



## Our Commitment

At Cellectis, patients are our priority. As a clinical-stage biopharmaceutical company that has been working to develop the future of cancer immunotherapies for over 19 years, we are familiar with the challenges that people living with cancer face every day. As such, we find it incredibly important for us to leverage our leadership in gene editing and in allogeneic CAR-T therapy development to bring new hope to cancer patients.

We plan to continue our commitment to a cure through the four main pillars of success our company has been built upon:

**Innovation:** As one of the leaders in the gene-editing space, we continue to utilize our protein engineering for best-in-class gene editing and CAR T-cell technologies, cell engineering and culture technologies as well as our innovative and robust gene-editing (TALEN®) platform.

**Leadership:** Cellectis is developing the first clinical proof-of-concept - UCARTs - for off-the-shelf CAR-T therapy to address multiple unmet cancer needs, with several ongoing clinical trials testing allogeneic product candidates.

**Pipeline:** We are pioneering robust first-in-class allogeneic CAR T-cell programs for different hematological malignancies.

**Manufacturing:** We work hard to develop and improve a comprehensive, scalable, efficient, and cost-effective manufacturing process to generate highly potent CAR-T therapies. In an effort to continue upon this pillar, two manufacturing facilities are being built to ensure autonomy and control over our intricate process.



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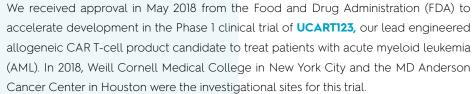
## Note from the Chairman and CEO



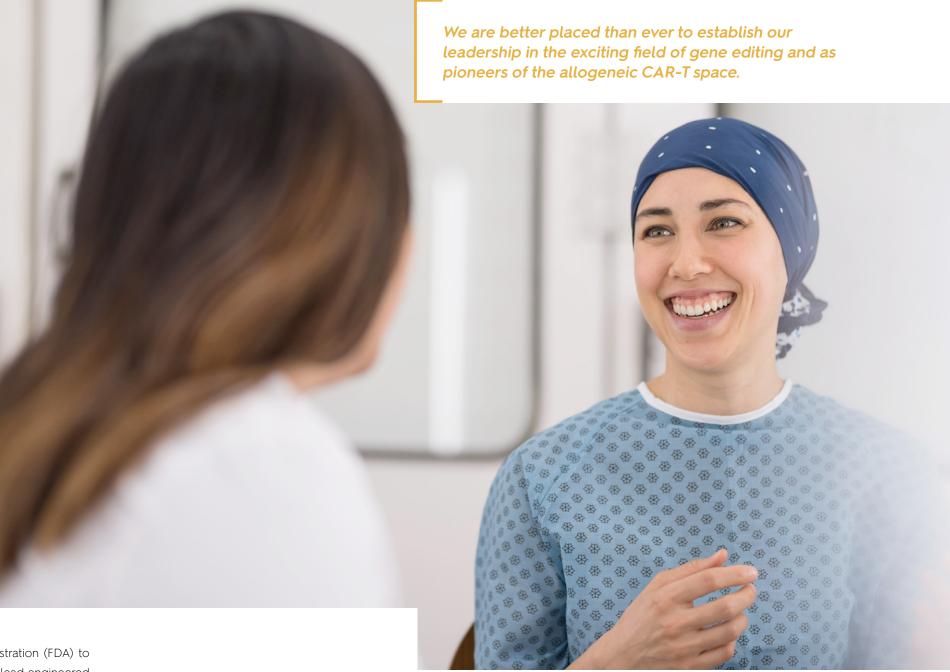
For Cellectis, 2018 was a crucial year in which we continued to develop a new generation of cancer therapies based on our flagship, high-precision TALEN® gene-edited CAR T-cells (UCARTs), while accelerating our transformation into a fully-fledged biopharmaceutical company.

With two wholly-controlled product candidates that had their IND granted in the U.S., and more to come in 2019, our partnerships with Allogene Therapeutics and Servier, and a successful financing round, we are strongly positioned to uphold our leadership in the exciting field of gene editing and as pioneers of the allogeneic CAR-T space.

Here are some of the highlights from 2018:



The FDA also approved our Investigational New Drug (IND) application to initiate a Phase 1 clinical trial for UCART22, Cellectis' second wholly-controlled TALEN® gene-edited product candidate, for the treatment of B-cell acute lymphoblastic leukemia (B-ALL) in adult patients. Following preclinical proof-of-concept in 2016, UCART22, which has the potential to target ALL, Non-Hodgkin Lymphoma and other B-cell malignancies, has proven to be highly efficient at eradicating tumors in vivo in vivo in preclinical research... We anticipate that the clinical trials will take place at MD Anderson Cancer Center, at the University of Chicago, and at Weill Cornell Medical College in New York City.



In April 2018, Allogene Therapeutics, Inc., a clinical-stage biotechnology company to develop allogeneic CAR-T therapies for different types of cancer, and Pfizer, Inc. entered into an asset contribution agreement, pursuant to which Allogene purchased Pfizer's portfolio of assets related to allogeneic CAR T-cell therapy. Following this asset contribution agreement, effective as of April 6, 2018, Allogene purchased Pfizer's portfolio of assets related to allogeneic CAR T-cell Therapy, including the Collaboration and License Agreement we signed with Pfizer in June 2014. Thus, Allogene acquired the exclusive rights to the 15 UCART cell therapies initially granted by Cellectis to Pfizer, as well as the Servier's U.S. rights to UCART19, the most advanced UCART product

UCART19 **UCART123** UCART22

**UCARTCS1** 



2018 Annual Report - Note from the Chairman and CEO

candidate exclusively licensed to Servier currently in clinical stage development Servier is leading the UCART19 clinical trials for adult and pediatric patients with relapsed or refractory CD19-positive B-cell acute lymphoblastic leukemia. We continue to be excited about our partnership with Allogene and Servier, and look forward to the years ahead.

In January 2019, we received approval from the FDA to start a clinical trial for our 3<sup>rd</sup> wholly-controlled product candidate UCARTCS1 for the treatment of multiple myeloma (MM). We believe that this product candidate has the potential to offer a totally new treatment approach for this disease, which affects more than 30,000 people each year in the U.S. alone. We anticipate that three sites will participate in the trial: MD Anderson, Weill Cornell Medicine and Hackensack Meridian.

In connection with our follow-on offering of 5,646,000 American Depositary Shares ("ADS") closed in April 2018, which resulted in gross proceed of \$175 million, we closed the sale of an additional 500,000 ADS at the public offering price of \$31.00 per ADS resulting in additional gross proceeds of \$15.5 million.

In 2018, we strengthened our management team with several senior appointments including Elsy Boglioli, former Partner and Managing Director at the Boston Consulting Group (BCG) and leader of BCG's biotech-focused business in Europe, as Chief Operating Officer. Elsy brings a wealth of biopharmaceutical industry experience at an exciting point in our development.

We also brought on board William (Bill) Monteith to the role of Senior Vice President U.S. Manufacturing and Thierry Ziegler, Ph.D., to the role of Head of Production. Bill joined Cellectis from Hitachi Chemical Advanced Therapeutics Solutions, where he was the Chief Operating Officer and Site General Manager for three manufacturing facilities. His appointment comes at a pivotal time for Cellectis, as the company moves closer to having internal manufacturing capability

with two state-of-the-art plants under development, including a 82,000 square-foot facility named IMPACT to be located in Raleigh, North Carolina, USA. This plant is Bill Monteith's responsibility, specifically the deployment of a proprietary, state-of-the-art, geneedited cell manufacturing plant for clinical and commercial supplies of our immuno-oncology UCART product candidates.

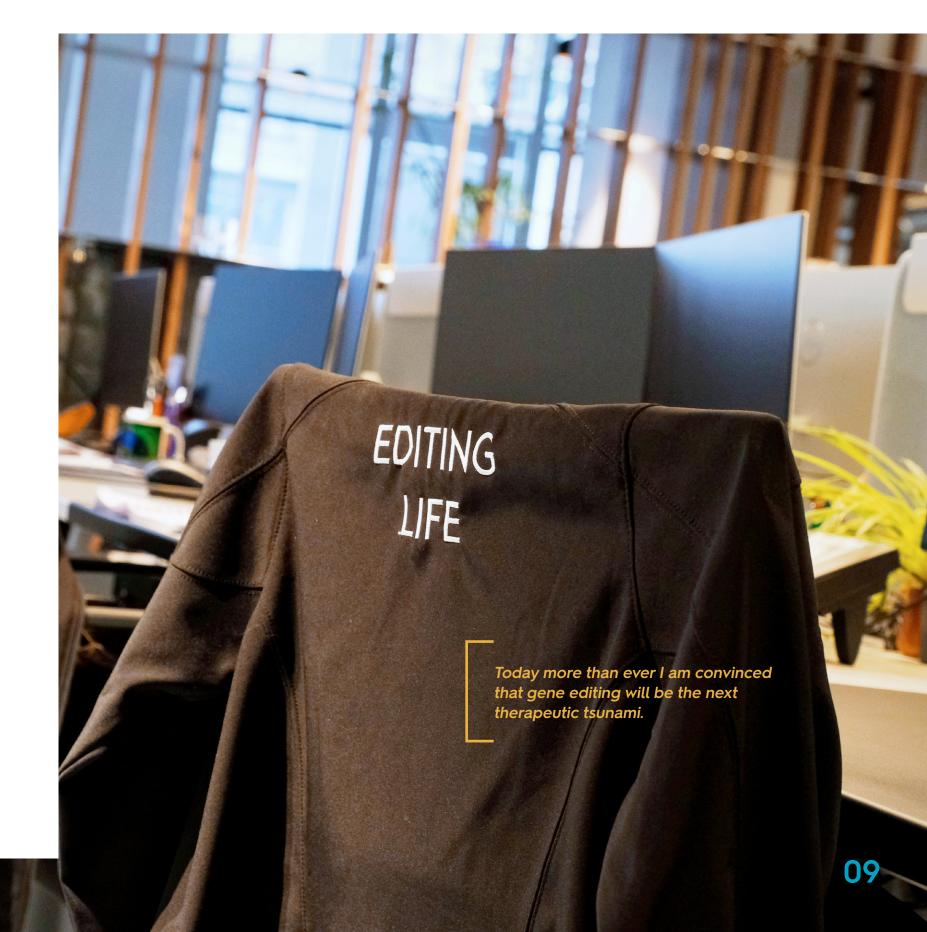
In addition, Thierry Ziegler joined Cellectis from Sanofi where he was Head of BioPharmaceutical Development. Thierry is our Head of Production and is handling the establishment of our SMART plant of 14,000 square-foot in Paris that will manufacture plasmids, vectors and other raw material for clinical supply. We expect this plant to go-live and begin supplying commercial material in 2020.

Today more than ever I am convinced that gene editing will be the next therapeutic tsunami. Other players have arrived on the scene, but as the pioneers in this area, we are confident our almost 20-year experience, strong partnerships, and encouraging clinical results will allow us to remain market leaders. The fact that competitors are now investing in gene editing serves to validate our approach. We welcome this new interest, as it will provide further momentum in this field, and ultimately get to patients faster.

UCART19 marked a medical first: to date we and our partner Servier are the only companies to have produced a gene-edited CAR-T product candidate used to treat patients. In 2019, we will continue to pursue our goal of bringing safe, effective cancer treatments based on immunotherapy to cancer patients everywhere.

I wish to thank the Cellectis team for their dedication and support in making 2018 such a productive year.

Dr. André Choulika Chairman and CEO of Cellectis





## Our key figures\*

## Our values

Our strong culture is rooted in the core values that make up the basis of our company. We pride ourselves on these 4 key areas:

#### Ingenuity

We value the ingenuity of our teams to address problems with new and creative solutions that set us apart from others in the industry.

#### Collaboration

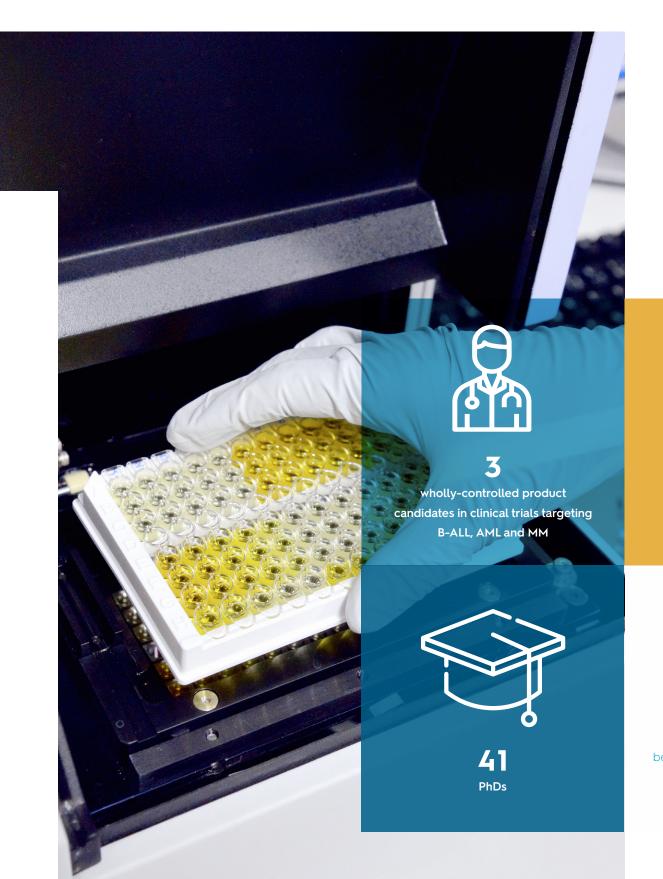
Our teams all have their strengths - but together, we create a super strength that allows us to work towards one unified goal - helping patients.

#### **Dedication**

Our dedication to our mission and patients is why we wake up and do what we do every day. Our team is passionate about using their ingenuity, collaboration and dedication to drive our initiatives.

#### People

All of these values culminate with one master value people. Whether it be our investment in our employees who work hard to produce quality, thoughtful work on a daily basis, or the patients who we remain committed to helping, we're in the business of health and wellbeing of people.





112 employees at Cellectis 85 in Paris, France office 27 in New York, NY office



54/46 46% of males







manufacturing plants

being built to allow Cellectis to remain in control of its production process (SMART in Paris, France & IMPACT in Raleigh, USA)







Not only are we focused on patients, but we are focused on investing in people at large.

At Cellectis, we value our employees, which transpires to a strong sense of work ethic and pride in the work we are doing every day. Our teams remain particularly engaged, as we value opinions and encourage collaboration across teams - and sites. Cellectis is located in life science focused hubs that not only emphasize the importance of helping patients, but provides a thinktank of ideas and cooperation where our employees can flourish.

#### Maintaining a consistent culture of transparency

Remaining True to Our Culture. At Cellectis, we have always had a culture that was invested in transparency and teamwork. Our team prides itself on its frequent meetings to discuss the state of the business, as well as the partnerships we have with internal and external stakeholders.

#### **Trainings**

Improving those who love to learn. Our team is filled with people who are invested in continuing to learn and be the best in their field. We invest in this desire for self-improvement by funding trainings, workshops and class opportunities for our employees. Cellectis believes in this so much, that it allows employees to include this as an aspect of individual performance during their yearly assessment.

#### Located in highly productive areas, Paris premises in the Biopark Building & NY premises in Alexandria Center for Life Science

Located in the center of it all. Between our Paris, France and New York, U.S. offices, both locations are positioned in the middle of the hustle and bustle of the scientific community. In Paris, our employees enjoy the great Biopark building that regroups laboratories and offices dedicated to life and health sciences. In New York, our offices are located in the Alexandria Center for Life Science, which houses a number of other biotechnology and pharmaceutical companies with a common goal: contribute to a better tomorrow. The team is able to frequently network and discuss ideas that give way to new and innovative research.

#### Involvement in volunteering that matters - CRI, patient advocacy

Listening to our employees. Cellectis works with eyes – and ears – wide open. We have listened to what employees find important and create opportunities for partnerships or volunteering with these organizations. We've now partnered with a number of organizations for research and patient advocacy purposes, to allow our employees to remain close to what inspires them.

# Our 2018 Accomplishments







#### **APPOINTMENTS**

Elsy Boglioli Named as Chief Operating Officer

March 13, 2018

CAR-T Pioneer Dr. Stephan A. Grupp to Join Cellectis Clinical Advisory Board September 19, 2018

Cellectis Appoints Bill Monteith as Senior Vice President U.S. Manufacturing

December 10, 2018







#### RESEARCH & CLINICAL DEVELOPMENT NEWS

Two Issued U.S. Patents Granted to Cellectis for CRISPR Use in T-Cells

February 13, 2018

Servier and Pfizer Announce Results of UCART19 First-in-Human Trials to Be Presented at the 44<sup>th</sup> EBMT (European Society for Blood and Marrow Transplantation) Annual Meeting

March 8, 2018

Cellectis and Allogene Therapeutics Intend to Continue Strategic Cancer Immunotherapy Collaboration to Accelerate Development and Commercialization of Allogeneic Off-the-Shelf CAR-T Therapies April 3, 2018 Assets Purchase Agreement for Pfizer's Allogeneic CAR-T Immuno-oncology Portfolio April 9, 2018

**Allogene Therapeutics Completes** 

Harvard's Wyss Institute Partners with Cellectis to Recode the Human Genome May 1, 2018

Approval of UCART123 Amendment in AML to Accelerate Clinical Development

May 22, 2018

FDA Grants Cellectis IND Approval for UCART22 in B-ALL

June 4, 2018

Cellectis Publishes Novel Methods to Improve the Clinical Use of Chimeric Antigen Receptor T-Cell Therapy in Scientific Reports

June 12, 2018

Cellectis Announces FDA Clearance of the IND for UCARTCSI, the First Allogeneic CAR-T to Treat Multiple Myeloma Patients

April 1, 2019



#### **FINANCE**

Cellectis Announces Closing of Following-On Offering

April 10, 2018





# Commitment to a Cure



Over 20 years ago, if you were told that you had a type of blood cancer, the options that oncologists had to choose from were extremely limited. As time has progressed, so has technology and the overall survival of people living with these diseases. One of the main technologies that has come to the forefront is gene editing.

In today's society, the FDA has granted marketing approvals for 2 autologous CAR-T therapies, which focus on leveraging a patient's own T-cells to create these treatments. However, patients have experienced serious limitations with these therapies, including high pricing and limited market access, highlighting the need to personalize medicine on a larger scale.

Our leading immuno-oncology product candidates, which we refer to as UCARTs, are all allogeneic CAR T-cell product candidates engineered to be used for treating the largest number of patients with a particular cancer type. UCARTs are off-the-shelf therapeutic product candidates, which means they are derived from healthy, pre-existing donor cells and not from the patient. UCARTs are our first therapeutic product candidates line that we are developing with our geneediting platform to address unmet medical needs in oncology.

We are committed to patients, and are working to ensure that our UCART product candidates will have the following benefits:



#### **Broad availability**

Making our UCART products truly off-the-shelf for patients will always be at the center of our ambition. By using cells from healthy donors and utilizing gene editing to make a therapy accepted by all patients, our ambition is to make these treatments available globally to any patient in need.

We are also working to target different therapeutic areas using our gene-editing technology, in hopes that we can expand our clinical trials and provide allogeneic therapies to more people living with cancer.

#### **Cost-effectiveness**

By removing the need for personalized manufacturing which autologous therapies are based on, allogeneic, off-the-shelf technology would make CAR-T therapy cost-effective. There are also lower logistical complexities and associated costs, as allogeneic products can be shipped within a few days worldwide, not only making it more affordable for patients, but also available faster.

#### **Novel features**

We remain committed to staying at the forefront of innovation and technological advancements. We take pride in the fact that we are consistently improving our technology to be even more specified, safe and controlled, to ensure that physicians can regulate the treatment at all times.

#### Compatibility

We are constantly taking into consideration the current standards of cancer care to ensure that our product candidates are designed to make sense for both patients and their prescribing oncologist. Better yet, we seek to address these standards of care head-on in hopes of improving the quality of



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life of those living with the disease. In early 2019, we published a scientific article\* that identifies and addresses a key pathway that plays a role in one of the major side effects of people who have received CAR-T therapy - cytokine release syndrome.

#### Consistency

Cellectis is developing immuno-oncology product candidates that are designed for optimal dosage, while reducing batch-to-batch variability. We are building two manufacturing facilities in France and the United States, so that we can further control our manufacturing process to ensure patients will receive the highest quality treatments, when approved.

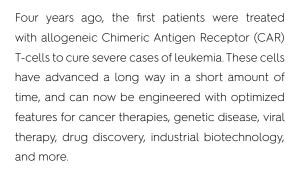


(\*) Granulocyte-macrophage colony-stimulating factor inactivation in CAR T-Cells prevents monocyte-dependent release of key cytokine release syndrome mediators, Mohit Sachdeva et al., Journal of Biological Chemistry

## Our Core Asset: **Gene Editina**

We believe gene editing will completely reshape molecular medicine within the next decade. Being a gene-editing company at our core, we've worked for almost 20 years in the space, benchmarking all the emerging technologies. We focus on our proprietary TALEN® gene editing technology because of its high precision, specificity and efficiency to edit a DNA sequences within a living cell.

Just as you would cut and paste with scissors and glue, or edit text by adding, removing, or replacing words, genome editing is an approach in which the physical composition of DNA is directly changed by adding, replacing, or removing DNA bases. As gene editing goes to the core of the cell, this unlocks the potential to treat people by curing the roots of their diseases instead of merely treating symptoms. As we continue to rethink the way diseases are treated over time, we are excited by the possibilities that offers gene editing and what it could mean for the future of medicine – for patients, doctors and the cancer treatment landscape at large.





Today, the use of gene editing isn't only applied to make deletions, but rather it is also being used to add advantageous attributes to the cells.

Up until recently, nuclease-based gene editing was primarily thought of as a means to remove functions from a cell through gene knock-out Although, as Cellectis' knowledge and understanding of gene editing has continued to progress, we have also developed novel applications for this technology. The first years of gene therapy have consisted in inserting at random positions therapeutic genes in to the DNA of target cells, with little control over how much and where DNA is inserted. Through gene editing, we are able to circumvent the issues of existing therapies and actually modify the cells much less extensively. Through technological advances in gene editing and also in the analytical domain (such as sequencing), we push the current limits to finely manipulate and control the outcomes of a desired genetic modification. Therefore, today, the use of gene editing isn't only applied to make deletions, but rather it is also being used to add advantageous attributes to the cells. Cellectis is also using TALEN® to control their on and off functions and essentially hijack the cells normal processes to allow it to make the decisions we want it to more naturally.

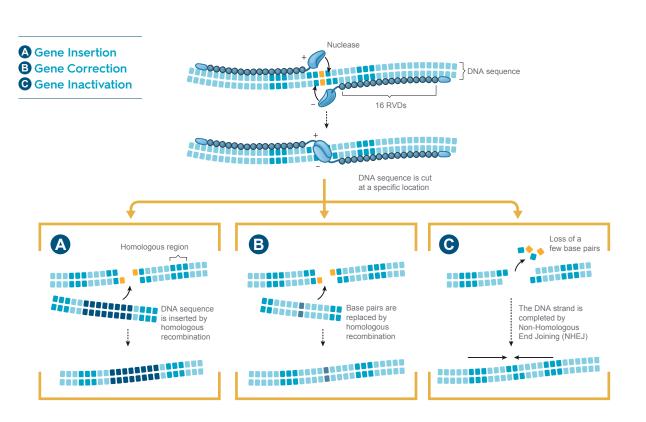
Certain genetic diseases would be difficult to treat without gene editing, but there is more potential that has yet to be revealed for gene-editing applications beyond the obvious. As such, in 2018 we began a project in partnership with Harvard called the Genome Write Project, in hopes of understanding how we can rewrite a cell's code and edit its genes on a global level, instead of the local level in which companies work on now. This project will aim to help us more profoundly understand the genome, and hopefully expose the full potential in which we can use it

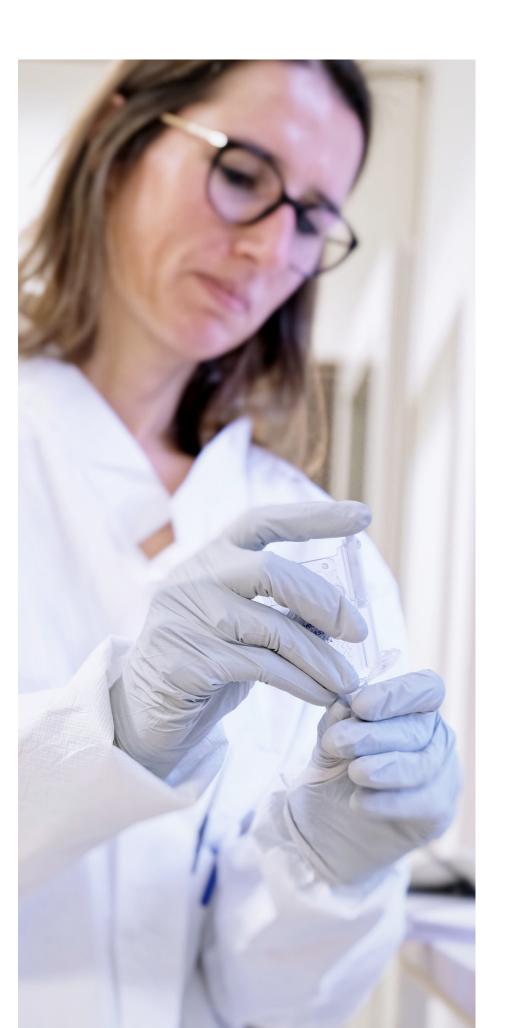
#### **Gene-edited CAR T-cells: how it works**

The immune system protects the human body from any external factors that might cause it harm, such as the flu that could cause you to get sick. The success of the immune system depends on its ability to discriminate between these external factors or unhealthy cells (non-self) and normal host (self) cells.

Cancer cells thrive, in part, because the immune system treats them as self, even though they sometimes express abnormal antigens. Breaking immune tolerance is an important aspect of most immuno-oncology based therapies because it enables the immune system to recognize and treat tumors, leading to the eradication of tumor cells.

We are using our TALEN® gene-editing platform to develop engineered T-cells that express a Chimeric Antigen Receptor (CAR), that are allogeneic but non-alloreactive, meaning they come from a third party donor but they can be injected in any patient because the gene that recognizes the non-self has been deleted, and that are compatible with specific medical regimens that cancer patients may undergo.





#### **CARs (Chimeric Antigen Receptors)**

Adoptive cell immunotherapies using CARs are one of the most promising approaches to fight cancer today. These approaches capitalize on our capacity to genetically modify immune cells (most often T-lymphocytes) to present at their surface an engineered modular protein, the CAR. This CAR allows the engineered cells to recognize a predefined protein present at the surface of cancer cells and induce the killing of these tumor cells. CARs are constructed by assembling specific domains from different proteins, each of which enables the chimeric molecule to carry out well defined functions. Today, the standard CAR architecture comprises an extracellular domain containing a region that recognizes the targeted tumor antigen and a spacer region that links it to the transmembrane domain (the part of the protein that spans the cellular membrane). This is followed by an intracellular domain, responsible for transmitting an activation signal to the cell upon antigen recognition, causing the CAR-engineered cell to attack and kill the tumor cell. 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 costimulatory receptor proteins that could enhance the 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, aiming to further increase the applicability of adoptive cell therapies. Cellectis has demonstrated that additional functional units, allowing detection, purification and depletion of CAR T-cells at will can be incorporated within the CAR architecture to improve our control of CAR-based therapies.



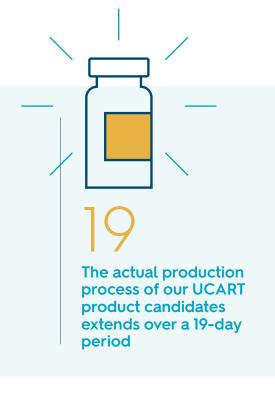
## Manufacturing

Over the past years, Cellectis has developed a sophisticated, proprietary manufacturing process for its UCART product candidates that involves significant financial resources, a series of sophisticated technical steps, and scientifically advanced gene-editing expertise.

In 2018, our manufacturing took a quantum leap towards industrialization when we developed new versions of the processes for production of three of our product candidates, UCART123, UCART22, and UCARTCS1, at a four months interval – a huge accomplishment Moreover, in 2019, we have started building our internal manufacturing capabilities, which will allow us to scale-up capacity, as well as compress timelines.

We are now closer than ever to the development and deployment of a solid, scalable, and industrial manufacturing process for our powerful cellular product candidates. With this strategy, Cellectis aims to manufacture industrial pharmaceutical products that are cost-effective, readily available off-the-shelf to broad patient populations in hospitals without the need for local cell manufacturing facilities, and easily distributed across all geographies.

As the industry leader in gene editing and allogeneic CAR T-cell development, Cellectis currently works with two contract manufacturing organizations (CMOs): CELL for CURE in France and Mol Med in Italy, to produce clinical batches of our UCART product candidates.



CELLforCURE, the largest commercial industrial facility for the production of innovative therapeutic cell therapies in Europe, is producing UCART123, our first wholly-controlled UCART product candidate, to serve the needs of Phase 1 clinical trial in acute myeloid leukemia (AML). In 2019 CELLforCURE was acquired by Novartis Oncology. The agreement we have with CELLforCURE will conclude this year.

Our CMOs produce materials based on specifications that we have first set in the processes developed by our in-house teams. The actual production process of our UCART product candidates extends over a 19-day period and involves multiple steps of cell handling, activating, engineering, amplification, purification as well as the final filling and freezing. It is then followed by 4 to 6 months of extensive quality control on the frozen product candidate in order to release it for use.

The Cellectis process development team is in charge of defining and optimizing each step of this process to ensure that the cells are healthy, the products consistent in quality, and that the whole production process is reliable and fully controlled. That team is also responsible for transferring the defined process to the CMO platform where the product will actually be manufactured.

In parallel, our internal analytical team develops the methods to analyze, measure, and characterize the product or its intermediates during the process. That team also establishes the assays to test the cells as well as safety, identity and potency criteria that the product needs to meet. In cell therapy, it takes strong analytics to release a clinical batch. The analytical development team is also responsible for transferring these assays and test methods to the CMO platform where the product will actually be tested and released.

The Cellectis manufacturing team then defines and sets up a comprehensive pharmaceutical supply chain with qualified contractors and vendors to ensure the procurement or manufacturing of pharmaceutical grade ingredients, raw materials or starting materials

such as cells, DNA, vectors, culture media, etc. That team also sets up and contracts the qualified CMO platform that will perform the final UCART batches' production, testing and release. The manufacturing team also monitors the transfer to clinical sites where the product candidates will be administered to the patients. A constant objective of the Manufacturing team lies in optimizing quality, yield and costs in manufacturing our UCARTs.

The entire production process must adhere to the strict manufacturing quality standards, guidelines, and regulations pertaining to the manufacturing of pharmaceuticals. These regulations are established by various government agencies, including the Food and Drug Administration (FDA) in the U.S. and the European Medicines Agency in Europe (EMA), in order to ensure the safety and efficacy of each batch of manufactured product candidates. These regulations are referred to as current Good Manufacturing Practices (cGMP) in the

U.S., or Good Manufacturing Practices (GMP) in Europe, and they apply to the design, monitoring and control of the manufacturing processes and facilities in order to ensure that they are consistent and controlled.

Unlike autologous CAR-T approaches derived from patient samples, Cellectis' manufacturing process allows us to make therapeutic UCART product candidates from healthy, tested, and qualified donor-derived T-cells. This off-the-shelf approach means lower production costs and, when deployed, accelerates administration and broadens availability of the treatment for patients. In addition, our process — powered by TALEN® and our proprietary PulseAgile electroporation technologies — inactivates genes in a highly efficient and gentle manner that avoids harming T-cells during processing. As a result, we can manufacture quality UCARTs with high yields and in bulk amounts.



This off-the-shelf approach means lower production costs and, when deployed, accelerates administration and broadens availability of the treatment for patients.

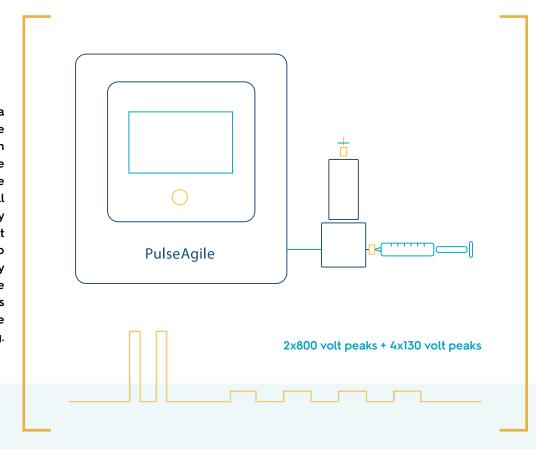
This represents an enormous step forward for cell therapy, as T-cells from one healthy donor and just one manufacturing run of UCART creates hundreds of product doses. As we scale up our manufacturing process and continue to develop Cellectis into an industrial company, we are also driving cell therapy's transition from the field of autologous individual grafts, into a real industry using off-the-shelf, broadly available allogeneic CART-cells pharmaceutical products.

The next step in this evolution will take place when our new 14,000 square-foot in-house SMART plant in Paris, France, begins to produce the first GMP batches of raw and starting material for clinical supply such as DNA and vectors. This is completed with the construction of a second manufacturing plant named IMPACT, located in Raleigh, North Carolina, designed to produce clinical and commercial UCART products. These new manufacturing plants will allow manufacturing

for both clinical supplies and commercial products pursuant to the Food and Drug Administration (FDA) and European Medicines Agency (EMA) guidelines and applicable regulations, and will be fully equipped to support a potential regulatory approval.

Having in-house manufacturing capacity will mark a paradigm shift in Cellectis' development. We are already gaining recognition as an industrial company, allowing us to attract highly experienced senior talent from the industry, such as Bill Monteith in the U.S., who has joined the company as Senior Vice President, U.S. Manufacturing from Hitachi Chemical Advanced Therapeutics Solutions, where he was the Chief Operating Officer and Site General Manager for three manufacturing facilities, and Thierry Ziegler, Ph.D., in Paris, who has joined the company as Head of Production from Sanofi where he was Head of BioPharmaceutical Development in France.

PulseAgile uses a particularly effective combination of high voltage peaks, that are optimized to create transient pores in the cell membrane, followed by lower voltage pulses that help mRNA migrate into the cells. This technology is optimized to preserve high cell viability and is thus suited for large-scale manufacturing.



## Our Products

As the recognized leader in gene editing and inventor of the allogeneic approach, Cellectis has a robust pipeline of first-in-class allogeneic CAR T-cell programs targeting hematological malignancies.

Our immuno-oncology therapeutic product candidates hold great promise for people living with various blood and bone marrow cancers, notably acute myeloid leukemia (AML), B-cell acute lymphoblastic leukemia (B-ALL) and multiple myeloma (MM). Together these diseases affect tens of thousands of patients worldwide each year, with low five-year survival rates.

The goal of our programs is to leverage our leadership in gene editing and allogeneic CAR-T development to make off-the-shelf therapeutic products both cost-effective and broadly available to cancer patients everywhere.

Each UCART product candidate targets a selected tumor antigen and bears specific engineered attributes, such as compatibility with specific medical regimens that cancer patients may undergo. UCART is the first therapeutic product candidate line that we are developing with our gene-editing platform to address unmet medical needs in oncology.

development program between Servier and Allogene, is the most advanced UCART product candidate. In June 2015, it marked a medical first when it was used with a young patient with relapsed or refractory ALL. The American Cancer Society's estimates for ALL in the United States for 2019 (including both children and adults) are about 5,930 new cases and about 1,500 deaths. To date, UCART19 remains the only gene-edited, off-the-shelf product candidate that has been successfully used to treat a patient. Tests continue in both adult and pediatric patients suffering from this cancer in partnership between Allogene Therapeutics, a U.S. clinical-stage biotechnology company which last year acquired the U.S. rights to UCART19, and Servier, which retains exclusive rights for all other countries. In the pooled data presented at the ASH 2018 conference in December, investigators observed a 67% complete remission rate in the overall population and an 82% complete remission rate in patients who received a three-drug lymphodepleting regimen. With these promising results, we hope this product candidate will begin Phase 2 trials this year.

UCART123, our first wholly-controlled product candidate, targets AML, a devastating cancer of the lymphoid line of blood cells that can cause bone marrow failure and death. In 2018, we received approval from the Food and Drug Administration (FDA) to accelerate development of our Phase 1 clinical trial to treat patients with AML. In the U.S. alone, there are 21,450 new cases expected for 2019, with 10,920 estimated deaths. Weill Cornell Medical College in New York City and the MD Anderson Cancer Center in Houston are the investigational sites performing this clinical trial.



malignancies, has proven to be highly efficient at eradicating tumors in vivo. Last June, the FDA approved our Investigational New Drug (IND) application to initiate a Phase 1 clinical trial for UCART22, our second wholly-controlled TALEN® gene-edited product candidate, for the treatment of B-cell acute lymphoblastic leukemia (B-ALL) in adult patients. Approximately 85% of ALL cases involve precursor B-cells.

designed to treat multiple myeloma (MM) offers a totally new treatment approach for this disease, which affects more than 30,000 people each year in the U.S. alone. We expect to begin clinical development in 2019 at MD Anderson, Weill Cornell Medicine and Hackensack Meridian.



Program	Indication	Target	Pre-clinical Phase 1
UCART19*	ALL	CD19	Mar. 2016 CTA Mar. 2017 IND (70A)
UCART123	AML	CD123	Feb. 2017 IND (70A)
UCART22	ALL	CD22	Jun. 2018 IND (5)
ALLO-501*	NHL	CD19	Jan. 2019 IND (50)
UCARTCS1	ММ	CS1	Jan. 2019 IND (1)
ALLO-715**	MM	ВСМА	
UCART22	NHL	CD22	
UCART123	HL	CD123	
UCARTCLL1	AML	CLL1	
ALLO-819**	AML	FLT3	

<sup>\*</sup> UCART19/ALLO-501 is exclusively licensed to Servier and under a joint clinical development program between Servier and Allogene.

Phase 2 / 3

<sup>\*\*</sup> Product candidates exclusively licensed to Allogene

# Transformative Innovation

As Cellectis has always been at the forefront of innovation and technological advancements, implementing disruptive features in our product candidates to meet unmet medical needs is a core aspect of our mission. As a pioneering gene-editing company at its core, we focus our know-how on elaborating immunotherapies using our expertise and TALEN® gene-editing platform to develop off-the-shelf gene-edited T-cells that express Chimeric Antigen Receptors (CARs) to target and destroy cancer cells. Cellectis is currently developing a pipeline of CARs targeting antigens present on cells from various types of cancer.

B-Acute Lymphoblastic Leukemia

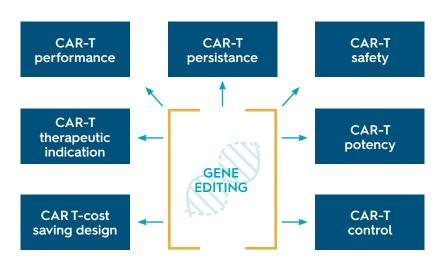
Acute Myeloid Leukemia Acute Lymphoblastic Leukemia

Hodgkin Lymphoma



Non Hodgkin Lymphoma

Using gene-editing technology, we are able to precisely and efficiently insert, replace, correct and/or inactivate genes at will. Cellectis is working on improving and expanding the potential of its allogeneic off-the-shelf UCART product candidates through gene editing by adding innovative features that will ultimately benefit patient treatments. Our goal is to improve engineered CAR T-cells' functionalities through the molecular engineering of the CAR architecture (proprietary pharmacologically controllable CAR or proprietary CAR-integrated suicide switch for safety), but also through multiplex gene editing thanks to our capacity to rapidly design optimal TALEN® combinations.





# Partnerships: Working Together to Build More



One of Cellectis' strengths is the solid partnerships we've forged with industry leaders who share our goal of developing allogeneic cancer therapies that will benefit patients around the world.

For development and commercialization of our UCART product candidates, we have joined forces with Servier, a leading French independent pharmaceutical company, and Allogene Therapeutics, a clinical-stage biotechnology company focusing on the development of allogeneic CAR-T therapies for cancer.

Cellectis and Servier are collaborating on five targets, including **UCART19**, our innovative cellular therapy candidate against lymphoid malignancies, with ongoing pediatric and adult trials sponsored by Servier in the UK, Belgium and France. Our highly complementary competencies and know-how give our teams the best chances of providing patients worldwide with a new generation of cancer treatments they need.

In April 2018, Allogene and Pfizer entered into an asset contribution agreement, pursuant to which Allogene purchased Pfizer's portfolio of assets related to allogeneic CAR T-cell therapy. Following this asset contribution agreement, effective as of April 6, 2018, Allogene purchased Pfizer's portfolio of assets related to allogeneic CART-cell therapy, including the Collaboration and License Agreement we signed with Pfizer in June 2014. Thus, Allogene acquired the exclusive rights to the 15 UCART cell therapy initially granted by Cellectis to

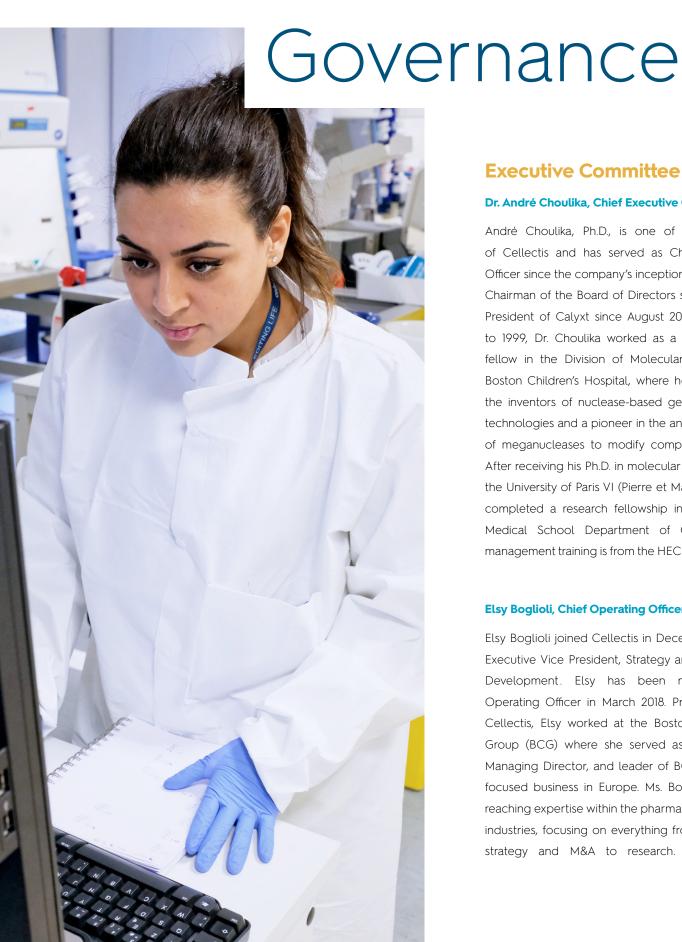
Pfizer, as well as the Servier's U.S. rights to **UCARTI9**. Founded and led by former Kite Pharma executives who brought clinical development acumen in cell therapy, Allogene is helping us to accelerate the development of allogeneic cell therapies for blood cancers as well as solid tumors.

For ongoing clinical trials, we have forged close relations with Weill Cornell Medical College in New York City and the MD Anderson Cancer Center in Houston, where we are developing UCART123, our first wholly-controlled product candidate that targets acute myeloid leukemia (AML), a devastating cancer of the lymphoid line of blood cells that can cause bone marrow failure and death. The clinical trial for AML is coordinated by principal investigator Professor Gail J. Roboz, M.D., Professor of Medicine at Weill Cornell Medicine and Director of the Clinical and Translational Leukemia Programs at Weill Cornell Medicine and NewYork-Presbyterian Hospital. The UCART123 clinical program at MD Anderson is led by Dr. Naveen Pemmaraju, M.D., Associate Professor, Dr. Marina Konopleva, Professor, and Professor Hagop Kantarjian, M.D., Department Chair, Department of Leukemia, Division of Cancer Medecine.

Cellectis and MD Anderson Cancer Center are also developing **UCART22** for B-cell acute lymphoblastic leukemia (B-ALL) in adults. The clinical trial, sponsored by Cellectis, is led by Dr. Nitin Jain, Assistant Professor, and Prof. Hagop Kantarjian, Chairman in the Department of Leukemia and University Chair in Cancer Medicine at The University of Texas MD Anderson Cancer Center in Houston.

On the manufacturing side, Cellectis forged longstanding partnerships with two contract manufacturing organizations (CMOs): CELLforCURE in France, which is now acquired by Novartis, and MolMed in Italy.





#### **Executive Committee**

#### Dr. André Choulika, Chief Executive Officer

André Choulika, Ph.D., is one of the founders of Cellectis and has served as Chief Executive Officer since the company's inception in 1999. He is Chairman of the Board of Directors since 2011 and President of Calyxt since August 2010. From 1997 to 1999, Dr. Choulika worked as a post-doctoral fellow in the Division of Molecular Medicine at Boston Children's Hospital, where he was one of the inventors of nuclease-based genome editing technologies and a pioneer in the analysis and use of meganucleases to modify complex genomes. After receiving his Ph.D. 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. His management training is from the HEC (Challenge +).

#### **Elsy Boglioli, Chief Operating Officer**

Elsy Boglioli joined Cellectis in December 2017 as Executive Vice President, Strategy and Corporate Development. Elsy has been named Chief Operating Officer in March 2018. Prior to joining Cellectis, Elsy worked at the Boston Consulting Group (BCG) where she served as Partner and Managing Director, and leader of BCG's biotechfocused business in Europe. Ms. Boglioli has farreaching expertise within the pharma and medtech industries, focusing on everything from corporate strategy and M&A to research. Ms. Boglioli







Dr. Philippe Duchateau



Dutang



Reynier



Dr. David Sourdive



graduated from Ecole Polytechnique in Paris, France and holds a master's degree in economy and management from Pompeu Fabra University in Barcelona, Spain.

Boglioli

#### Dr. Philippe Duchateau, Chief Scientific Officer

Philippe Duchateau, Ph.D., joined Cellectis in 2001 to pioneer the field of gene editing and has served as Chief Scientific Officer since 2012. After receiving his Ph.D. in 1993 in biochemistry and molecular biology at the Institut Pasteur (Lille, France), he completed a research fellowship from 1993 to 2001 at the University of California, San Francisco, within the Cardiovascular Research Institute. Dr. Duchateau has led Cellectis' Research department since 2004.

#### **Eric Dutang, Chief Financial Officer**

Eric Dutang, Certified Public Accountant in France, joined Cellectis as Deputy Chief Financial Officer in May 2015. Eric began his career as a financial auditor with KPMG, first in Paris for five years and then in New York for two years. He worked for publiclytraded companies in France and the U.S. including Vivendi, Veolia Environnement, and Cablevision. He then became a member of the transactions and advisory teams in Paris for seven years where he carried out acquisitions/disposals for both publiclytraded companies and private equity funds. Eric holds a Master of Finance and Executive MBA from HEC Paris (France)/Babson Massachusetts (USA).

#### **Stephan Reynier, Chief Regulatory** and Compliance Officer

Stephan Reynier, M.Sc., joined Cellectis in April 2011. He has served as Chief Regulatory and Compliance Officer since 2014 with the responbilities of ensuring a speedy and successful development of the UCART product family by establishing close interactions with regulatory agencies such as the EMA and the FDA, while securing compliance to applicable regulations, regulatory guidelines and quality assurance standards. From his previous positions as Senior Director at Voisin Consulting Life Sciences and European Associate Director of Medical Affairs at Gilead sciences, Mr. Reynier has extensive experience in the design and implementation of regulatory strategies for the development of drugs and biologics, with a strong focus on cell and gene therapy. Mr. Reynier graduated as Agro-Engineer in France and received a Master of Science in Chemical Engineering from the University of Toronto, Canada

#### Dr. David Sourdive, Executive Vice **President Technical Operations**

David Sourdive, Ph.D., is a co-founder of Cellectis and joined the Board of Directors in 2000. Dr. Sourdive holds the position of Executive Vice President, Technical Operations, with the mission to develop the Company's industrial and technological basis as well as to deploy its operations in the pharmaceutical arena. Dr. Sourdive combines a strong scientific expertise

with experience in managing industrial programs, bringing innovative technologies to industrial fruition. He served as Executive Vice President, Corporate Development, from 2008 to 2016. In addition to his role at Cellectis, David Sourdive graduated from École Polytechnique, received his Ph.D. in molecular virology at Institut Pasteur, and completed a research fellowship in the Emory University Department of Microbiology and Immunology. His management training is from the HEC (Challenge +) and his decade-long experience in industrial program management was acquired at the French Department of Defense (DGA) prior to Cellectis' inception.

#### Marie-Bleuenn Terrier, General Counsel

Marie-Bleuenn Terrier joined Cellectis as Legal Counsel in 2008, and was appointed General Counsel in 2013. Prior to joining Cellectis, she worked as Legal Counsel for Pfizer from 2004 to 2006, and for Boehringer Ingelheim from 2006 to 2008. Marie-Bleuenn Terrier has served as secretary of the Board of Directors of Cellectis since 2015. She holds a Master's degree in Law from the Panthéon La Sorbonne University in Paris.

#### **Board of Directors**

#### Dr André Choulika, Ph.D.

Chairman of the Board of Directors and CEO

#### **Laurent Arthaud**

Independent Director\*

#### **Pierre Bastid**

Independent Director\*

#### Dr. Rainer Boehm, M.D.

Independent Director\*

#### **Alain Godard**

Independent Director\*

#### Hervé Hoppenot

Independent Director\*

#### Dr. Annick Schwebig, M.D.

Independent Director\*

#### Dr. David Sourdive, Ph.D.

Executive Vice President Technical Operations

\*Independent Director according to Nasdaq rules

### **Committee of the Board of Directors**

#### **Audit and Finance Committee**

Laurent Arthaud, Independent Director

Pierre Bastid, Independent Director Compensation Committee

Alain Godard, Independent Director

Dr. Annick Schwebig, Independent Director

#### **Clinical Advisory Board**

**Prof. Catherine Bollard,** Director, Center for Cancer and Immunology Research, Children's Research Institute, Children's National Health System and Professor of Pediatrics and Immunology, The George Washington University, Washington DC

**Prof. Hervé Dombret**, Head of the Leukemia Unit at the Hôpital Saint Louis, Paris, and Director of Clinical Research in the Hematology, Immunology and Transplantation Unit, University of Paris Diderot, Paris, France

**Dr. Stephan Grupp,** Chief of the Cellular Therapy and Transplant Section, Director of the Cancer Immunotherapy Program, and Director of Translational Research in the Center for Childhood Cancer Research at the Children's Hospital of Philadelphia

**Prof. Ola Landgren**, Chief of Myeloma Service at Memorial Sloan Kettering Cancer Center, New York, NY

**Dr. Marcela Maus,** Director of Cellular Immunotherapy at the Massachusetts General Hospital, Boston, MA

**Prof. Ghulam J. Mufti,** Professor of Hematooncology and Head of Department, King's College Hospital, Department of Hematological Medicine, London, UK

**Prof. Dietger Niederwieser,** Professor of Medicine, Head of the Division of Hematology and Medical Oncology at the University of Leipzig, Germany

**Prof. Kanti Rai,** Professor of Medicine and Molecular Medicine, Hofstra Northwell School of Medicine, Hempstead, NY

**Prof. Catherine Thieblemont,** Professor of Hematology in the Paris VII- University, France and Head of the Hemato-Oncology Unit of St- Louis Hospital, Paris, France

**Prof. Koen van Besien,** Director of the Stem Cell Transplant Program and Professor of Medicine at Weill Cornell Medical College, New York, NY

#### **External Auditors**

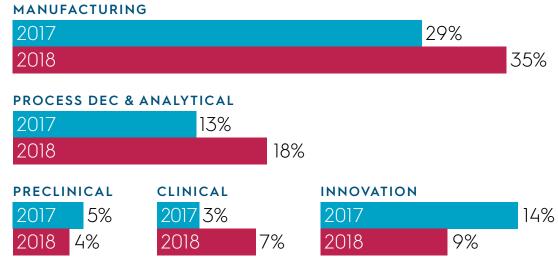
#### **Statutory Auditor**

Ernst & Young

JMH Conseil



#### Significant R&D expenditures



#### **Composition of capital**

as of December the 31st, 2018

INSTITUTIONAL INVESTOR FRANCE	4,17%	1,768,100
FREE FLOAT OTHER		
	16,01%	6,792,339
INDUSTRIAL PARTNERS (INCL PFIZER)		
	6,57%	2 ,789,252
INSTITUTIONAL INVESTORS U.S.		
	31,14%	13,211,764
INSTITUTIONAL INVESTORS EUROPE & OTHER		
	13,46%	5,711,300
FREE FLOAT FRANCE		
	9,23%	3,914,802
COMPANY RELATED HOLDER		
	19,43%	8,242,512
TOTAL		
	100%	42.430.069

## Balance sheet - Assets

STATEMENTS OF CONSOLIDATED FINANCIAL POSITION - \$ in thousands, except per share data

December 31, 2017	December 31, 2018
1,431	1,268
7,226	10,041
1,004	1,891
9,661	13,199
250	275
2,753	2,971
9,524	17,173
13,713	15,333
296,982	451,889
323,221	487,641
332,882	500,840
	1,431 7,226 1,004 9,661 250 2,753 9,524 13,713 296,982 323,221

# Balance sheet - Equity and Liabilities

	December 31, 2017	December 31, 2018
LIABILITIES		
Shareholders' equity		
Share capital	2,367	2,765
Premiums related to the share capital	614,037	828,525
Treasury share reserve	(297)	0
Currency translation adjustment	1,834	(16,668)
Retained earnings	(253,702)	(326,628)
Net income (loss)	(99,368)	(78,693)
Total shareholders' equity - Group Share	264,872	409,301
Non-controlling interests	19,113	40,970
Total shareholders' equity	283,985	450,272
Non-current liabilities		
Non-current financial liabilities	13	1,018
Non-current provisions	3,430	2,681
Total non-current liabilities	3,443	3 699
Current liabilities		
Current financial liabilities	21	333
Trade payables	9,460	15,883
Deferred revenues and deferred income	27,975	20,754
Current provisions	1,427	1,530
Other current liabilities	6,570	8,369
Total current liabilities	45,453	46,869
TOTAL LIABILITIES AND SHAREHOLDERS' EQUITY	332,882	500,840

## Income statement

STATEMENTS OF CONSOLIDATED OPERATIONS
Full year — \$ in thousands, except per share amounts

	For the year ended December 31, 2017	For the year ended December 31, 2018
Revenues and other income		
Revenues	25,188	12,731
Other income	8,528	8,528
Total revenues and other income	33,715	21,432
Operating expenses		
Royalty expenses	(2,620)	(2,739)
Research and development expenses	(79,227)	(76,567)
Selling, general and administrative expenses	(44,750)	(47,248)
Other operating income (expenses)	232	31
Total operating expenses	(126,366)	(126,523)
Operating income (loss)	(92,650)	(105,091)
Financial gain (loss)	(11,032)	16,758
Net income (loss)	(103,683)	(88,333)
Attributable to shareholders of Cellectis	(99,368)	(78,693)
Attributable to non-controlling interests	(4,315)	(9 640)
Basic net income (loss) attributable to shareholders of Cellectis per share (\$/share)	(2,78)	(1,95)
Diluted net income (loss) attributable to shareholders of Cellectis per share (\$/share)	(2,78)	(1,95)

## Cash flow statement

STATEMENTS OF CONSOLIDATED CASH FLOWS
For the year ended December 31, 2018 — \$ in thousands

	For the year ended December 31, 2017	For the year ended December 31, 2018
Cash flows from operating activities		
Net loss for the period	(103,683)	(88,333)
Reconciliation of net loss and of the cash provided by (used in) operating activities		
Adjustments for		
Amortization and depreciation	3,371	2,377
Net loss (income) on disposals	40	20
Net financial loss (gain)	11,032	(16,759)
Expenses related to share-based payments	50,418	37,218
Provisions	2,908	(468)
Other non cash items	2	_
Interest (paid) / received	1,371	6,905
Operating cash flows before change in working capital	(34,540)	(59,040)
Decrease (increase) in inventories	(109)	(37)
Decrease (increase) in trade receivables and other current assets	(549)	(3,696)
Decrease (increase) in subsidies receivables	305	(8,257)
(Decrease) increase in trade payables and other current liabilities	(335)	9,374
(Decrease) increase in deferred income	(17,099)	(6,480)
Change in working capital	(17,787)	(9,096)
Net cash flows provided by (used in) operating activities	(52,327)	(68,137)
Cash flows from investment activities		
Proceeds from disposal of property, plant and equipment	7,164	1,262
Acquisition of intangible assets	(273)	(171)
Acquisition of property, plant and equipment	(2,383)	(4,715)
Net change in non-current financial assets	(125)	221
Sale (Acquisition) of current financial assets	(2,598)	39,025
Net cash flows provided by (used in) investing activities	1,784	35,623
Cash flows from financing activities		
Increase in share capital net of transaction costs	2,930	186,382
Shares of Calyxt issued to third parties	38,257	49,942
Decrease in borrowings	(41)	(127)
Treasury shares	120	297
Net cash flows provided by financing activities	41,266	236,494
(Decrease) increase in cash	(9,277)	203,981
Cash and cash equivalents at the beginning of the year	254,568	256,380
Effect of exchange rate changes on cash	11,089	(8,860)
Cash and cash equivalents at the end of the period	256,380	451,501

#### DETAILS OF KEY PERFORMANCE INDICATORS BY REPORTABLE SEGMENTS Full year — \$ in thousands

For the year ended December 31, 2017

For the year ended December 31, 2018

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	Plants	Therapeutics	Total reportable segments	Plants	Therapeutics	Total reportable segments
External revenues	508	24,680	25,188	236	12,495	12,731
External other income	239	8,290	8,528	178	8,523	8,701
External revenues and other income	747	32,969	33,715	414	21,018	21,432
Royalty expenses	(390)	(2,230)	(2,620)	(595)	(2,144)	(2,739)
Research and development expenses	(6,057)	(73,170)	(79,227)	(8,638)	(67,929)	(76,567)
Selling, general and administrative expenses	(13,143)	(31,607)	(44,750)	(21,067)	(26,180)	(47,248)
Other operating income and expenses	6	225	232	(50)	81	31
Total operating expenses	(19,584)	(106,782)	(126,366)	(30,351)	(96,172)	(126,523)
Operating income (loss) before tax	(18,837)	(73,813)	(92,650)	(29,937)	(75,154)	(105,091)
Financial gain (loss)	0	(11,032)	(11,032)	1,420	15,339	16,758
Net income (loss)	(18,837)	(84,846)	(103,683)	(28,517)	(59,816)	(88,333)
Non controlling interests	4,315	-	4,315	9,640	-	9,640
Net income (loss) attributable to shareholders of Cellectis	(14,522)	(84,846)	(99,368)	(18,877)	(59,816)	(78,693)
R&D non-cash stock-based expense attributable to shareholder of Cellectis	967	22,623	23,590	838	16,852	17,689
SG&A non-cash stock-based expense attributable to shareholder of Cellectis	4,990	20,345	25,335	5,218	11,655	16,873
Adjustment of share-based compensation attributable to shareholders of Cellectis	5,957	42,968	48,925	6,056	28,507	34,563
Adjusted net income (loss) attributable to shareholders of Cellectis	(8,565)	(41,877)	(50,443)	(12,821)	(31,309)	(44,130)
Net cash used in operating activities	(12,785)	(39,542)	(52,327)	(20,252)	(47,885)	(68,137)

\*Cellectis

Cellectis 8 rue de la Croix Jarry - 75013 Paris - France 430 East 29th Street - New York, NY 10016 - USA e-mail: media@cellectis.com website: www.cellectis.com

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#### Disclaimer

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## EDITING LIFE

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