

Improving life through genome engineering

April, 30 2013

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Contents

- Introduction: biotech environment and Collectis' positioning
- 2012 highlights and changes to the Group's organization
- Three key areas for development
- Financials
- Outlook

Biotech industry

The strong development of BIOTECHNOLOGIES today is underpinned by a range of scientific knowledge and expertise:

- I. Access to genomic information
- II. Genome engineering
- III. Metabolic engineering
- IV. Protein engineering
- V. Large-scale DNA synthesis
- VI. Cellular engineering



- Reading
- Writing
- Composing
- Creating
- Imprinting
- Modeling

Those who are able to master all or part of these foundations of modern biology now have outstanding potential for development and value creation.

Group's strategic positioning

Collectis is a biotechnology group, a market leader in Europe

- * developing totally new treatments for diabetes and cancer,*
- * offering groundbreaking solutions for researchers worldwide,*
- * designing particularly innovative seeds.*

Collectis in brief

- Main development milestones:
 - ✓ 1999: Creation
 - ✓ 2005: Development of an industrial nuclease production technique
 - ✓ 2007: IPO, acquisition of technologies and creation of subsidiaries (2008-2010)
 - ✓ 2011: Acquisition of Cellartis

- 2012 revenues: €21 M

- Headcount: 230 staff

- Locations: France, Sweden and USA

- Range of technologies at the forefront of global R&D:
 - ✓ Protein and genome engineering
 - ✓ Cellular engineering
 - ✓ New area for development: metabolic engineering

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Changes to Group organization in 2012

- **Post-acquisition Group organization**

- ✓ Integration of Cellartis
- ✓ Support function rationalization / optimization
- ✓ Increase in marketing investments
- ✓ Focus on a select number of high-potential projects
- ✓ Organization of activities around 3 main divisions
- ✓ Strengthening of the therapeutics division

- **Strengthening of the shareholding structure**

- ✓ Redemption of the convertible bonds subscribed for in November 2011 into shares, for €50 M

Current structure: 3 main business units



- Management functions
- Upstream research
- Support functions

Tools and services business unit

Research tools
Production tools
Service offering



**PROFITABILITY IN
THE SHORT-TERM**

Plants business unit

Development of features
Strategic partnerships



**PROFITABILITY IN
THE MEDIUM-TERM**

Therapeutics business unit

Cancer: leukemia
Regenerative medicine: diabetes



**PROFITABILITY IN
THE LONG-TERM**

A strong management team

- André Chouluka, Chairman and CEO
- David Sourdivé, Executive Vice President Corporate Development
- Mathieu Simon, Senior Vice President, CEO of Collectis Therapeutics
- Pierre Schwich, Chief Financial Officer
- Philippe Valachs, Company Secretary
- Xavier Champavère, Deputy CEO of Collectis bioresearch
- Jean-Charles Epinat, Deputy CEO of Collectis bioresearch
- Luc Mathis, CEO of Collectis Plant Sciences
- Philippe Duchateau, Chief Scientific Officer

A strong governance

- André Choulika
- David Sourdivé
- Pierre Bastid
- Laurent Arthaud
- Annick Schwebig
- Alain Godard
- Kaminvest

- Institut Pasteur (observer)

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Tools and services Business Unit

Recognized expertise across the value chain

From genotype to phenotype and biological tests

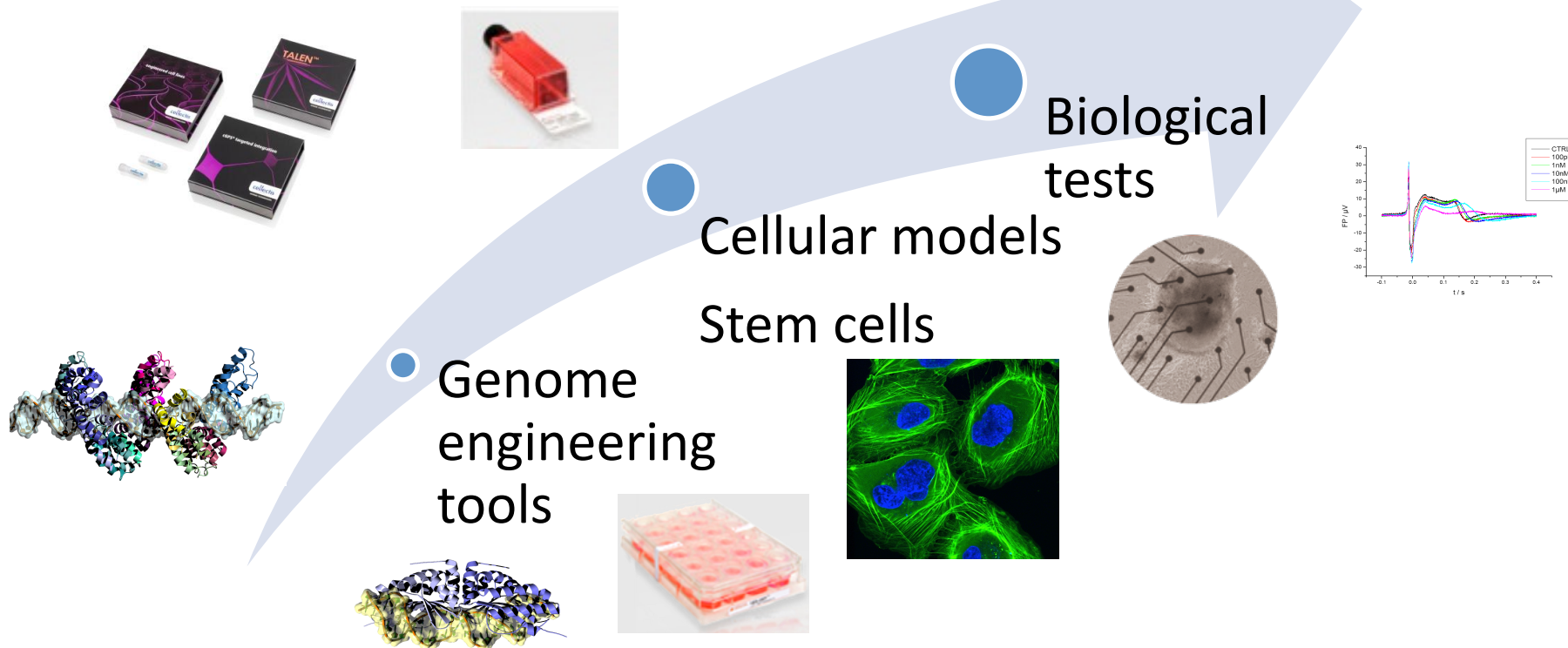
Engineering tools, Cells, Bioassays
Products, Services, Ad Hoc Programs



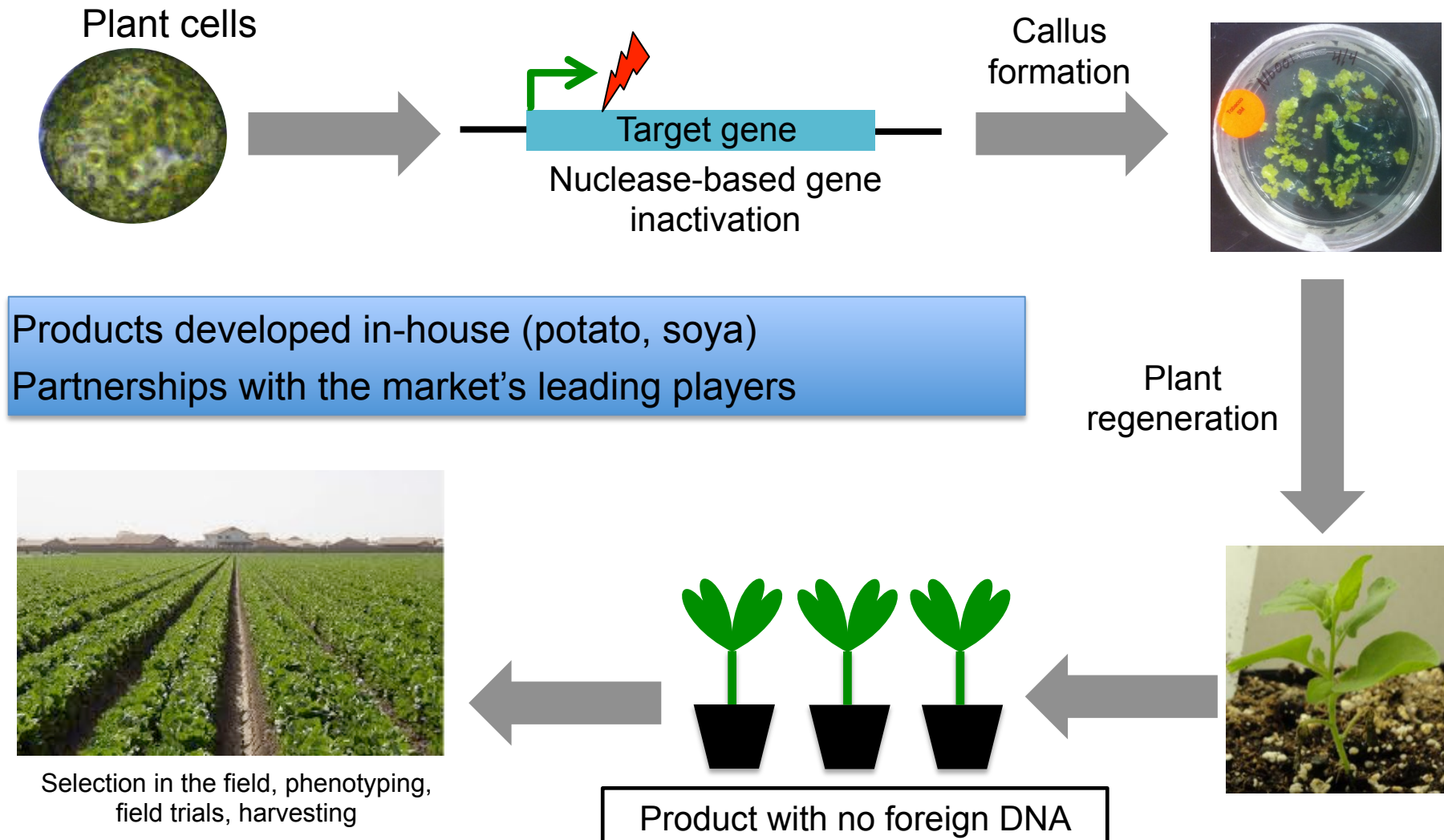
Industrial integration



Growing value creation



Plants Business Unit: dedicated platform



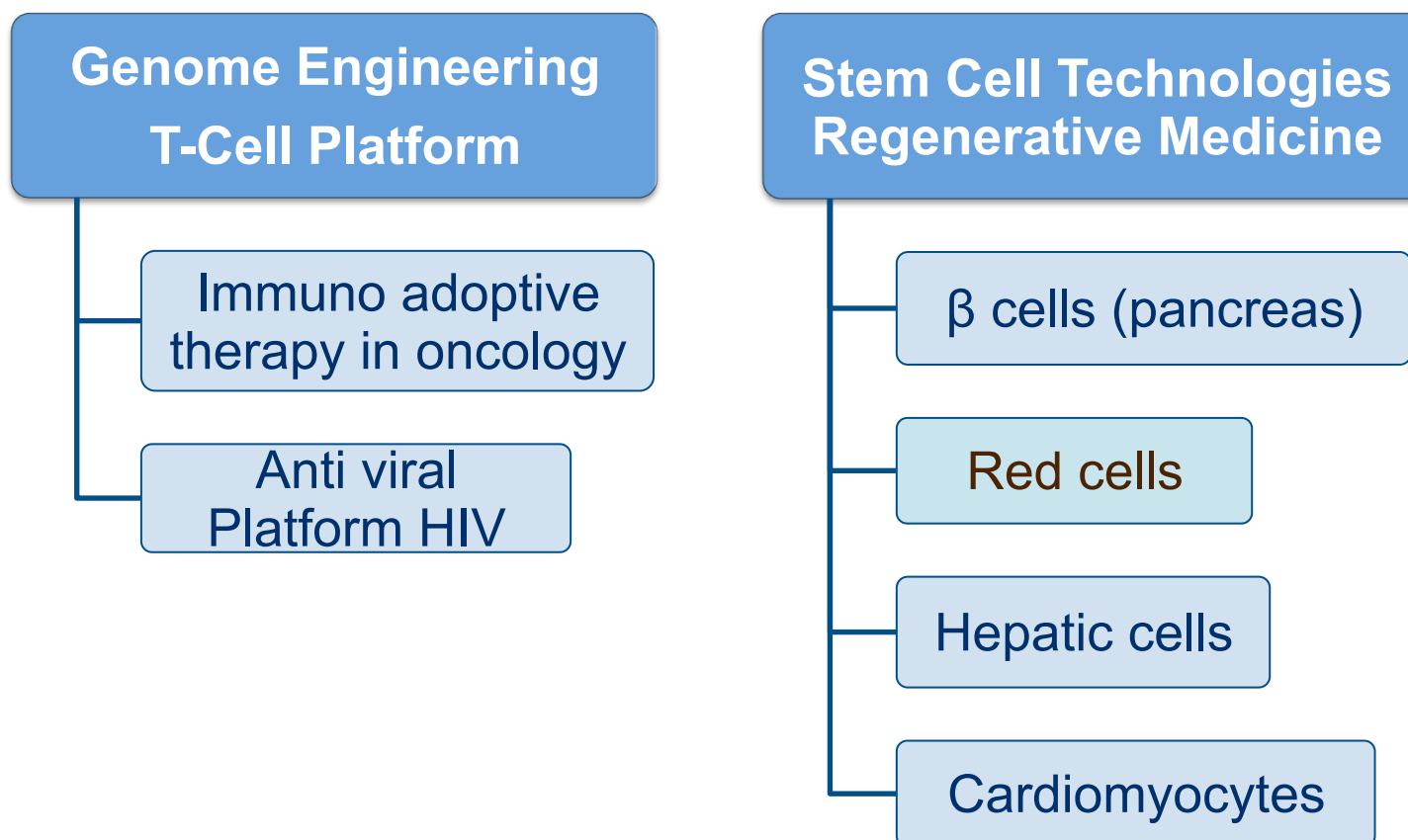
Business Unit: Therapeutic

- Started in 2008.
- 20 dedicated people.
- Key people:
 - ✓ Dr. Mathieu Simon M.D., Managing Director, CEO (Pierre Fabre, Wyeth Pharmaceuticals, USA).
 - ✓ Dr. Andy Scharenberg M.D., CSO (Children Hospital, Seattle).
 - ✓ Dr. Julianne Smith Ph.D., Head of T-cell engineered platform, (University of Columbia, NYC).
 - ✓ Dr. Petter Bjorquist Ph.D., VP Head of Regenerative Medecine (Göteborg, Sweden).
- 2 sites:
 - ✓ Paris, France (T-cell platform).
 - ✓ Göteborg, Sweden (Regenerative Medecine).

Today a discovery unit:
tomorrow a biopharmaceutical company.

Collectis core technologies

Acquisition of Cellartis AB
(Sweden)



An innovative risk avoiding and cost-conscious development model

- Early partnerships to maximize knowledge transfer, clinical development and regulatory activities while minimizing cost:
 - ✓ Collectis / Novo Nordisk alliance in diabetes.
 - ✓ Collectis / EFS in red cell transfusion.
 - ✓ Collectis / University College of London (UCL) in oncology.
- CTx client and partner of Collectis for TALEN™, Meganucleases and Cell lines.

Stem cells and cell therapy

Press Release

23 October 2008

Novo Nordisk, Cellartis and Lund University enter into a collaboration to develop insulin-producing cells from stem cells for the treatment of diabetes

Novo Nordisk A/S, a world leader in diabetes care, Cellartis AB, a forefront stem cell biotechnology company, and Lund University Stem Cell Center today signed a collaborative research agreement for the development of insulin-producing cells from human stem cells. The collaboration aims to develop a cell therapy for the treatment of insulin-dependent diabetes and, in the longer term, a cure for diabetes.



LUND UNIVERSITY
Faculty of Medicine



Diabetes, a major public health burden

- 370 million people in 2012, 550 million people by 2030.
- 72.4 billion USD by 2018 (therapeutic devices and drug discovery).
- Novo Nordisk, a solid leader in this field: 27,4% MS in 2011.
- Type 1 diabetes: 10% of diabetic population.
 - ✓ Auto immune disease (2 Mio American diagnosed).
 - ✓ Medium average age: 18 years old.
 - ✓ About 70 000 children aged 14 years are developing T₁ MD per year.

Diabetes, a major public health burden

Insulin replacement is the life saving first line treatment for T₁ MD (2 billion USD in sales). However due to young age of patients development of disease modifying treatment remain a major medical need.

- **Immunological approaches:**

- ✓ AG - specific vaccines
- ✓ CD3 – specific monoclonal antibodies
- ✓ Otelixizumab / Teplizumab

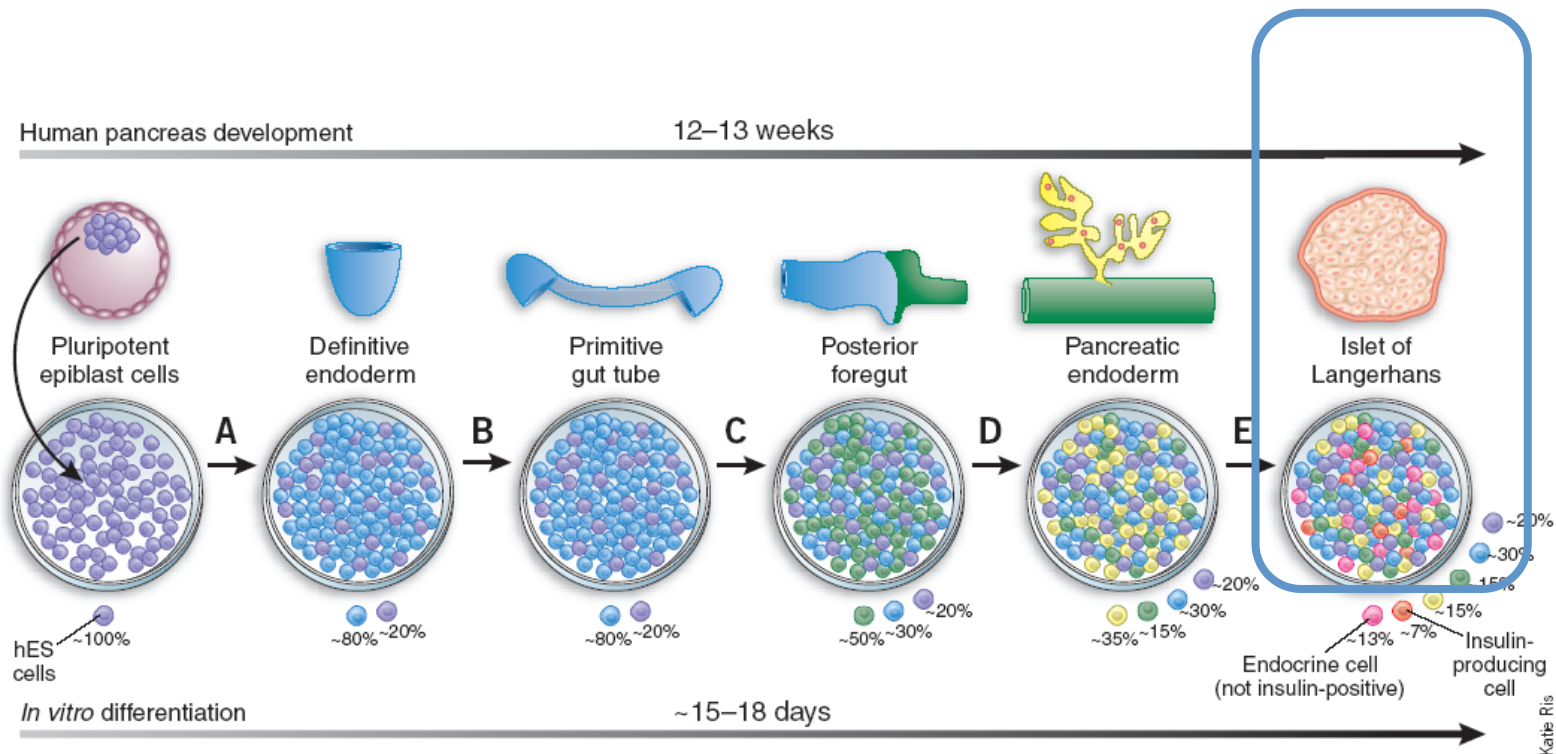
- **Cell therapies / regenerative medicine (10-12 years horizon)**

- ✓ Collectis / Lund / Novo Nordisk
- ✓ ViaCyte (40 Mio USD California Stem cell brand)
- ✓ Betalogics (Johnson & Johnson)

Novo Nordisk / Collectis development plan

- Generation of beta functional cells:
 - ✓ Endocrine progenitors (2012) → Q₁/Q₂ 2013
 - ✓ Beta cells (2013)
- GMP grade hESC lines / compliant with EMA and FDA
 - ✓ Derivation + master cell banks
 - ✓ Working cell banks → Q₂ 2013
 - ✓ Characterization + safety
- Validation of encapsulation method → Q₄ 2013
- VP scaling and GMP production (cells and device) → Q₂ 2014
- POP: cells + device in diabetic pigs → Q₁ 2015
- Clinical development / First in humans → Q₃ 2015

Development of insulin producing β -cells from hES cells



Madsen OD, Serup P Nat. Biotech.2006

Terms of Novo Nordisk / Collectis partnership

- 5-year research collaboration program. Started October 2008 and will continue beyond Oct 2013.
- Total deal value > €100 M plus FTE cost.
- Revenue during 2012: €1.8m including an annual fee of €1m.
- Today 8 FTEs (each €110k). Potentially 5 additional FTEs (each €200k) for the generation of clinical grade stem cell lines.
- Royalty between 6-12% of Net Sales with clauses reducing the royalty to a minimum of either 2.5% or 3.5% of Net Sales.

Terms of Novo Nordisk / Collectis partnership

Milestone	Amount
Milestone 1: Robust protocol for generation of glucose-sensitive insulin-producing beta-cell	EUR 3m
Milestone 2: Establishment of 1st GMP cell line	EUR 1m
Milestone 3: First patient dosed in a Phase I trial	EUR 2m
Milestone 4: First patient dosed in a Phase IIb trial or equivalent clinical proof of concept study	EUR 3m
Milestone 5: First patient dosed in a Phase III trial	EUR 4m
Milestone 6: First NDA filing for Product	EUR 5m
Milestone 7: Approval 1st major market (US or in the EU)	EUR 7.5m
Milestone 8: Approval 2nd major market (US or in the EU)	EUR 7.5m
Milestone 9: First year aggregate annual Net Sales during a calendar year in the Territory reach EUR500m	EUR 10m
Milestone 10: First year aggregate annual Net Sales during a calendar year in the Territory reach EUR1b	EUR 20m
Milestone 11: First year aggregate annual Net Sales during a calendar year in the Territory reach EUR2b	EUR 52m
Total potential milestones	EUR115.0m

CTx First in class engineered T-cell platform

CTx is developing the new generation of immune adoptive therapy through new genome engineering technologies providing allogenic ready for use T-cells in oncology.

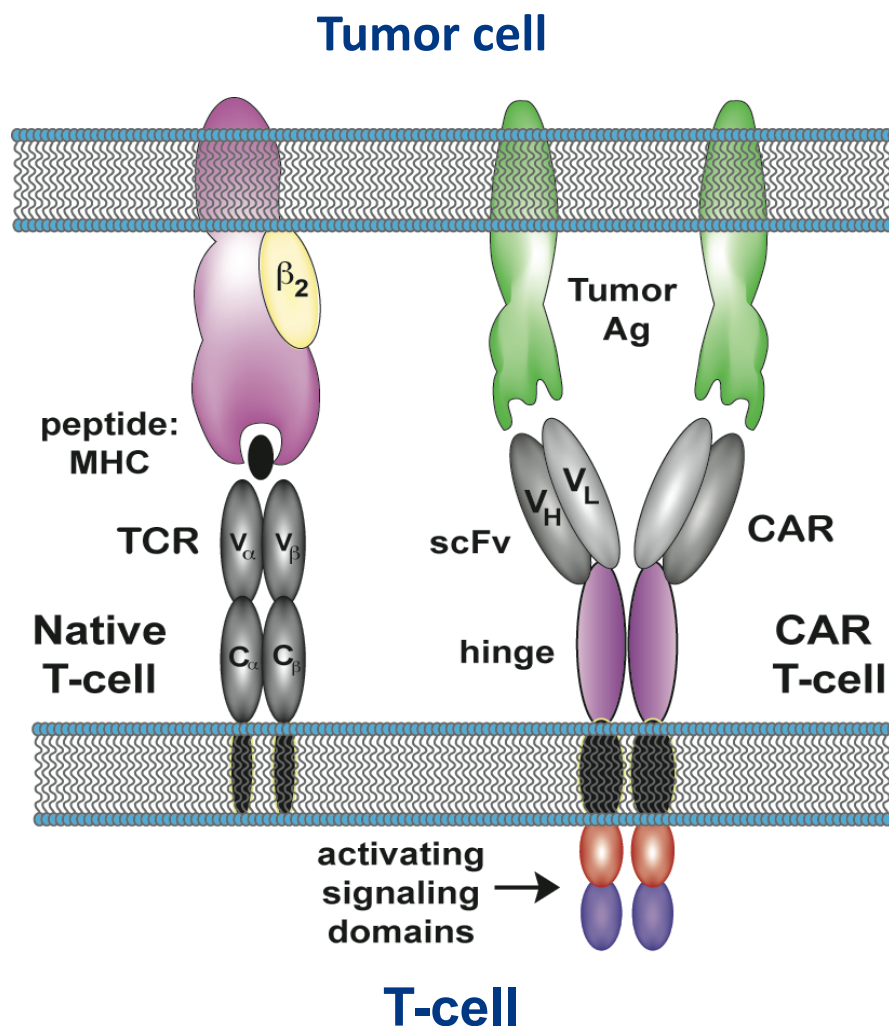
Today:

- **Non-targeted therapies**
 - ✓ Radiotherapy
 - ✓ Chemotherapy
- **Targeted therapies**
 - ✓ Monoclonal antibodies
 - ✓ Kinase inhibitors

Tomorrow:

- **Genetically modified serial killer T-cells**
 - ✓ Unprecedented efficacy but limitations due to autologous settings.
- **Collectis allogenic platforms**
 - ✓ Engineered of off-the-shelf T-cells with no alloreactivity and unprecedented efficacy.

Re-targeting T-cells to Tumors with CARs



- 4th generation: autologous T-cells retargeted to tumor antigens via chimeric antigen receptors (CARs)
 - ✓ CARs = membrane bound mAbs that target T-cells to tumors
 - ✓ T-cells replicate in vivo
 - ✓ T-cells properties can be controlled by genome editing = low toxicity; high efficacy
- Limitations: patient specificity

The New York Times

March 20, 2013

Cell Therapy Shows Promise for Acute Type of Leukemia

By DENISE GRADY

A treatment that genetically alters a patient's own immune cells to fight cancer has, for the first time, produced remissions in adults with an acute leukemia that is usually lethal, researchers are reporting.

In one patient who was severely ill, all traces of leukemia vanished in eight days.

"We had hoped, but couldn't have predicted that the response would be so profound and rapid," said Dr. Renier J. Brentjens, the first author of a new study of the therapy and a specialist in leukemia at Memorial Sloan-Kettering Cancer Center.

The treatment is experimental, has been used in only a small number of patients and did not work in all of them. But experts consider it a highly promising approach for a variety of malignancies, including other blood cancers and tumors in organs like the prostate gland.

The new study, in five adults with acute leukemia in whom chemotherapy had failed, was published Wednesday in the journal *Science Translational Medicine*.

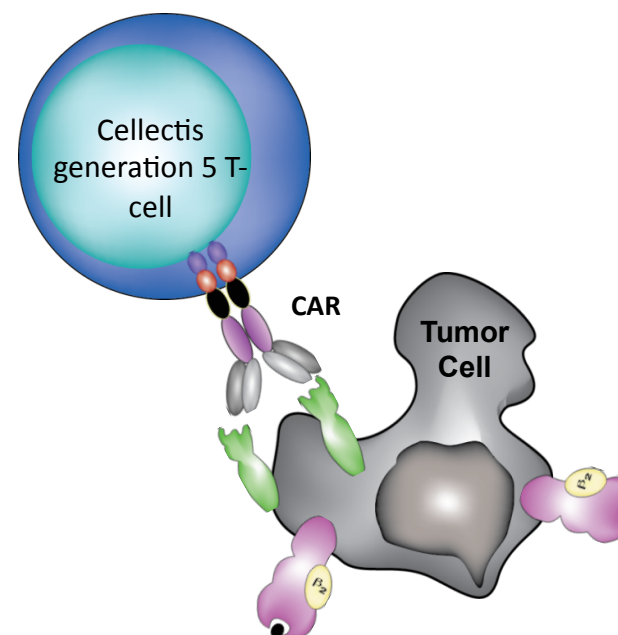
The treatment is similar to one that pulled a 7-year-old girl, Emma Whitehead, from death's door into remission nearly a year ago, and that has had astounding success in several adults with chronic leukemia in whom chemotherapy had failed. The treatment regimen that saved Emma and those adults was developed at the University of Pennsylvania. Related studies have also been done at the National Cancer Institute.

But this cell-therapy approach had not been tried before in adults with the disease that Emma had, acute lymphoblastic leukemia. This type of blood cancer is worse in adults than in children, with a cure rate in adults of only about 40 percent, compared with 80 percent to 90 percent in children. The disease is not common. Each year in the United States, it affects about 2,400 people older than 20, and 3,600 younger. Though there are fewer cases in adults, there are more deaths: about 1,170 adults die each year compared with 270 deaths in people under 20.

In adults, this type of leukemia is a "devastating, galloping disease," said Dr. Michel Sadelain, the senior author of the new study and director of the Center for Cell Engineering and the Gene Transfer and Gene Expression Laboratory at Memorial Sloan-Kettering Cancer Center in Manhattan.

“Off-the-shelf” T-cells: the 5th generation of mAbs

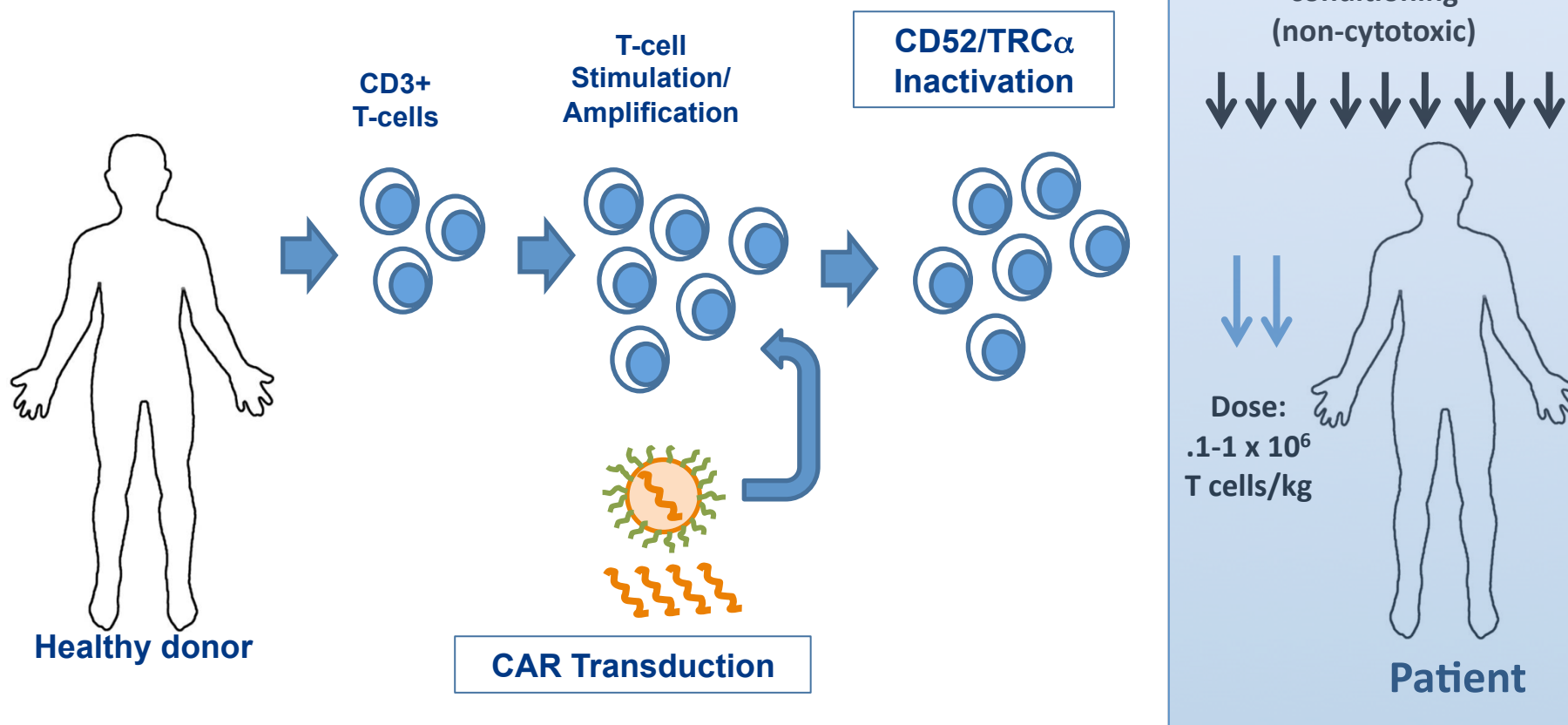
- Engineered “off-the-shelf” T-cells
 - ✓ Retargeted via chimeric antigen receptors (CARs)
 - ✓ T-cells properties controlled by disruption of key immune regulatory genes
 - No alloreactivity: available off the shelf
 - Non-toxic engraftment
 - Can be rendered tumor evasion resistant
 - Low CoG
 - Broad market access



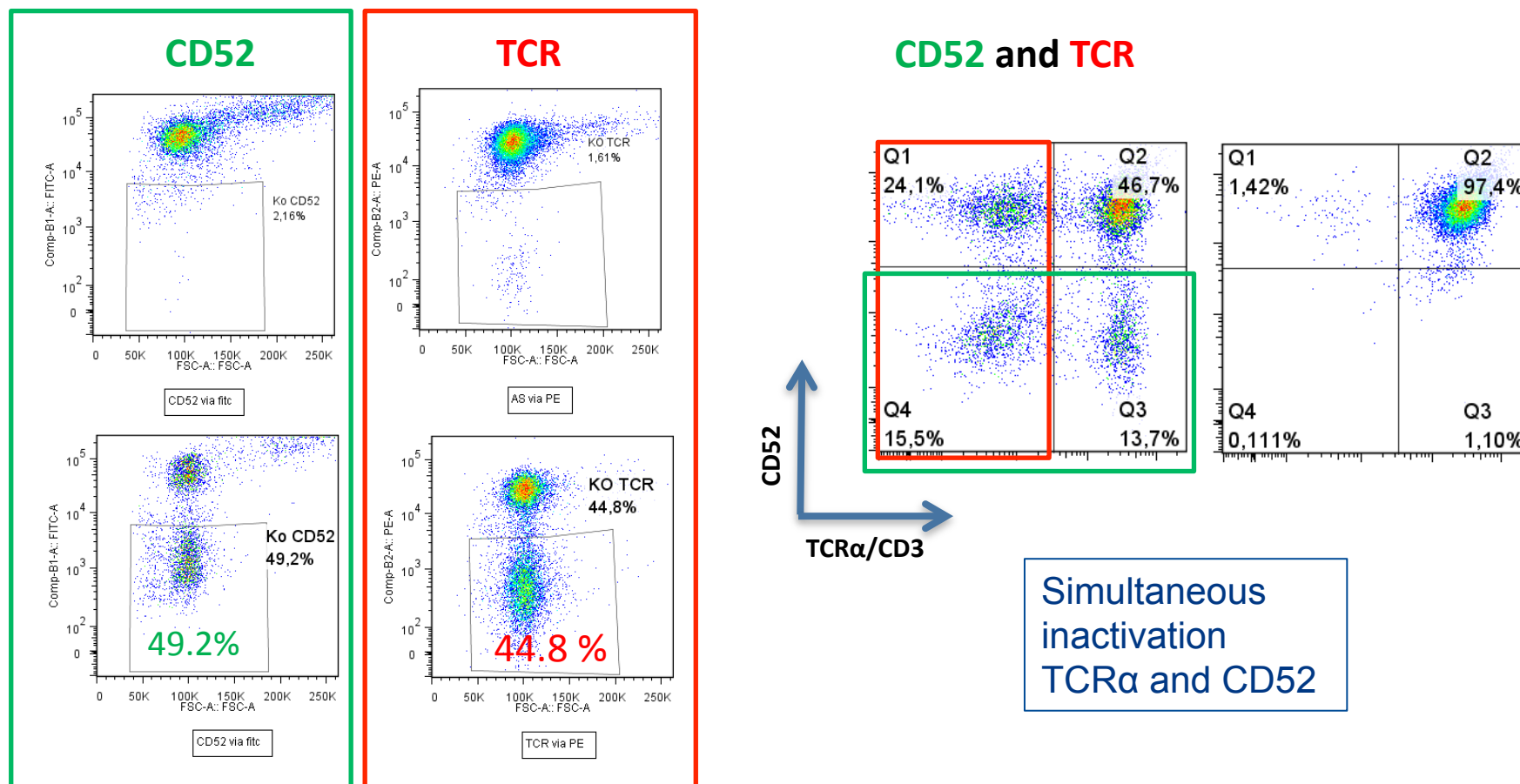
« off-the-shelf » T-cells engineered both for specificity and functionality are precise tumor targeted mAb conjugates that will set new standards for efficacy and safety

UCART19 process development

CLL (Chronic Lymphocytic Leukemia)



UCART19: a cost effective industrialization process

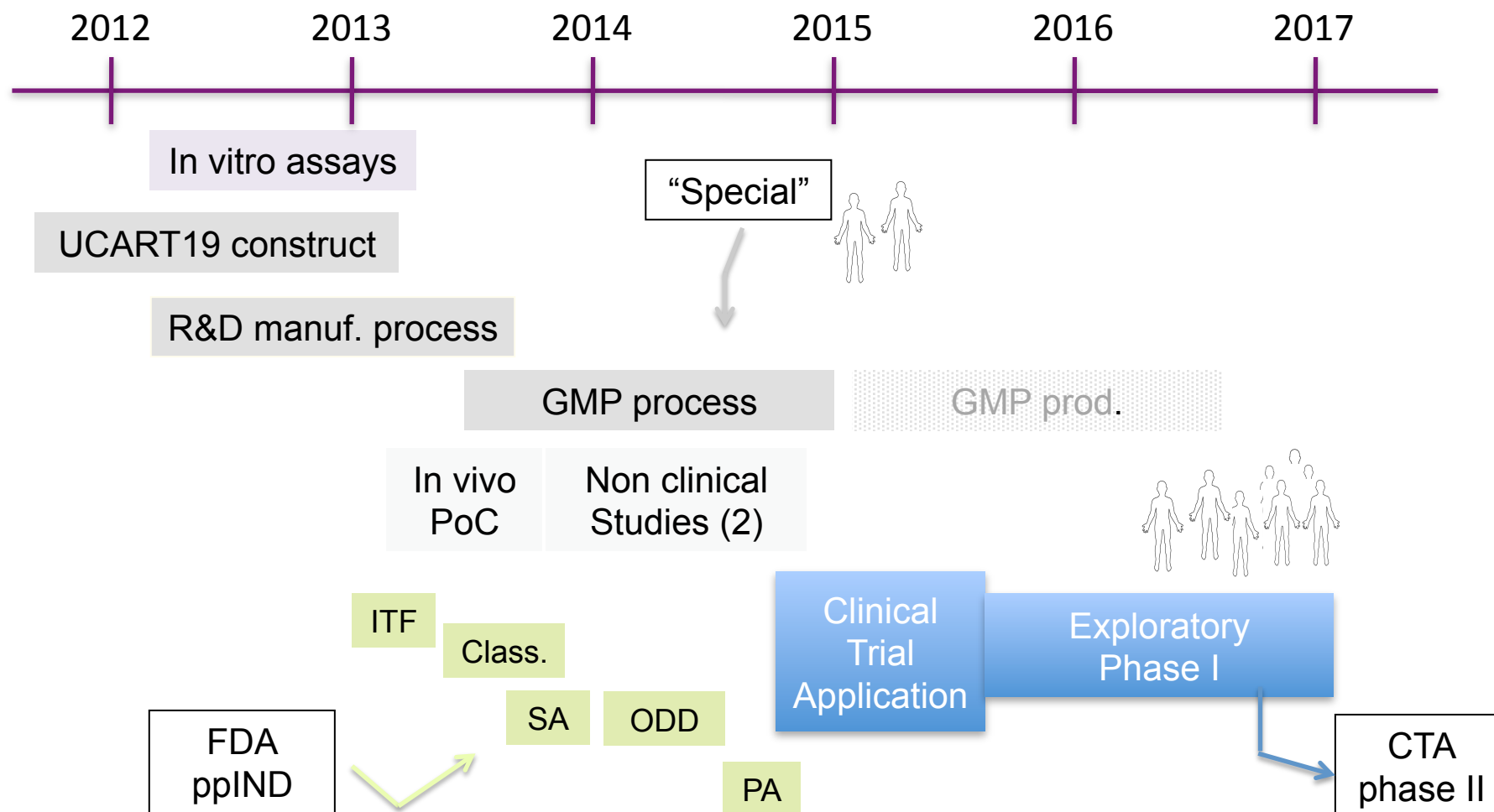


UCART19 Development plan

1. Target specific, high risk orphan population for Proof-of-Concept, « *Adult relapsed/refractory CLL patients* », with further possibility of extension of indication to other B-Lymphomas.
2. Share risks of process development by concomitant in-house/UCL co-development of a *small manufacturing scale* (demonstration of feasibility).
3. Early validation with regulatory agency (ITF*, Scientific Advice) of the chosen options : *limited non-clinical experiments*, use of supportive data from *compassionate treatment*, cells pooling, infusion of UCART19 as a salvage therapy in *lymphodepleted patients*,...
4. Conservative approach for First-in-Man clinical study with a short, easy to set up, low number of patients, exploratory study to answer the main questions: *is allogeneic approach safe?* Do the *cells expand (dosing) and target tumors?*

(*): ITF, Innovative Task Force

UCART19 Development plan



Class: classification / SA: scientific Advice / ODD: orphan drug designation / PA: protocol assistance / ppIND: pre-pre Investigation New Drug meeting

U-CART19 in CLL: a new treatment paradigm

- CLL market estimated at \$550Mio in 2012: \$820Mio in 2017 – CAGR 5 years + 8%
- 20 / 37% Fludarazine resistant treatment
- New treatment Algorithm: 192 clinical studies ongoing in USA.
 - ✓ Monoclonal antibodies
 - ✓ Kinase inhibitors (2nd line)
 - ✓ Cell therapies in rescue therapies patients (3rd line / 2nd line)
- 16 000 patients in rescue therapy
 - ✓ 80% allogenic
 - ✓ 20% autologous

Peak sales potentially at \$100 000 treatment cost (125Mio – 225Mio*)

* depending availability to move upstream in indication flow

Well-positioned and promising product portfolio

	Lead Id.	Lead Opt.	Preclinical	Phase I
<i>Oncology</i>				
Blood cancer Lymphoid leukemia Target: CD19			2013	*2015
Solid tumors Lung, pancreas, colorectal cancer Target: 5T4			nd	nd
<i>Virology</i>				
HIV Target: CCR5			2013	2015
Cytomegalovirus - CMV Target: GR			2013	2015
<i>Regenerative medicine</i>				
Diabetes Target: beta cells Collectis / Novo Nordisk alliance			2013	2015
Other applications hemophilia Target: hepatocytes			nd	nd

* 1st clinical trial Q2 2014 in partnership with University College London

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Comprehensive income statement

(In 000' €)	2012	2011
Sales	11 301	9 928
Other Revenues	9 731	6 065
Total Revenues	21 032	15 993
Cost of sales	(1 535)	(2 515)
Gross Margin	19 497	13 478
R&D cost	(18 981)	(12 306)
Sales, General & Administrative cost	(19 528)	(20 589)
Other Operating Income & Expenses	(753)	(110)
Operating Income	(19 764)	(19 526)
Financial Income	(1 312)	133
Income Tax	(1 193)	(4 445)
Profit (loss) of the period	(22 270)	(23 838)
Attributable to owners of the parent	(21 855)	(23 838)
Attributable to non controlling interest	(414)	
Differences arising on translation of assets	1 258	54
Comprehensive Income (Loss)	(21 012)	(23 783)
Attributable to owners of the parent	(20 598)	
Attributable to non controlling interest	(414)	

Financial position statement

ASSETS (in 000'€)	2012	2011
Intangible assets	37 821	35 202
Tangible assets	5 484	6 619
Financial Assets	1 422	960
Differed tax assets	3 392	4 483
Non Current Assets	48 119	47 265
Inventories and Trade receivables	17 107	12 109
Cash and cash equivalent	21 808	42 384
Current Assets	38 916	54 492
	87 036	101 757

LIABILITIES (in 000'€)	2012	2011
Common stock and paid-in capital	131 984	80 397
Accumulated deficit	(50 449)	(27 996)
Net income	(21 856)	(23 838)
Stockholders' Equity	59 680	28 564
Non controlling interest	2 086	-
Total Equity	61 766	28 564
Long term debt	3 303	52 088
Non current provisions	525	305
Non Current Liabilities	3 828	52 393
Short term debt	988	1 213
Trade payables	20 452	19 587
Current Liabilities	21 441	20 800
TOTAL LIABILITIES AND EQUITY	87 036	101 757

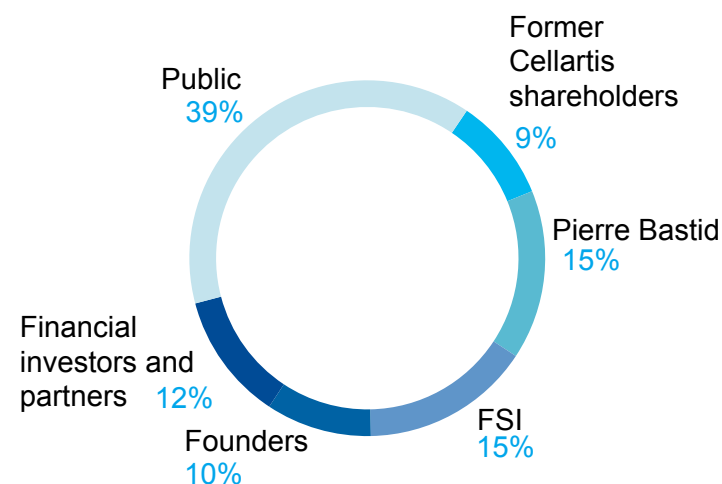
Cash flow statement

(In 000' €)	2012	2011
Profit (loss) for the period	(22 270)	(23 838)
Adjustments for non cash items	7 344	9 121
(Increase) / Decrease in Working Capital	(5 041)	3 984
Interest received /(paid)	224	555
Net cash flows from operating activities	(19 743)	(10 178)
Acquisition of development costs	(3 391)	(2 763)
Acquisition of other intangible assets	(250)	(332)
Acquisition of property, plant and equipment	(507)	(2 945)
Acquisition of other non current asset	(462)	(383)
Impact of change in consolidation scope	-	(16 271)
Net cash used in investing activities	(4 610)	(22 694)
Share Capital	2 704	1 717
Borrowings	282	51 097
Proceeds from lease-back operations	764	466
Sale and purchase of treasury shares	(25)	(15)
Bonds issuance cost	-	(2 099)
Net cash from (used in) financing activities	3 725	51 167
Net increase (decrease) in cash and cash equivalents	(20 628)	18 295
Cash and cash equivalent at end of the period	21 808	42 384

Shareholding structure built to support growth

- Stronger majority shareholder position
- French and foreign institutional investors on board for the long term
- Shareholding structure in line with growth strategy
- Float of almost 40%
- Collectis share (ALCLS.PA) on the stock market
 - ✓ €120 M market capitalization (March 31, 2013)
 - ✓ Significant increase in liquidity
 - 20,000 shares traded / day in 2012
 - 16,000 shares traded / day in 2011

Breakdown of capital at Dec 31, 2012
(20.5 million shares*)



* Fully diluted capital: 25.5 million shares

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Outlook

I. Economic balance → increase in 'Tools' and 'Plants' sales

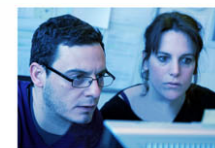
II. Value creation:

❖ Reinvestment of cash flow generated → development of totally new drugs

❖ Partnership strategy → Pharma, Agro, Energy

❖ Acceleration of growth → targeted acquisitions

III. Top 3 biotech market capitalizations in Europe over the medium term



Thank you for your attention

Cellestis SA
8 rue de la Croix-Jarry
75013 Paris - France

<http://www.cellestis.com/>
investors@cellectis.com
actionnaires@cellectis.com

tel: +33 (0) 1 81 69 16 00

