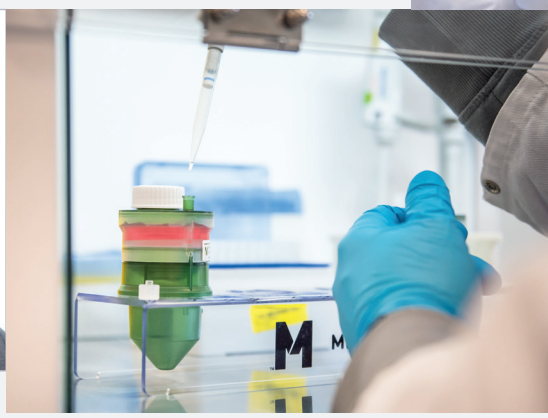
"We will continue to be guided by our "We care, we cure" mantra. Our goal is to be involved in developing this personalized medicine and to be able to offer patients more than palliative treatments."

MICHEL LUSSIER, CHAIRMAN OF THE BOARD

Key Highlights 2014
Building a Global Specialty Therapeutics Company



Dr. Georges Rawadi



JANUARY 2014

The **U.S. Food and Drug Administration** (FDA) authorized the Company's Investigational New Drug (IND) application for clinical testing of **C-Cure®** as a treatment targeting heart failure using the MyoStar™ injection catheter, this clinical trial will commence once we receive further clearance from the FDA.

MARCH 2014

Appointment of **Hanspeter Spek** as an Independent director of the Company. As past President Global Operations of Sanofi, Mr. Spek represents a major addition to the Company's Board of Directors.

MAY 2014

The European Medicines Agency (EMA) **certifies the quality data for C-Cure®** and delivers the certificate of Advanced Therapy Medical Products (ATMP).

JUNE 2014

Completion of a **capital raise of €25 million** fully subscribed by Medisun International Ltd.

JUNE 2014

Celyad appoints **Dr. Georges Rawadi** as VP Business Development.

SEPTEMBER 2014

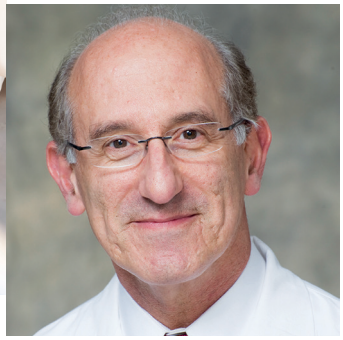
First interim **safety data analysis for C-Cure® in CHART-1.** DSMB concluded that C-Cure® and C-Cath$_{ez}$® showed no safety issues.

OCTOBER 2014

Company **strengthened** the long standing research and development **collaboration with the Mayo Clinic** giving the company **a preferred access** to the new technologies developed at the Mayo Clinic Center for Regenerative Medicine, with a view towards future licensing.

"Our goal is to build a global and sustainable specialty therapeutics company by leveraging our proven expertise in cell therapies and drug development to create breakthrough treatments to change disease outcomes."

DR CHRISTIAN HOMSY, CEO



Dr. Warren Sherman

CorQuest

MAYO CLINIC

Dr. Vincent Brichard

NOVEMBER 2014

Acquisition of **CorQuest Medical Inc.** and its unique heart access platform. Appointment of **Dr. Warren Sherman** as Chief Medical Officer.

DECEMBER 2014

Enrolment of the 240th patient in the CHART-1 trial.

JANUARY 2015

The Group **entered the immuno-oncology** space with acquisition of OnCyte **CAR T-cell portfolio** from Celdara Medical, LLC. To support the development of the newly acquired portfolio, the Group appointed **Dr. Vincent Brichard as Vice President Immuno-oncology.**

MARCH 2015

Successful capital raising of €32 million through a private placement of ordinary shares to qualified institutional investors in the United States and Europe at a price of €44.50 per share.

MARCH 2015

Company received product-specific **pediatric waiver for C-Cure®** from European Medicines Agency (EMA) – confirming focus on adult populations.
The Company also confirmed plans for a geographical expansion in the US with **a new U.S.-based manufacturing facility in Rochester, Minnesota, and a Boston based U.S. headquarters.**

MARCH 2015

Celyad completed patient enrolment of its European Phase III clinical trial, **CHART-1** trial in Europe and Israel.

MARCH 2015

Successful completion of a futility analysis for C-Cure®. DSMB reviewed unblinded safety and efficacy data from CHART-1 and determined that the data did not support discontinuation of the trial on the basis of futility. Furthermore, the DSMB recommended the continuation of the trial with no changes to the protocol.

Celyad's **mission, vision & strategy**

What makes Celyad **unique** is its **combination** of **scientific, manufacturing, clinical** and **regulatory know-how** in addition **to its proven translational expertise** and ability to **bring** product candidates through various stages of **development**.

Celyad
we care · we cure

At Celyad, our mission is to focus on translating breakthrough cell-based research into innovative treatments to improve the outcome of severe diseases. We aim to achieve this by harnessing the mechanisms by which the human body responds to disease and make those mechanisms more effective by leveraging on breakthrough technological advancement in cell therapies and medical devices, or both.

To achieve this goal, Celyad combines world class expertise in cell engineering and a strong knowledge base to identify and further advance transformative treatments that bring value to patients, worldwide.

The Company will continue to strengthen and extend its strong intellectual property portfolio with the goal of becoming a global specialty therapeutics company.

Celyad built its model on partnering with leading edge researchers such as Mayo Clinic, Harvard Medical School and Dartmouth College, and develops those programs from bench to commercial applications.

Product pipeline and therapeutic areas

Celyad focuses on indications that represent a high unmet medical need in the world. Cardiovascular diseases and cancers are the first two areas Celyad identified and focuses on.

Celyad's lead product candidate in cardiovascular disease y is C-Cure®, an autologous cell therapy using adult engineered cells for the treatment of ischemic heart failure. In oncology the company plans to develops CAR-T cell therapies for the treatment of various different cancers. NKG2D CAR T-Cell is an autologous T-cell transduced with an NKG2D receptor present on Natural Killer (NK) cells that binds to numerous types of cancer cells, including blood cancers and solid tumors.

Oncology

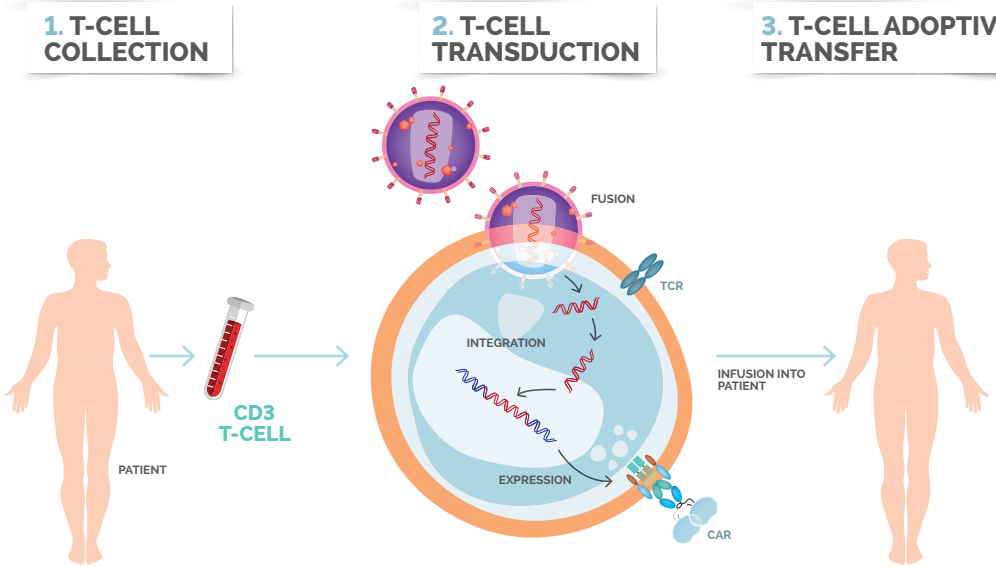
Cancer is the second leading cause of death in the United States after cardiovascular diseases, according to the U.S. Centers for Disease Control and Prevention. Cancer accounts for nearly one out of every four deaths in the United States, according to the American Cancer Society. In 2014, there were an estimated 1.6 million new diagnosed cancer cases and over 550,000 cancer deaths in the United States alone.

Focus on immuno-oncology

Immuno-oncology represents an innovative approach to cancer treatment by **teaching the body's own immune system to fight against cancer cells**. Today's most advanced treatment options - which have seen a dramatic acceleration over the last 18 months - are the **CAR T-cell therapies**. This therapy represents the future hope for effective cancer treatment in very sick patients.

How does it work?

The patient's immune T-cells are collected and engineered to express special chimeric antigen receptors, or CARs, on their surface that enable them to recognize a specific protein on cancer cells (called "tumor antigen"). These engineered "CAR T-cells", are then infused back into the patient where, with guidance from the chimeric receptor, they multiply, recognize and kill the cancer cells that have the tumor antigen on their surfaces. So far, CAR T-cell therapies targeting the CD19 antibody have demonstrated promising results in the treatment of certain blood cancers.

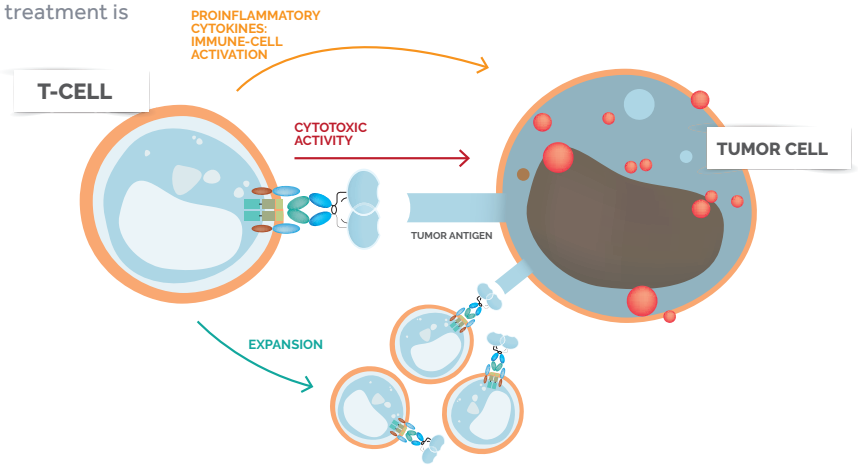


Oncology

Celyad technology: CAR technology using NK cells receptor

The technology acquired by Celyad is different from the classic CAR technologies in the sense that it uses human **Natural Killer cells (NK cells) as receptors**. NK cells are lymphocytes of the **innate immune system**, which can eliminate targets directly and kill cells and secrete cytokines that assist in establishing an adaptive immune (T-cell) response. The major benefit of using those NK cells receptors in cancer treatment is that they have the potential to target a broad range of cancers such as lymphoma, colorectal, ovarian cancer and myeloma.

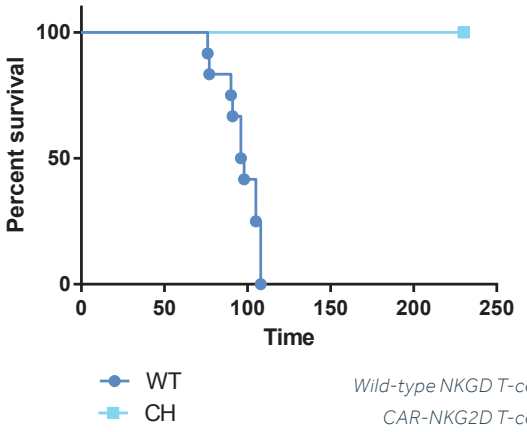
Unlike CD19 CAR T-cell therapy, which only targets one tumor antigen, CAR T-cell products using human NK cells receptors have the potential to target a broad range of cancers. Indeed, human natural receptor target ligands which are present on numerous tumor types.



Results in animal models

NKG2D CAR T-CELLS INDUCE LONG-TERM TUMOR FREE SURVIVAL IN ANIMAL MODELS

FIGURE A



Wild-type NKGD T-cells (n=12)
CAR-NKG2D T-cells (n=12)

In figure A, a first group of mice were injected with ovarian tumor cells and then treated with unmodified NKG2D T-cells, also called wild-type NKG2D T-cells (dark blue color). A second group of mice (light-blue color) was injected the same ovarian tumor cells as the first group, but they were treated with engineered NKG2D CAR T-cells, i.e lymphocyte T-cells on which a CAR has been artificially added to express NKG2D on their surfaces. In the control group treated with wild-type NKG2D T-cells all animals developed tumors and died.

On the opposite, in the group of mice treated with NKG2D CAR T-cells, all animals survived for a long-term period without developing any tumors.

This data indicates that NKG2D CAR T-cell treatment results in long-term tumor free survival in animal models.

In addition to ovarian cancer model, NKG2D CAR T-cell has also demonstrated efficacy in other cancer models such as multiple myeloma, lymphoma, melanoma and colon cancer.

NKG2D CAR T-CELLS INDUCE DURABLE ANTI-TUMOR IMMUNITY

FIGURE B

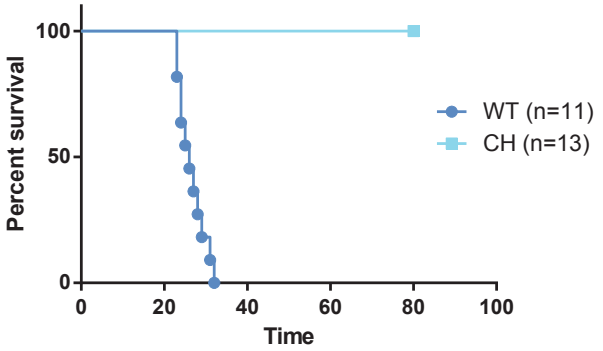
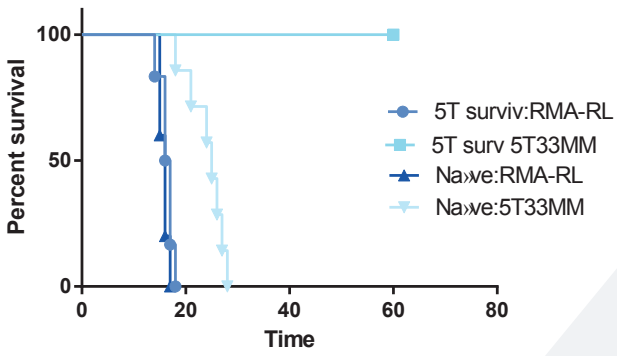
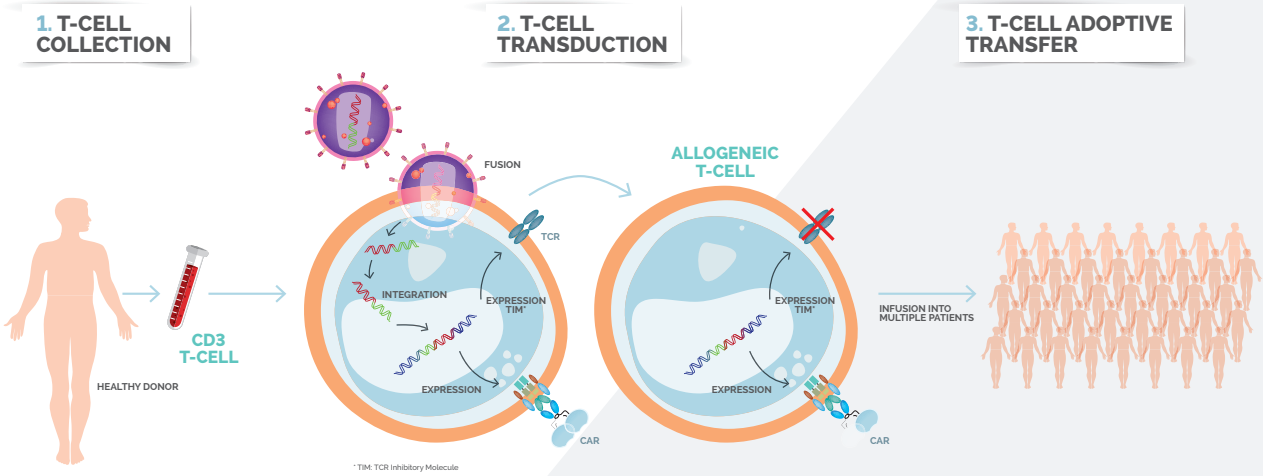


FIGURE C



In a following experiment shown by Figure C, we have used survivor animals (light blue color) of the previous experiment (Figure B) to re-challenge with the same multiple myeloma tumor cells or with a different tumor cells. Survivor animals that were re-challenged with the same multiple myeloma tumor cells showed resistance and did not develop any tumor, whereas survivors that were re-challenged with a different tumor cells developed tumors and died. Control naïve animals developed tumors and died in response to both tumors cells. These data showed that NKG2D CAR T-Cells are capable of inducing durable anti-tumor immunity in preclinical models.

Allogeneic platform



An allogeneic platform enables the production of "off-the-shelf" CAR T-cell products from healthy donors.

The injection of a T-cell into a receiver (patient), different from the donor, leads to a severe rejection response in which TCR, a molecule present at the surface of T-Cells, is largely responsible. Our allogeneic platform is based on the engineering of T-cells from healthy donors that, in addition to CAR, also express TCR Inhibitory Molecules (TIMs).

TIMs inhibit TCR function allowing the T-Cells to persist when injected into patient.

We believe that our allogeneic platform may allow us to manufacture "off-the-shelf" products to treat thousands of cancer patients.

Moreover, this platform can be applied not only to Celyad CAR T-Cell product candidates, but also to any other CAR T-cells.

Oncology

NKG2D CAR T-Cell

Celyad's lead product candidate NKG2D CAR T-cell, an autologous CAR T-cell therapy, will first be the subject of a Phase I clinical trial to assess safety and feasibility of the treatment for blood cancer indications such as Acute Myeloid Leukemia (AML) and Multiple Myeloma, but we believe it may also be able treat cancers such as breast, colorectal, lung, liver, ovarian and bladder cancer.

Portfolio of pharmaceutical products

	PRODUCTS	INDICATION	DISCOVERY	PRE-CLINICAL	PHASE I	PHASE II	PHASE III
oncology							
CART T-CELL	**NKG2D**	CAR T-Cell therapy using NKG2D, a Natural Killer Cell receptor					
	NKp30	CAR T-Cell therapy using NKp30, a Natural Killer Cell receptor					
	B7H6	CAR T-Cell therapy using B7H6, a Natural Killer Cell receptor					
	T3 (Allogeneic)	Allogeneic T-Cell platform					

"To date, NKG2D CAR T-Cell therapies have demonstrated the prevention of tumor development and increased survival in preclinical animal models, suggesting that NKG2D CAR T-Cell has the potential to become a new, viable treatment option for cancer patients."

DR CHRISTIAN HOMSY, CEO

Cardiovascular Disease

Cardiovascular diseases, which are diseases of the heart and blood vessels, are the largest cause of mortality in the world. According to the World Health Organization, in 2012, approximately 31% of all global deaths were attributable to cardiovascular diseases. Cardiac diseases can be broadly divided into diseases linked to impairment of blood flow to the heart muscle, or ischemic causes, and diseases linked to other causes, or non-ischemic causes, such as hypertension and metabolic disorders. If left untreated, cardiac diseases can lead to heart failure (HF), a condition in which the heart is unable to pump enough blood to meet the body's metabolic needs.

Ischemic Heart failure

Heart failure (HF) is a very serious condition in which the heart has been damaged and cannot pump enough blood to meet the body's metabolic needs. As it is a natural evolution of most cardiac diseases HF is also very common. HF affects 1% to 2% of the adult population in developed countries and approximately 5.7 million patients were diagnosed with HF in the United States in 2012, according to the American Heart Association. The prevalence of HF is increasing due to an aging population and the increasing prevalence of major cardiovascular risk factors, such as obesity and diabetes. Population studies published in Nature Reviews Cardiology have estimated that one in five people over the age of 40 will develop HF during his or her lifetime. The long-term prognosis associated with heart failure is dire, with approximately 50% mortality at five years following initial diagnosis, according to a 2014 report from the American Heart Association. HF patients vary in their symptoms from very mild, through shortness of breath during moderate exercise, and then shortness of breath during light exercise. In the most severe stages, patients are exhausted even at rest.

Today HF cannot be cured or repaired, and most of the current therapies only reduce the severity of symptoms. Drug therapies in particular are aimed at relieving suffering and improving quality of life. While some medical devices (such as pacemakers and heart pumps) have improved the function of a damaged heart, no currently available heart failure treatment has demonstrated an ability to generate new muscle tissue within the scarred regions of a heart. As such, regenerative therapies, that have the goal of rebuilding an organ that has become non-functional, when approved, would offer new hope to patients who otherwise have limited choices.

The Cardiopoiesis platform

Celyad is developing the breakthrough proprietary Cardiopoiesis platform, which is based on fundamental research and proprietary technology from Mayo Clinic. This novel platform is designed to drive the differentiation of multipotent stem cells into new cardiac progenitor cells. While most organs (such as the skin and bone) have a greater or lesser capacity for self-repair of damage, the heart does not have this capacity: it does not harbour large quantities of cardiac stem cells (CSCs) it can use for self-repair and the CSCs that are present in the heart are in a dormant state. Fundamental research at Mayo Clinic uncovered the mechanisms in the embryo that make an embryonic stem cell become a heart cell. This led to the identification of a 'Cardiopoietic' combination of proteins signaling the transformation of generic adult stem cells from

other tissues into cardiac progenitor cells. The Cardiopoiesis platform aims to replicate the normal processes of cardiac development in the embryo, without attempting to permanently or temporarily modify the genome of the cell. As such, the platform aims to recapitulate what nature does, while at the same time turning on every patient's reparative potential. The platform is also highly versatile and could be applied to various stem cell sources.

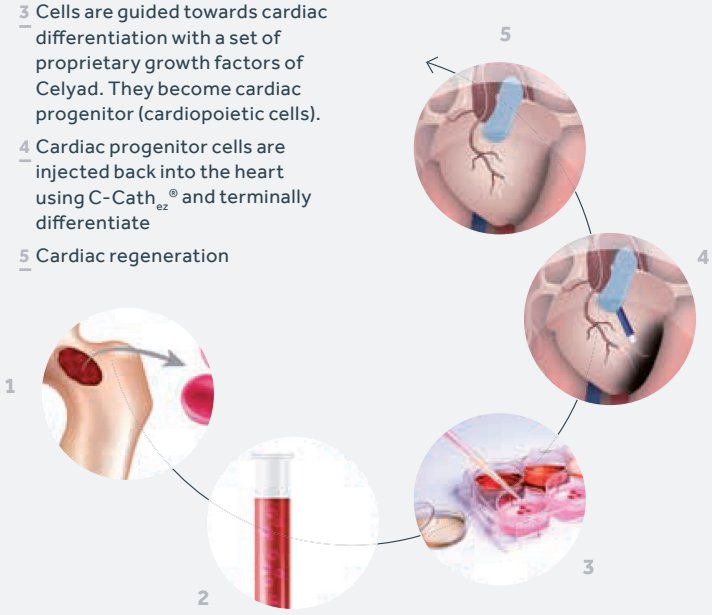
C-Cure®

C-Cure® is Celyad's lead product candidate in cardiovascular disease and is based on the Cardiopoiesis platform. C-Cure® is being developed for ischemic HF and consists of a patient's own cells harvested from bone marrow, treated with the Cardiopoietic growth factors and then re-injected into the heart. It is designed to produce new autologous heart muscle cells which behave identically to those lost without carrying the risk of rejection.

C-Cure® has two modes of action:

- directly through the proliferation, engraftment and terminal differentiation of the injected cells; and
- indirectly through the beneficial effect of the factors excreted by the transplanted cells on the host's own resident cardiac stem cells.

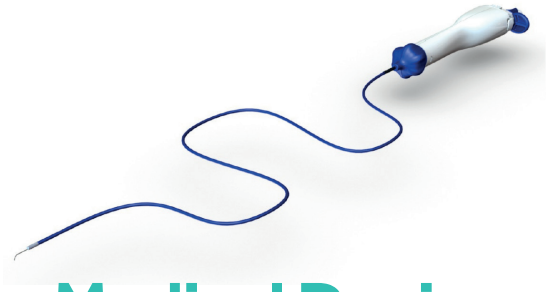
1 Bone marrow is drawn from the patient
2 Stem cells are selected and expanded
3 Cells are guided towards cardiac differentiation with a set of proprietary growth factors of Celyad. They become cardiac progenitor (cardiopoietic cells).
4 Cardiac progenitor cells are injected back into the heart using C-Cath$_{ez}$® and terminally differentiate
5 Cardiac regeneration



Portfolio of pharmaceutical products

	PRODUCTS	INDICATION		DISCOVERY	PRE-CLINICAL	PHASE I	PHASE II	PHASE III
cardiology								
CELLS	**C-Cure**	Congestive Failure	Heart	**CHART-1 – EMA APPROVED CLINICAL STUDY**				
				CHART-2 – FDA - APPROVED IND*				

** Pending FDA clearance on C-Cath$_{ez}$® to begin the trial.*



Medical Devices

C-CATH$_{ez}$®

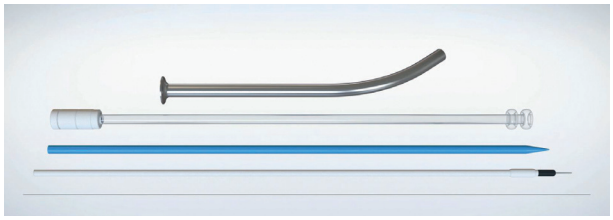
Celyad has developed a proprietary technology aimed at maximizing the delivery efficiency of regenerative therapeutics to the heart. C-Cath$_{ez}$® is an intra-myocardial delivery catheter, designed to reduce risk of myocardium perforation, increase needle stability and deliver enhanced fluid dynamics to improve retention. C-Cath$_{ez}$® obtained CE mark in April 2012 and is therefore available for clinical use worldwide and commercial use outside of the U.S.

Heart Access Technology

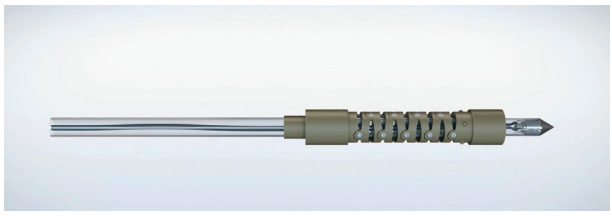
Celyad's heart access technology is designed to enable cardiologists to take a unique access route directly to the patient's left atrium, enabling the deployment of catheters or other necessary instruments for use in the treatment of various indications such as mitral valve disorders and structural heart diseases, conditions often linked to heart failure.

Celyad's heart access technology comprises a number of instruments which allow for quick, user friendly and easy trans-thoracic access to the heart.

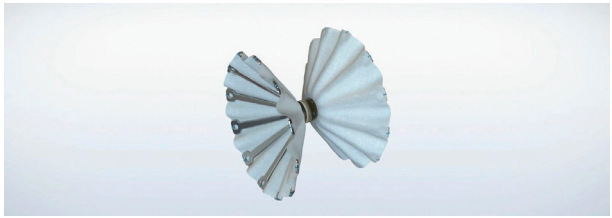
HEART ACCESS SHEATH



MITRAL VALVE NEO-CHORDAE



CLOSURE DEVICE



Portfolio of medical devices

PRODUCTS	INDICATION	DISCOVERY	PRE-CLINICAL	MARKET AUTHORIZATION
C-Cath$_{ez}$	Intramyocardioal Injection Catheter			
Heart Access Sheath	Hearth Access Sheath allowing easy and quick delivery of cardiac therapeutic devices			
Mitral valve neo-chordae	Mitral valve defects			
Closure device	Closing device post transcatheter intervention			

Believe in team

The talent, the expertise and the commitment of our teams have made and will continue making Celyad a leader in engineered cell therapies. Celyad's team is committed to making fundamental changes to the treatment of high unmet medical needs in cardiovascular disease and oncology and is continually pushing back the limits of the science and the technology.

"We care. We cure"
is our credo.

Celyad strives to create value through its people, seeking to attract the best candidates from all backgrounds and developing an exciting culture to help them realize their full potential. We are passionate, proactive, open-minded and committed. We only trust the higher standards of integrity and scientific excellence.

Celyad
we care · we cure

Christian Homsy

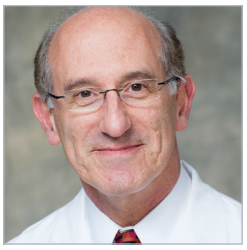
Michel Lussier

Patrick Jeanmart

Peter De Waele

Vincent Brichard

Georges Rawadi



Warren Sherman

Board of directors

The Board of directors is composed of 11 members, one of which is an executive director (as a member of the Executive Management Team), LSS Consulting SPRL, represented by **Christian Homsy**, Chief Executive officer and co-founder, and 10 of which are non-executive directors, including five independent directors. The non-executive board members are **Michel Lussier**, Chairman and co-founder; **William Wijns**, co-founder and permanent representative of Cardiovascular Onderzoek Aalst CVBA; **Serge Goblet***, owner of the holding Tolefi SA; R.A.D. Life Sciences BVBA represented by its permanent representative **Rudy Dekeyser**, managing partner of LSP Health Economics Fund, and former managing director of the Vlaams Instituut voor Biotechnologie (VIB); Pienter-Jan BVBA, represented by its permanent representative **Chris Buyse**, managing director of Life Science Research Partners VZW and non-executive director of multiple private biotech companies; **Jean-Marc Heynderickx**, CEO of Nextgen Group and former CEO of the Louis Delhaize Group; **Chris de Jonghe**, Group Manager venture capital at PMV and non-executive director of multiple private companies; and **Hanspeter Spek**, former President Global Operations and member of the Executive Committee of Sanofi; **Danny Wong**, chairman and executive director of National Investments Fund Limited, a company listed in Hong-Kong.

The current independent directors are R.A.D. Life Sciences BVBA, represented by its permanent representative, Rudy Dekeyser, Pienter-Jan BVBA, represented by its permanent representative, Chris Buyse, Jean-Marc Heynderickx, Chris De Jonghe and Hanspeter Spek.

Board Committee

The Board of Directors has set-up a *Nomination and Remuneration Committee*. This Committee is composed of four non-executive directors, respectively Pienter-Jan BVBA, represented by its permanent representative, **Chris Buyse, Hanspeter Spek** and R.A.D. Life Sciences BVBA, represented by its permanent representative, **Rudy Dekeyser**. The Committee is chaired by **Michel Lussier**.
In March 2015, the board nominated an *Audit Committee* within the Board of Directors. The audit committee consists of three members, all non-executive and independent directors: Pienter-Jan BVBA, represented by its permanent representative, **Chris Buyse**, R.A.D. Life Sciences BVBA, represented by its permanent representative, **Rudy Dekeyser** and **Chris De Jonghe**. Previously, the audit function was carried out by the entire Board of Directors.

Executive management team

The Executive Management Team is composed of the senior management of the Company. The Executive Management Team is responsible for submitting the Board of Directors with vision and the strategy of the Company, and for executing the day-to-day management of the Company.

The team consists of:

Christian Homsy,
representative of LSS Consulting SPRL,
acting as Chief Executive Officer
Patrick Jeanmart,
representative of PaJe SPRL,
acting as Chief Financial Officer
Peter De Waele,
representative of Advanced Therapies Consulting Ltd., acting as VP Research & Development
Vincent Brichard,
representative of ViaNova SPRL,
acting as VP Immuno-oncology
Georges Rawadi,
VP Business Development
Warren Sherman,
Chief Medical Officer

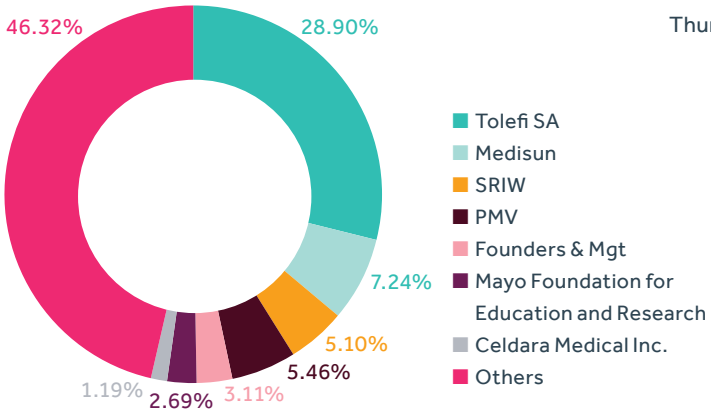
**acting in his own name and as permanent representative of Tolefi SA.*

Information to shareholders

Shareholding structure

As of 2 March 2015 and capital increase of €32 million, Celyad SA has a total of 7,847,187 outstanding shares and 347,930 outstanding warrants. The shareholding structure can be summarized as follows:

SHAREHOLDER STRUCTURE AS PER MARCH 31, 2015



2015 financial calendar

All announcements will be made post close of markets

Tuesday 5 May 2015: Annual Shareholders meeting

Tuesday 19 May 2015: Q1 2015 Business Update

Tuesday 25 August 2015: 2015 Half Year Financial and Operational results half year 2015

Thursday 19 November 2015: Q3 2015 Business Update

Analyst coverage

NAME	BANK/FIRM	WEBSITE
Sachin Soni	Kempen & co	www.kempenresearch.nl
Mark Pospisilik	Kempen & Co	www.kempenresearch.nl
Martial Descoutures	Invest Securities	www.invest-securities.com
Arnaud Guerin	Portzamparc, groupe BNP Paribas	www.portzamparc.fr
John Savin	Edison Group	www.edisongroup.com
Roderick Verhelst	Petercam	www.petercam.com
Bruce D. Jackson	Lake Street Capital Markets	www.lakestreetcapitalmarkets.com
Hugo Solvet	Bryan Garnier	www.bryangarnier.com
Jason Kolbert	Maxim Group	www.maximgrp.com

Share Price performance

Financial services

The financial services for the shares of the Company are provided by BNP Paribas Security Services.

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Glossary

Acute Myeloid Leukemia (AML)	AML is a type of cancer that affects the blood and bone marrow. It is characterized by an overproduction of certain immature white blood cells, called myeloblasts or leukaemic blasts.
Autologous cells	Cells that are from the same donor as the recipient.
Cardiac Progenitor Cells (CPCs)	A cardioprogenitor cell is a cellular phenotype with the capacity to yield myocardial tissue and blood vessels upon differentiation.
Cardiac Stem Cells (CSCs)	Cells that can give rise to all of the major cell types in the human heart.
Cardiopoiesis	Process to drive stem cells towards the cardiac lineage.
Cardiopoietic Cells (CPCs)	Cells that are precursors of fully differentiated cardiac muscle cells. In the lab, CPCs can be generated from stem cells by culture in the presence of a specific cocktail of cardiotrophic factors discovered at the Mayo Clinic.
CAR T-Cell	A CAR-T cell is a T lymphocyte (a type of white blood cells) in which a DNA construct, coding for a receptor, has been introduced artificially. The result of this engineered cell is that the T lymphocyte express the CAR (Chimeric Antigen Receptor) on its surface and is able to recognize a specific target through new engrafted receptor.
Heart Failure (HF)	Heart Failure is a condition in which the heart has been damaged and cannot pump enough blood to meet the body's metabolic needs. HF can be of ischemic or non-ischemic origin: – Ischemic Origin (Coronary Artery Disease); – Non-ischemic Origin; • Hypertension: high blood pressure; • Other conditions such as heart valve disease, congenital heart defect, endocarditis (infection of the heart valves) and/or myocarditis (infection of the heart muscle). The failing heart keeps working but not as efficiently as it should. HF patients cannot exercise because they become short of breath and tired. In the most severe forms, even slight exercises like walking a short distance are impossible.
In vivo (experiments)	Experiments done in animal living systems.
Left Ventricular Ejection Fraction (LVEF)	The fraction of blood pumped out of the left ventricle with each heart beat.
ligand	A ligand is molecule, as an antibody, hormone, or drug, that binds to a receptor.
Multiple Myeloma (MM)	MM is a cancer of plasma cells. Plasma cells are mature B lymphocytes, a type of white blood cell, that help to fight infection by producing special proteins called antibodies or immunoglobulins. In myeloma, large numbers of abnormal plasma cells called myeloma cells are made in the bone marrow.
NK cell or Natural Killer cell	NK cells are lymphocytes of the innate immune system, which can eliminate targets directly and destroy cells (e.g upon viral infection, or tumor cells)
Stem cells	Stem cells are primal cells. Stem cells retain the ability to renew themselves by division and can differentiate into a diverse range of specialised cell types. Stem cells can be found in adult tissues (adult stem cells), embryos (embryonic stem cells or ESCs) or umbilical cord blood.
TCR	TCR is a molecule found on the surface of T lymphocytes (or T cells) that is responsible for recognizing antigens bound to major histocompatibility complex (MHC) molecules.

Concept and realization
The Crew Communication - www.thecrewcommunication.com

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Albe De Coker

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Cardiovascular disease
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