



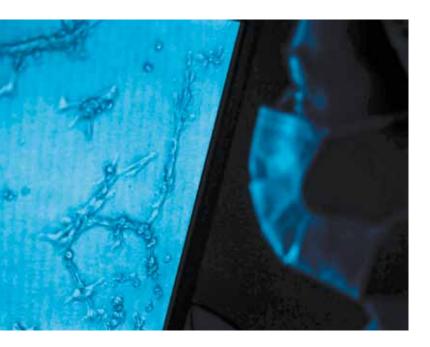
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### Disclaimer

This report and the information contained herein do not constitute an offer to sell or subscribe, or a solicitation of an offer to buy or subscribe, for shares in Cellectis in any country. This report contains forward-looking statements that relate to the Company's objectives based on the current expectations and assumptions of the Company's management and involve risk and uncertainties that could cause the Company to fail to achieve the objectives expressed by the forward-looking statements that follow.

## A key player in the field of immuno-oncology A revolution is taking place in the field of ad with engineered CAR T lymphocytes (eCAF



ith the active support of the Board of Directors, the management worked to accelerate the Group's therapeutic focus in a background of particularly dynamic global competition.

At the end of 2013 fiscal year, Cellectis was a fully operational, focused, agile and stronger group; effectively structured to meet its stated ambition: to be a key player in the field of oncology and to play a full part in the therapeutic revolution taking place in the field of adoptive immunotherapy to fight cancer with engineered CAR T lymphocytes (eCART).

At the heart of this revolution is genome engineering. Cellectis is capitalizing on its 14 years of technological expertise by relying on its flagship tools, TALEN<sup>™</sup> and meganucleases, and on Pulse Agile the stateof-the-art technology of electroporation, to create a new generation of immunotherapy aiming to treat leukemias and solid tumors.

This new approach, based primarily on the use of TAL nucleases, alters the T cell's genome to give it new properties. In particular, the engineered T cell can be transformed into a non alloreactive allogeneic product, can be compatible with standard cancer treatments or can be modified to overcome checkpoint inhibition.

This skill, combined with an acknowledged know-how in the reprogramming of T cells places Cellectis in a very strong position in the global effort of companies involved in the development of innovative therapeutic solutions, especially in the field of oncology.

Whether in regard to liquid or solid tumors, Cellectis is already developing new classes of therapeutic products that may transform the way in which diseases are treated, and will enable us to treat pathologies with unmet medical needs.

2013 was marked by an extremely aggressive transformation of the competitive environment in the field of genome engineering tools that made us suddenly question the Group's economic model and adapt its organization accordingly.

In the space of just 3 years, under the pressure of spectacular technological advances, the sale price of a gene editing nuclease has fallen drastically. But it is without doubt the introduction of CRISPR technology that has overturned this market's economic model.

# optive immunotherapy to fight cancer RT).

First published at the beginning of 2013, the encouraging results of CRISPR technology took less than six months to become an industrial reality offering the players concerned, primarily the academic world, experimental tools whose low designing costs obliterate the development in the short term of an alternative market in conditions of profitability compatible with existing cost structures.

We have responded to the structural transformation of the tools and services market by adapting our operating structures and drastically reducing resources allocated to the marketing and sales of those products.

During the second half of 2013, the Group has put in place an Employment Protection Plan involving a significant reduction in the payroll. On the date of publication of this activity report, the Group has 95 employees.

In late 2013, as part of the focus of the Group's operating structure, Ectycell was merged into Cellectis bioresearch. At the same time, the *"Caisse des Dépôts et Consignations"* increased its shareholding with a capital increase of 3.5 million euros enabling it to hold 24.5% of the new structure.

During the first quarter of 2014, Cellectis finalized two significant transactions that have come to reflect the Company's strategy.

Firstly, as we announced on 17 February 2014, the signing of a cooperation agreement with Servier to develop and market 6 product candidates using engineered T lymphocytes to target leukemias and solid tumors. As part of this agreement, Servier made an initial payment of 7.55 million euros. The maximum total financial value of this contract is potentially in excess of 750 million euros, including up to 105 million euros for each of the 6 product candidates potentially developed.

Secondly, in early March, following a private placement, several US investment funds specializing in biotechnology acquired a holding in the Company, reinforcing its equity by more than 20 million euros. The decision of OrbiMed Healthcare Fund Management, venBio, Ridgeback Capital Management LLC, Aquilo Capital Management, Merlin Nexus and additional funds to invest confirms the validity of the technological and economic model deployed by Cellectis and illustrates the immediate potential of the Company.

Throughout the 2013 financial year, then, Cellectis has been reconciling the past and considering future prospects for therapeutics.

This was no easy task, and we are proud to have achieved the first stage of this strategy.

The acceleration of the Group's therapeutic focus is as much the will of the management, with the constant support of the Board of Directors, as an overriding need in view of the spectacular changes in the biotechnology arena in the past years.

Our approach to life sciences is part of the industrial transformation taking place worldwide, which is creating a new order and providing a focus for innovation and inexhaustible growth.

Strengthened by your trust, we are forging ahead. Our initial commercial success in the field of therapeutics is encouraging. We feel sure that this is just the beginning.

On behalf of our management team and all Cellectis employees, we want to thank you for your enduring loyalty and ongoing support.

> ANDRÉ CHOULIKA Chairman and Chief Executive Officer

# About Cellectis

ellectis is a biopharmaceutical company focused on oncology. The company's mission is to develop a novel generation of therapies based on engineered T cells to treat cancer. Cellectis capitalizes on its 14 years of expertise in genome engineering, based on TALEN™, meganucleases and the state-of-the-art electroporation technology Pulse Agile, to create a new generation of cancer immunotherapy for treating leukemias and solid tumors. Cellectis adoptive cancer immunotherapy for chronic and acute leukemias is based on the first allogeneic T cell Chimeric Antigen Receptor (CAR) technology. CAR technologies are designed to target surface antigens expressed on cells. These new treatments could reduce toxicities associated with current chemotherapeutics and have the potential for curative therapy. The Cellectis Group is focused on life sciences and uses leading genome engineering technologies to build innovative products in various fields and markets.

**Legal form:** French *société anonyme* corporation with board of directors

ISIN code: FR0010425595 – ALCLS Listing date: February 6, 2007 Stock indexes: Alternext Allshare, Next Biotech, Oseo Innovation Number of shares outstanding at December 31, 2013: 21,082,320

Share capital at December 31, 2013: €1,054,116 Market capitalization at December 31, 2013: €48.5m Reuters: ALCLS.PA Bloomberg: ALCLS: FP

**Industrial property:** Cellectis has a rich, diversified intellectual property portfolio comprised of 108 patent families and 330 patents pending (as of January 1<sup>st</sup>, 2014). The continued development of these assets and the protection of the Company's scientific assets are guaranteed by the quality of our science, as well as by actions taken to raise awareness about intellectual property issues. Cellectis also encourages its employees to publish, which in turn contributes to the dissemination and visibility of its scientific expertise worldwide.

### Milestones

1999: Cellectis is founded

2005: Development of a process for the industrial production of nucleases

2007: Listing on the NYSE Euronext Alternext market in Paris

2008 – 2010: Acquisition of technologies and establishment of subsidiaries

2010: Acquisition of all assets of the American company CytoPulse Inc.

The acquisition included Hybrimune electrofusion technology and Pulse Agile technology for RNA transfection by electroporation. Pulse Agile is now the standard technology for RNA transfection of T cells.

2011: Acquisition of the Swedish company Cellartis 2013: Launch of the program Scéil™

### Contact

Cellectis – Investor Relations 8 rue de la Croix Jarry – 75013 Paris – France Phone: +33 (0)1 81 69 16 00 E-mail addresses: investors@cellectis.com, actionnaires@cellectis.com www.cellectis.com

Cellectis securities services: Société Générale Securities Services (affiliate 042)

### Listing market:

NYSE Euronext Alternext, Paris Ticker: ALCLS.PA Staff:

95 as of April, 2014

# The Cellectis Group

### CELLECTIS

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CANCER THERAPY T CELL PLATFORM ADOPTIVE IMMUNOTHERAPY SOLID AND LIQUID TUMORS CART INNOVATION

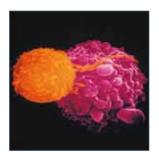
### CELLECTIS PLANT SCIENCES

A LEADER IN PLANT GENOME ENGINEERING WHOLLY-OWNED SUBSIDIARY FOUNDED IN 2010 LOCATED IN NEW BRIGHTON MINNESOTA, USA

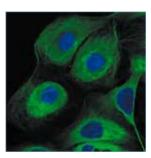
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### CELLECTIS BIORESEARCH

RESEARCH SOLUTIONS AND CUSTOM SERVICES 75,5% OF THE SHARE CAPITAL HELD BY CELLECTIS, 24,5% HELD BY CAISSE DES DÉPÔTS FOUNDED IN 2008 LOCATED IN PARIS, FRANCE









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# activities

### Disruptive innovation in oncology by gene editing and T cell CARs

At Cellectis, we are developing innovative cancer products based on engineered T cells armed with a Chimeric Antigen Receptor (CAR) to target liquid and solid tumors. Cellectis' state-of-the-art genome engineering technologies take T cell CAR technologies to the next level. An engineered T cell can in particular be converted into an allogeneic product or resist existing cancer treatments, or it can overcome checkpoint inhibition. Cellectis is focusing on certain types of cancer, particularly leukemia (B cells malignancies) and solid tumors (12 antigenic targets).

T cells are natural cells that are present in all humans and survey potential infections and contaminations. They permanently screen for non-self intrusion in the body and when they detect an infection, they kill contaminated cells and start amplifying significantly until the infection is resolved. T cells screen non-self intrusions in the body by a receptor called the T Cell Receptor or TCR. These specific killing and amplifying properties of T cells are exploited by researchers to convert T cells into cancer killing machines. T cells are modified by genome engineering to give them new properties. T cells will receive a Chimeric Antigen Receptor (CAR) that will specifically target a specific type of cancer in order to kill the cancer cells and induce amplification. T cell CARs will therefore fight cancer cells as if they were an infection. The next level of potency is brought by Cellectis' technologies. T cells are genetically engineered to gain or lose properties, for example, by suppressing the expression of the TCR or allowing the T cell to overcome checkpoint inhibition or indeed to resist existing cancer treatments or standard of care. Cellectis isolates large numbers of cells from the immune systems of healthy individuals. These cells are then genetically reprogrammed to specifically target and destroy cancer cells. Known as allogeneic or "donorderived" T cells, these protective cells of the immune system are engineered to avoid attacking the recipient's healthy tissues and rendered resistant to the most widely used lymphodepleting chemotherapies.

Allogeneic T cells engineered by Cellectis may be used to overcome the limitations of autologous or "patient-derived" adoptive immunotherapies, eventually making it possible to treat many patients using a standardized, off-the-shelf therapeutic product. Adoptive immunotherapy using T cell CARs is our flagship project. Cellectis' potential links us to the latest cancer breakthroughs as we develop new treatments in partnership with large pharmaceutical companies.

### **Engineered T Cell Therapy**

Genome engineering of T cells is the paradigm shift that will take T cell CAR technologies to the next level. Engineered T cells are the result of turning a therapeutic process into a pharmaceutical product adapted to the patient needs and standard of care, and can be seen as the future of adoptive immunotherapy.

The immune system is crucial in protecting the body against diseases. It prevents and fights infections caused by viruses, bacteria and other diseases. It also eliminates transformed cells that could become cancerous. The immune system consists of a vast number of molecules, structures, processes and cells that act in a coordinated manner. Of particular importance in the immune system are T cells, also called T lymphocytes.

During an infection, T cells are able to detect non-self molecules through the T Cell antigen Receptor (TCR); they are then activated and trigger defense mechanisms. Several types of T cells can initiate a variety of responses upon activation: they can kill infected cells directly or interact with other immune cells to induce them to participate in protecting the body against disease.

Sometimes the immune system is not able to contain the disease because of defects in the T cell response or because the cancer or the infectious agent has evolved to escape the immune response. For example, some tumors express on their surface a molecule called PDL1 that is able to tame the activity of T cells and therefore support tumor growth.

Decades of research have shown that it is possible today to improve the ability of T cells to fight diseases by genome engineering. For example, T cells can be engineered by adding a new gene (called a Chimeric Antigen Receptor or CAR) that will target them and boost their ability to recognize and destroy specific cancer cells. Another possibility for T cells is to inactivate an existing gene that damages the immune response.

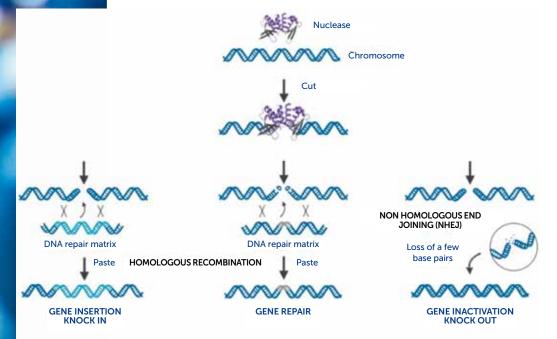
The possibilities provided by T cell genome engineering are endless. Very sophisticated strategies can be designed at will to open the door for a new era of treatments in indications such as cancer, autoimmune diseases and infectious diseases.



### What's genome engineering?

The principle of genome engineering is simple: it involves modifying the DNA of an individual or species. Genetics has demonstrated the link between the physical attributes of cells and their genes, and thereby shown how particular genes are implicated in certain diseases or cell attributes. Genome engineering enables species' genes to be modified in order to change certain attributes, to correct an error, or to add a new trait of physiological interest. This approach is not new: cross-breeding different plants or selecting the best animals for reproduction is based on the same principle. The aim is to improve cells by giving them the best possible attributes. The targeted approach of genome engineering is predictable, safer and more effective than earlier techniques. Knowledge of the location and sequence of genes in human beings is now very well known, even though the mechanisms of these genes are still not fully known. Our understanding in this field allows us to intervene on genes directly.

There are three possible strategies to do this:



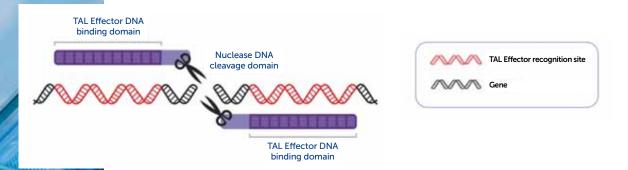
- Insertion is used to add a new attribute to the genome. For example in drug discovery, or in order to overcome a genetic defect.
- Correction is used to replace an existing defective sequence (which generally impacts the gene's functions) by a functional sequence. For example, to treat a genetic defect.
- Inactivation is used to prevent the expression of a gene. This approach can be used to modify a T cell to make it non alloreactive.

# Cellection Control <p

# Cellectis' ultra-precise gene editing tools: nucleases

These ultra-precise tools make it possible to edit the genome of any organism. The real power in genome engineering is being able to choose exactly where to edit a gene. Editing genes can be disabling a functional gene, correcting a gene, replacing or inserting a DNA sequence. Pioneer in the field of gene editing, Cellectis has over 14 years of expertise and knowledge in nucleases and DNA reconstruction, with products of highest quality, precision, and efficacy. At Cellectis, we design nucleases that cut a specific "gene of interest" in the genome. Cellectis is a leader in two types of nucleases:

TAL nucleases, or TALEN<sup>™</sup>, are the state-of-the-art of gene editing. TALEN<sup>™</sup> are proteins that attach themselves to DNA in a specific way and cut, at a very high efficiency and specificity, their target. Cellectis is the world specialist that can modify TALEN<sup>™</sup> on demand to target any given genetic sequence with high precision. The main advantage of TALEN™ is their target recognition system based on a simple, easyto-predict code. TAL nucleases are extremely precise, specific to their target and efficacious, due in part to the length of their 30<sup>+</sup> base pairs binding site. They have many applications in genome engineering and their specificity and high efficacity make them world best technology for therapeutic applications. Cellectis uses TALEN<sup>™</sup> for its therapeutic applications. TALEN™ are the most precise (genomic targeting can be performed within a 6 base pair range), specific (recognition site is of  $30^+$  base pairs), and efficacious (in example, TCR $\alpha$  can be knockedout routinely with over 85% efficacy in T cells) tool of gene editing. In addition, vectorization of TALEN™ is simple and easy.



• Meganucleases are a unique type of naturally occurring nuclease found in many single-celled organisms. They are extremely precise DNA scissors that look for a specific "binding site". These binding sites range from 16 to 30 or more base pairs long. Once the meganuclease has cut the DNA at the binding site, the surrounding cell activates its maintenance and repair system (for example, homologous recombination), which corrects the DNA molecule based on an identical copy (gene correction) or a fragment that has been specifically introduced into the cell (gene insertion or "knock-in"). This is the equivalent of cutting and pasting in a word processor. When a gene just needs to be inactivated rather than replaced, the broken DNA is reattached or "ligated", thus inactivating the target gene (this is called a "knock-out").

# Chimeric Antigen Receptors (CARs) for Cancer Immunotherapy

Chimeric Antigen Receptors (CARs) are artificial molecules that, when present at the surface of immune effector cells, will enable them to recognize a desired protein (antigen) and trigger the killing of cells harboring this antigen at their surface (target cells).

These receptors are one of the most promising approaches to fight cancer, through the development of adoptive cell transfer therapies. Indeed, immune cells (most usually T-lymphocytes) can be engineered to express a CAR able to recognize proteins present at the surface of cancer cells. Upon cell-to-cell contact between effector and targeted cells, antigen recognition will activate the effectors, giving them the signal to attack their targets, and leading ultimately to the killing of cancer cells. In addition, this activation will lead to an amplification of the CAR T cells in thousands in order to erradicate the tumor cells.

CARs are constructed by assembling domains from different proteins, each of which enables the chimeric molecule to carry out specific functions. The most common CAR architecture comprises an extracellular domain containing a region that recognizes the targeted antigen and a spacer region that links it to the transmembrane domain (the part of the protein that spans the cellular membrane). This is then followed by an intracellular domain, responsible for transmitting an activation signal to the cell upon antigen recognition, causing the CAR-engineered cell to attack the tumor cell.

Chimeric Antigen Receptors (CARs) have emerged as a powerful approach to retargeting of T cells to kill tumor cells that express specific surface target proteins. To date, CAR architectures have utilized a single polypeptide chain, mandating the serial appending of cytoplasmic signal transduction domains in order to enable a configuration that provides both T cell activation and co-stimulation. Cellectis has developed a novel multi-subunit CAR architecture based on FceRl, the high affinity IgE receptor that offers the potential for inclusion of multiple cytoplasmic signaling domains at their natural juxta-membrane positions, allowing improved functionality of the CAR. In addition, the multi-chain structure facilitates the implementation of multiple recognition domains, permitting the recognition of patterns of antigen expression. The novel multi-subunit architecture will allow the construction of chimeric antigen receptors with both improved activity and specificity and thus an expanded range of applications.

The target-binding moiety is usually derived from an antibody, while the intracellular portion can include, besides the domain leading to cell activation and cytotoxic response, one or more domains from co-stimulatory receptor proteins that enhance proliferative capacity and survival of the "therapeutic" cells.

Cellectis is currently developing a collection of CARs targeting antigens present on cells from various types of cancer, as well as a proprietary multi-chain architecture of these artificial receptors, aiming to further increase the efficacy of adoptive cell therapies in the future.

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# Cellectis' lead product candidate, UCART19

UCART19 is a best in class allogeneic engineered T cell product for treatment of CD19 expressing hematologic malignancies, initially developed in Chronic lymphocytic leukemia (CLL) and Acute lymphoblastic leukemia (ALL). Engineered allogeneic CD19 T cells currently stand out as a real therapeutic innovation for treating various types of leukemia and lymphoma.

UCART19 is a dynamic cellular product designed to become active, proliferate, secrete cytokines and kill tumoral CD19<sup>+</sup> B-cells following administration to lymphopenic patients. UCART19 activation is driven by contact between its anti-CD19 Chimeric Antigen Receptor (CAR) and CD19 on either CD19<sup>+</sup> tumor cells.

UCART19 activation leads to eradication of CD19<sup>+</sup> expressing cancer cells through T cell mediated cytotoxicity and potentially pro-inflammatory cytokine production.

Cellectis approach with UCART19 is based on the preliminary positive results from clinical trials using products based on the CAR technology and has the potential to overcome the limitation of the autologous current approach by providing an allogeneic, frozen, "off-the-shelf" cell based medicinal product.

### Chronic lymphocytic leukemia (CLL)

CLL is a blood cancer in which malignant, long-lived lymphocytes accumulate in the blood, bone marrow, spleen, and lymph node. Symptomatic patients with CLL commonly exhibit lymphadenopathy and in advanced stages anemia, neutropenia, and thrombocytopenia with a predisposition to repeated infections. Prognosis depends on the disease stage at diagnosis as well as the presence or absence of high-risk markers. CLL is the most common leukemia in the western world (1/3 of all new leukemia cases) with an incidence of 4:100 000/ year. CLL primarily affects the elderly, with the median age of 69 years. Efforts are ongoing to develop Chimeric Antigen Receptor adoptive immunotherapies. The main objective of the CAR T cell therapy is now to demonstrate the complementarity of this treatment to eradicate Minimum Residual Disease. The initial results in the published CAR clinical trial are very encouraging.

### Acute lymphoblastic leukemia (ALL)

Acute lymphoblastic leukemia (ALL) is a clonal disease of the bone marrow in which immature lymphoid precursors are arrested in development (with abnormal expression of genes, as a result of chromosomal translocations), proliferate and replace the normal hematopoietic cells of the marrow and in other organs, particularly the liver, spleen, and lymph nodes. ALL patients present symptoms related to infiltration by leukemic cells of the marrow or organs, or symptoms relating to the decreased production of normal marrow element resulting to varying degrees in anemia, thrombocytopenia, neutropenia, lymphadenopathy and splenomegaly.

Approximately 6000 new cases of ALL are diagnosed in the USA each year (1000 in France), leading to about 1400 deaths in 2013 (SEER data). Most occur in children, but 40% are in adults 20> years or older. About 80% of all children with ALL are cured. In contrast, the cure rate of adult ALL has remained at 20-40% over the past 30 years.

# Therapeutic indications

### Leukemia

Leukemia is a cancer that originates in the blood stem cells (immature blood cells) which are found in the bone marrow. The blood stem cells can become either lymphoid stem cells or myeloid stem cells. Lymphoid stem cells turn into lymphocytes, a type of white blood cell. Lymphocytes are usually found in the blood and various parts of the lymphatic system, particularly in the lymphatic ganglia and the spleen. Lymphocytes manufacture antibodies, whose role is to fight infections.

### Acute lymphoblastic leukemia

Acute lymphoblastic leukemia (ALL) is an abnormal proliferation of lymphoid stem cells blocked at an early stage of differentiation. ALL develops rapidly, within a few days or a few weeks of the first symptoms. Acute lymphoblastic leukemia accounts for approximately 20% of adult leukemias and more than one third of cancers in children.

### **Chronic lymphoid leukemia**

Chronic lymphoid leukemia (CLL) is a disease of the blood characterized by an excess of white blood cells in the blood and which develops slowly (chronic). In the case of chronic lymphoid leukemia, the B lymphocytes produced by the bone marrow accumulate in the blood, the ganglia, the spleen and the bone marrow, instead of dying within a few days or months to be replaced by others. It is the most common leukemia, affecting mainly people aged over 50.

### Acute myeloid leukemia

Acute myeloid leukemia (AML) is due to the proliferation of blasts - cells that give rise to white blood cells that have become tumoral - in the bone marrow which can then no longer ensure the production of healthy blood cells. The frequency of acute myeloid leukemias increases after the age of 40, the average age being 65.

### **Multiple myeloma**

Multiple myeloma, more commonly known as Kahler's disease, is a disorder of the bone marrow caused by an uncontrolled proliferation of plasmocytes (blood cells of the family of white blood cells) specialized in the production of antibodies. In Kahler's disease, the plasmocytes that proliferate all come from one abnormal plasmocyte. Multiple myeloma is a relatively rare cancer. This disease affects mainly people aged over 60.

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### Solid tumors

Cancerous solid tumors, identifiable as a localized mass of cells, differ from cancers of the blood cells, such as leukemias, whose cancerous cells circulate in the blood or lymph and are dispersed into the body. The majority of cancers are solid tumors. Two types of solid tumor are differentiated:

- carcinomas arise from epithelial cells (skin, mucosa, glands).
- sarcomas, less common, arise from cells of the connective tissue (known as "supporting" tissue).

### **Pancreatic cancer**

Pancreatic cancer is characterized by an anarchic proliferation of cells which forms a mass of tissue, i.e. a tumor, in the pancreas. Adenocarcinoma, which accounts for 95% of these tumors, is situated in the exocrine cells of the pancreas and is the most common type of pancreatic cancer. Although it is relatively rare, pancreatic cancer is one of the most aggressive.

### Non-small cell lung cancer

Non-small cell lung cancer (NSCLC) is an epithelial tumor of the lung. The most common forms of NSCLC are epidermoid carcinoma, large-cell carcinoma and adenocarcinoma, but there are other rarer forms. Non-small cell lung cancer (NSCLC) accounts for between 80 and 85% of lung cancers.

### Glioblastoma

Multiform glioblastoma is a brain tumor which will affect the astrocytes, cells of the central nervous system. It is the most common brain cancer in adults and the most aggressive.

### Our therapeutic products

### Pipeline

Hematopoietic tumors	Discovery	Preclinical	Phase I
UCART19 (partnering with Servier) Acute Lymphoblastic Leukemia (ALL), Chronic Lymphatic Leukemia (CLL)			2015
UCART123 Acute Myeloid Leukemia (AML)		Q4 2014	
UCART33 Acute Myeloid Leukemia (AML)		Q4 2014	
<b>UCART-BCMA</b> Multiple myeloma (MM)		Q2 2015	
<b>UCART38</b> Multiple myeloma (MM)		Q2 2015	

	Discovery	Preclinical	Phase I
Solid tumors	V		
UCART5T4 Multiple potential solid tumor indications (Pancreatic cancer; Non-small-cell lung carcinoma NSCLC)		Q4 2014	
UCART-EgfrVIII Glioblastoma		Q4 2014	
S-3		2015	
S-4		2015	
S-5		2015	
S-6		2015	
S-7		2015	

### Development of a medicinal product takes place in several stages:

- **Research:** from identification of the target to development of the drug candidate.
- **Preclinical:** validation of the concept and its safety and efficacy in animal models.
- **Clinical:** testing of the candidate medication in humans, generally in several phases:
  - **Phase I:** administration of the product candidate to a small group of healthy volunteers or patients to find out how the target works in the human body.
  - Phase II: administration of the product to a

larger group of patients to test its efficacy, to define the appropriate dose and to continue the assessment of its safety.

- **Phase III:** assessment of efficacy and tolerability in situations close to current practice. A dossier may then be submitted to the health authorities in order to obtain marketing authorization.
- **Phase IV:** studies performed after marketing authorization.

It must be expected to take an average of 8 to 12 years before a new medicinal product is launched on the market.





### Cellectis plant sciences, Healthier Food for a Better Life

### The overall objective of Cellectis plant sciences is to bring to the market crops with improved health characteristics that will benefit to the consumers.

Founded in 2010, Cellectis plant sciences is based in New Brighton, Minnesota (United States). Cellectis plant sciences has developed a platform to improve the agronomic and quality value of crops for the food and agriculture industries. It is involved in a network of collaborations that include global seed companies (Bayer, Limagrain, Monsanto, SESVanderhave among others), as well as leading Healthcare (Mitsubishi Tanabe) and food companies. Cellectis plant sciences is developing innovative products with prominent partners in order to secure access to the market.

The process used to develop products is based on technologies (such as TALEN<sup>™</sup>) invented by scientists at University of Minnesota, widely adopted by the scientific community worldwide and exclusively licensed to Cellectis. Several governmental agencies have indicated that the resulting products would be regulated as mutagenesis products. The expertise and commercial network include a range of high valuable plants with healthier characteristics: soybean, potato, canola and wheat, and can be adjusted to virtually any crop on a need basis.

The activities of Cellectis plant sciences are focused in three main areas:

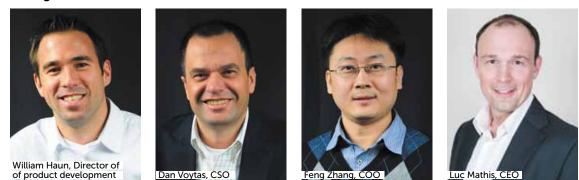
- developing a pipeline of potato products
- developing a portfolio of traits in various crops including soybean, canola and wheat
  offering access to its platform to agri-food companies and co-develop valuable
- new varieties The high-potential of Cellectis plant sciences activities and products opens up the

prospective of a significant growth and a significant increase in value over the next few years as a result of the first traits being validated in field trials (in-house or with partners).

### Pipeline

In house programs	Initiation	Phenotype	Scale up	Commercialization
Non trans fat soybean oil			2014-2016	2019
Potato traits Cold induced sweetening		2014	2015-2017	N.D.
Enzymatic browning Disease resistance		2015	2016-2018	N.D.

### Management team



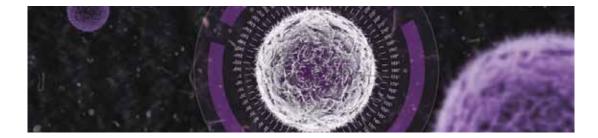
# Research solutions, custom-engineered production tools and bespoke services

Created in 2008, Cellectis bioresearch is an expert provider of tools and services combining targeted DNA editing and stem cells. Located in Paris, Cellectis bioresearch was built upon key technologies such as induced pluripotent stem cells (iPS cells) and genome engineering, and has developed expertise in nuclease technology and genetic targeting.

Since its inception, Cellectis bioresearch has commercialized different solutions for market participants in the life sciences sector:

- tools for specific applications, notably drug discovery and testing;
- engineered products;
- services adapted to all cell engineering projects.

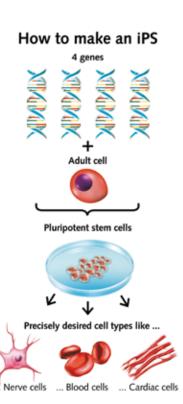
For more information: www.cellectis-bioresearch.com



### The Scéil™ program

Launched in July 2013, Scéil™ is the first opportunity for individuals to store their own induced pluripotent stem cells (iPS cells) so as to benefit, if necessary, from future regenerative medicine treatments. The program's availability in various geographic regions is subject to prevailing laws and regulations.

Find out more about Scéil: www.sceil.com



### Corporate social responsibility

Guided by a deep respect for humanity, Cellectis has for some years pursued an approach which consists of taking account of the social and environmental impact of its work, in order to adopt best practice and thus contribute to social improvement and environmental protection. By keeping the benefit to humanity at the heart of our priorities and by aligning our behavior and actions with our values of respect, integrity and transparency, we are daily building relationships based on enduring trust with our internal and external partners.

### Responsibility towards our team members and our stakeholders

As a company quoted on the stock market, Cellectis affirms its clear intention to define its CSR policy, its ethical commitment and also its responsibility towards all stakeholders: team members, shareholders, suppliers, clients, partners and society in general.

### **Better health for all**

First and foremost, our mission is to develop a new generation of immunotherapy to treat leukemias and solid tumors, using engineered CART cells. These treatments reduce the toxicity associated with current chemotherapy and have the potential to cure. Every member of the Company's staff is committed to maximizing the number of innovative health products available in the near future.

### A solid ethical charter

Ethical conduct implies that all should conform to the laws and regulations currently in force. This also means that we respect the corporate values and principles promulgated in our charter. These great principles concern the governance of the Group, the right to work and the protection of those who work in the Company. We maintain a working environment conducive to diversity and integration, implement responsible practices and respect the highest ethical standards at all stages, from research and development to marketing.

### **Environmental awareness**

The Group has instituted various measures to help preserve the environment. We also support initiatives to promote greater environmental responsibility.

### Training: investment in the Group's human capital

Our training plan bears witness to our commitment to developing the skills of our team members. It expresses our priorities and guarantees that all have equal access to training. We have considered our choice of training courses, how we implement these, the targeted profiles which we hope to shape as a priority, and the status we give to the needs expressed by the staff of the Group. This plan is a vehicle for social dialogue with all the actors in the Company.

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# Tuned in with our shareholders

In 2013, Cellectis experienced a particularly difficult trading year due to a strong focus of the Company on therapeutics and a massive turnaround in the tools market, which was a significant proportion of its turnover. The collapse in sales of tools and services together with the refocus of the strategy on therapeutic activities, while still maintaining the agro-industrial activities led the Group to change the cost structure. This shift has increased the volatility of Cellectis activities and has had a strong impact on its share price with an historic low hit in December 2013.

In this very unsettled climate, Cellectis has made it a priority to maintain a constant link with its shareholders, especially those who had a strong buy-in for the strategy and those who are showing concerns. The Shareholder Relations department has therefore responded to numerous letters, emails and phone calls and has constantly kept the relevant pages of the Internet site up to date. The Company's management has continued with the program of meetings with shareholders that started in 2012, with three new meetings arranged this year: one in Paris in February in partnership with the Federation of Personal Investors and Investment Clubs (Fédération des Investisseurs Individuels et des Clubs d'investissement (F2IC)), another in March in Lyon, again with F2IC and the final one in Pau in December in partnership with the weekly financial paper Le Revenu as part of "Finance Week", sponsored by the Ecole Supérieure de Commerce. André Choulika, Chairman and CEO of Cellectis, chaired this final meeting of the year, which took place on December 2. He explained the strategic focus of the Group with regard to high potential therapeutic activities, especially in the development of adoptive immunotherapy against certain forms of leukemias and solid tumors, and its agro-industrial activities which center on the creation, either alone or in partnership with another company, of traits for agricultural biotechnology.



The General shareholders' assembly took place on June 14, 2013 at the Cellectis head office, located in Paris, easily accessible via public transport. In his opening address, André Choulika gave a very informative presentation about the Group, of its achievements and its objectives. Mathieu Simon, Executive Vice-President responsible for the development of therapeutic activities, gave a detailed explanation of the potential of engineered T cells equipped with a Chimeric Antigen Receptor (CAR) based on the latest genome engineering technology from Cellectis, which will enable both liquid and solid tumors to be targeted. His statement gave rise to numerous questions from shareholders, who came to express their opinions in person.

During the year, the Group has issued eighteen press releases, which is an average of one every three weeks. In addition to the regulatory financial publications, these press releases highlight significant events for Cellectis. In January and September the Group also sent two letters to shareholders. Very comprehensive, these bi-annual publications give a detailed review of the highlights of the last six months, summarize the latest Group news and provide a clear outline of all information useful for shareholders.

On request, we can provide our shareholders with specific documents, such as the annual report and the letter to shareholders (half-yearly). Please do not hesitate to contact our Shareholder Relations department if you have any questions, comments or suggestions.

The summarized financial statements included in this document are derived from the Group's consolidated financial statements, which are prepared in accordance with IFRS. The consolidated financial statements for the year ended December 31, 2013 were approved by the Board of Directors at its meeting of April 10, 2014 and have been certified without qualification by the Group's Statutory Auditors.

### Balance sheet – Assets

In thousands of euros	December 31, 2013	December 31, 2012
Intangible assets*	6,621	37,821
Property, plant and equipment	3,869	5,484
Financial assets	1,150	1,422
Deferred tax assets	-	3,392
Non-current assets	12,001	48,119
Inventories	367	707
Operating receivables	12,018	16,400
Cash and cash equivalents	7,559	21,808
Current assets	19,945	38,916
TOTAL ASSETS	31,946	87,036

(\*) The reduction in the "Intangible assets" item compared with 2012 is due to the depreciation of goodwill relating to the acquisition of Cellartis AB in November 2011 (impact of  $\leq$ 25.7 million) and the capitalized development expenses of the "tools and services" segment (impact of  $\leq$ 3 million).

### Balance sheet – Equity and liabilities

In thousands of euros	December 31, 2013	December 31, 2012
Share capital and share premium account	134,298	131,985
Reserves	(68,232)	(50,668)
Net profit (loss), Group share	(61,033)	(21,896)
Equity attributable to equity holders of the parent	5,032	59,420
Equity attributable to non-controlling interests	(216)	2,086
Total equity	4,815	61,506
Long-term debt	3,375	3,303
Non-current provisions	437	513
Total non-current liabilities	3,812	4,088
Short-term debt	691	988
Operating payables	20,174	20,452
Current provisions*	2,454	-
Total current liabilities	23,319	21,441
TOTAL EQUITY AND LIABILITIES	31,946	87,036

(\*) Current provisions include a sum of €1.9 million for the Employment Protection Plan - PSE launched at the end of 2013 and rolled out during the first half of 2014.

### **Income statement**

In thousands of euros	2013	2012
Sales*	7,706	11,301
Other operating income	8,817	9,731
Total revenue	16,523	21,032
Cost of sales	(614)	(1,535)
Gross margin	15,909	19,497
Research and development costs	(24,914)	(19,008)
Selling, general and administrative expenses	(22,080)	(19,528)
Depreciation of goodwill	(25,683)	-
Other operating income and expenses	(1,590)	(753)
Operating profit (loss)	(58,384)	(19,792)
Financial income (expense)	(335)	(1,325)
Corporate income tax**	(3,392)	(1,193)
PROFIT (LOSS) FOR THE YEAR	(62,111)	(22,310)

(\*) The reduction in sales (-32%) is due in the main to the sharp decline in the market for genome engineering tools.

(\*\*) The corporate income tax figure corresponds to depreciation of deferred tax assets.

### Cash flow statement

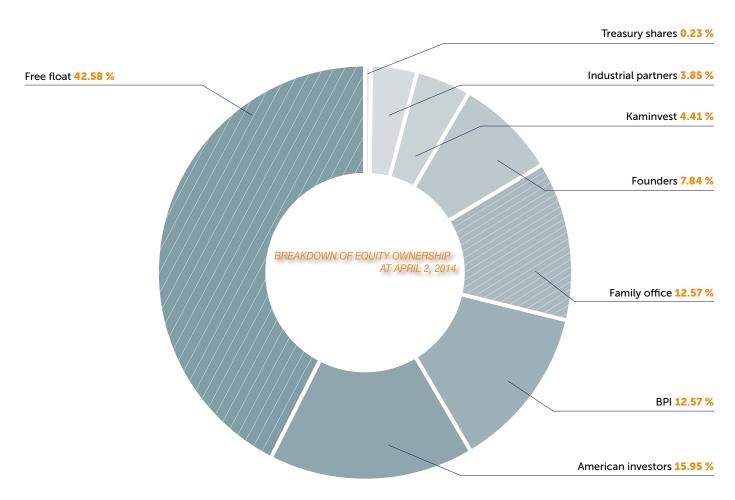
Net profit (loss) for the year	(62,111)	
		(22,310)
Non-cash transactions	39,456	7,344
Operating cash flow before change in working capital	(22,655)	(14,926)
Change in working capital	4,129	(5,041)
Interest received / (paid)	(33)	224
Net cash from (used in) operating activities	(18,560)	(19,743)
Cash payments in respect of capitalized development expenses	(895)	(3,391)
Purchases of other intangible assets	(62)	(250)
Purchases of property, plant and equipment	(429)	(507)
Purchases of other non-current assets	(122)	(462)
Net cash from (used in) investment activities	(1,509)	(4,610)
Capital increase*	5,818	2,704
Cash receipts from sale and lease-back transactions	-	764
Repayable loans and advances	(384)	282
Sale and purchase of treasury shares	-	(25)
Net cash from (used in) financing activities	5,434	3,725
Effect of foreign exchange rate changes	438	-
Net change in cash and cash equivalents	(14,197)	(20,628)
Net cash at the beginning of the year	21,808	42,384
Foreign exchange translation adjustment	(53)	53
Net cash at the end of the year	7,559	21,808

(\*) The "Capital increase" item relates to the increase in capital subscribed by the Caisse des Dépôts et Consignations at the subsidiary Cellectis bioresearch ( $\in$ 3.5 million) and the exercising of 605 000 share purchase warrants by Kepler Capital Markets SA under the equity line contract entered into with it ( $\in$ 2.3 million).

### Income statement

Amid still challenging and volatile market conditions, the share price varied between  $\leq 6.97$  on January 1, 2013 and  $\leq 2.30$  on December 31, 2013 with its highest closing price being  $\leq 7.83$  on February 25 and its lowest being  $\leq 2.11$  on December 17. The daily average volume of shares traded was 95,586, or nearly five times the average recorded in 2012.





# Governance

### **Executive Committee**

André Choulika, PhD, Chairman and Chief Executive Officer André Choulika is the Chairman, CEO, and founder of Cellectis. Dr Choulika is a pioneer in the analysis and use of meganucleases to modify complex genomes. After receiving his PhD in molecular virology from the University of Paris VI (Pierre et Marie Curie), he completed a research fellowship in the Harvard Medical School Department of Genetics. Later, while working in the Division of Molecular Medicine at Boston Children's Hospital, he developed the first approaches to meganuclease-based human gene therapy. Dr Choulika also has management training from the HEC (Challenge +).

### **Mathieu Simon, MD, Executive Vice President**

After graduating from medical school at the University of Paris in 1982, Dr Mathieu Simon embarked upon an illustrious international career in the pharmaceutical sector. After serving as Director of Marketing and Sales at Wyeth France, he became Group Vice President of Marketing and Clinical Affairs for Wyeth Pharmaceuticals in the United States, and later led several of the Wyeth Group's biggest regional subsidiaries in the Benelux countries, Italy, Greece, and the Balkans. In 2010, Dr Simon was named Senior Vice President of Pharma Global Operations at Pierre Fabre Médicament. He joined the Cellectis Group in 2012.

### David Sourdive, PhD, Executive Vice President Corporate Development

David Sourdive, PhD, is a graduate of the École Polytechnique. He is VP of Corporate Development and co-founder of the company. After completing his PhD in molecular virology at the Institut Pasteur, he joined one of the leading laboratories in viral immunology, at Emory University in Atlanta, Georgia (United States). His work there was focused on immunological memory. Before co-founding Cellectis, he directed the biotechnologies laboratory of the Centre d'études du Bouchet for the French Ministry of Defense. He also has management training from the HEC (Challenge +).

### Philippe Duchateau, PhD, Chief Scientific Officer

Philippe Duchateau received his PhD in biochemistry and molecular biology from the University of Lille and the Institut Pasteur. He joined Cellectis in 2001 after nine years at the Cardiovascular Research Institute of the University of California, San Francisco (United States). He previously headed Cellectis' Research department, starting in 2004.

### **Thierry Moulin, Chief Financial Officer**

Thierry Moulin is a graduate of Rouen Business School with over 30 years' professional experience and joined Cellectis as CFO in 2014. After starting out as an auditor, Thierry Moulin went on to specialize in the administrative and financial management of industrial groups (AIRSEC Industries, Süd-Chemie) in France and internationally, particularly in Japan. Before joining the Group, Thierry Moulin was a partner at TMBB Consulting and an expert in interim management.

### **Philippe Valachs, Company Secretary**

Philippe Valachs, Cellectis Company Secretary, became a partner in public affairs consulting firm Archimède Consultants in 2003 and, from 2004 to 2008, served as Associate Director of the think tank Cercle des Économistes. An economist by training, he began his career in the field of international consulting before working at France's Ministry of Industry and Foreign Trade from 1991 to 1993. He then joined Compagnie Générale des Eaux (now Vivendi), where he was named Chief of Staff to the Chairman in 1996. He then set out on a new business venture, co-founding Europe's first web television provider, Canalweb, in 1999.

### The Board of Directors: protecting the company's interests

### André Choulika, PhD, Chairman of the Board of Directors

### Laurent Arthaud, Director

Laurent Arthaud is a graduate of the École Polytechnique and the l'École Nationale de Statistique et d'Administration Économique. He has previously served as Vice President of Aventis Capital, an investment subsidiary of the pharmaceuticals group Aventis, and President of Pharmavent Partners, before being appointed to hold the position of Deputy CEO at CDC Entreprises in 2006. A subsidiary of the Caisse des Dépôts, CDC Entreprises handles private equity investments in small and medium sized growth companies. Laurent Arthaud also directs InnoBio, an investment fund managed by CDC Entreprises as part of the FSI France Investissement program. InnoBio invests in biotechs alongside France's biggest pharmaceutical laboratories.

### **Pierre Bastid, Director**

A graduate of the École Centrale de Lyon and INSEAD, Pierre Bastid spent 20 years in senior executive positions at major international business groups such as Schlumberger, Schneider Electric, Valeo and Thomson.

### Alain Godard, Independent Director

Alain Godard is a graduate of the École Nationale Supérieure Agronomique de Toulouse. He began his agronomy career in 1967 in Africa as a researcher at the l'Institut de Recherche pour les Huiles et Oléagineux (institute for research on oils and oleaginous plants). In 1975 he joined Rhône-Poulenc Agrochimie, where he held several executive positions before becoming Chairman and CEO of the company in 1991. During this time he successfully developed major processes in workflow decentralization and staff empowerment.

In 1997 he was appointed to the executive committee of the Rhône-Poulenc group, overseeing operations in the field of animal and plant health as well as the group's Asia region. In 1999 he was an active player in the merger of Hoechst and

Rhône-Poulenc, which resulted in the founding of Aventis. He was then named chairman of the management board of Aventis Cropscience and appointed to the group's executive committee. He left Aventis in 2002 to build up a consulting business in plant biotechnology and management.

### Institut Pasteur, Non-voting Director, represented by Pascale Augé

### Kaminvest, Director, represented by Roger J. Hajjar

Dr Roger J. Hajjar is a graduate of Harvard Medical School. He completed his residency in internal medicine as well as his fellowship in cardiology at Massachusetts General Hospital in Boston. He is a professor at the Mount Sinai School of Medicine in New York, and has directed the Cardiovascular Research Center there since January 2007. Before coming to Mount Sinai, he served as director of the Cardiology Laboratory for Integrative Physiology & Imaging at Massachusetts General Hospital and Associate Professor of Medicine at Harvard Medical School. He also worked as a staff cardiologist at the Heart Failure and Cardiac Transplant Center in Boston. Dr Hajjar is a co founder of the company NanoCor Therapeutics Inc., as well as co founder and Scientific Advisory Board member of Celladon Corporation in the United States.

### **Annick Schwebig, Director**

A graduate of the University of Paris medical school, Dr Annick Schwebig worked for 17 years as a senior manager at the biopharmaceuticals company Bristol-Myers Squibb. In 2000 she founded the French subsidiary of Actelion, of which she is now Chairman and CEO. Actelion is a biopharmaceuticals company specializing in innovative treatments to serve unmet medical needs.

She is also Vice Chairman of the LEEM's Biotechnologies Committee, which coordinates studies on cell therapies and nanomedicine, as well as Secretary General of ARIIS.

### Mathieu Simon, MD, Director

**David Sourdive, PhD, Director** 

# The Medical Advisory Board: driving performance

The Medical Advisory Board is in charge of setting the course for Cellectis' therapeutic strategy. It presents the Executive Committee with methods and strategies designed to achieve Cellectis' objectives; it then assesses the resulting work and outcomes.

### **Professor Malcolm K. Brenner**

MD, PhD, Baylor College of Medicine, Houston United States

### **Professor Dario Campana**

MD, PhD, National University of Singapore Republic of Singapore

### **Professor Hervé Dombret**

MD, Hôpital Saint-Louis, Paris, France

### Professor Alain Fischer

MD, PhD, Hôpital des enfants malades Necker, Paris, France

### **Professor Véronique Leblond**

MD, Hôpital Pitié-Salpêtrière, Paris, France

### **Professor David Linch, MD**

University College London Medical School, London, United Kingdom

### **Professor Ton Schumacher**

PhD, Netherlands Cancer Institute, Amsterdam, The Netherlands

### **Doctor Mathieu Simon**

MD, Chairman of the Medical Advisory Board, Executive Vice-President of Cellectis Cellectis

8 rue de la Croix Jarry 75013 Paris e-mail: media@cellectis.com website: www.cellectis.com

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