CellCAN
Regenerative Medicine and Cell Therapy Network

MOBILIZING KNOWLEDGE TO ENABLE OPTIMAL CELL & GENE THERAPY MANUFACTURING ACROSS CANADA

FIRST MANDATE REPORT

2014 | 2018

Centre intégré universitaire de santé et de services sociaux de l'Est-de-l'Île-de-Montréal

Québec

NCE
Networks of Centres of Excellence of Canada

FHMR fondation de l'hôpital maisonneuve-rosemont

The field of regenerative medicine and cell & gene therapy is rapidly evolving thanks to excellence in fundamental research and new front-line technologies.

COLLABORATION AND INFORMATION SHARING BETWEEN RESEARCHERS, REGULATORS, FUNDING AGENCIES AND THE INDUSTRY ARE ESSENTIAL.

VISION

Our vision is that cell & gene therapy manufacturing in Canada must operate under a **common seal of quality** to increase capacity and rapidly and effectively migrate innovative treatment concepts into standard clinical practice.

MISSION

Our mission is to improve the quality, safety and feasibility of cell & gene therapy in Canada through **optimal manufacturing practices**.

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MESSAGE FROM THE CHAIR OF THE BOARD

WILLIAM BROCK

As a survivor of acute myelogenous leukemia, I am honoured to be CellCAN's Chair of its Board of Directors. I have been a director with CellCAN since its inception in 2014 and have witnessed first-hand the tremendous impact CellCAN has achieved in cell, tissue and gene therapy manufacturing. Our mission to mobilize knowledge is both ambitious and essential. Stem cells bring hope to patients and physicians with the promise of new treatments for previously incurable diseases. Creating common standards and a seal of quality for the production of cell, tissue and gene therapies will benefit all Canadians.

AS A PATIENT, I WAS ABLE TO FIND LIFE-SAVING TREATMENT RIGHT HERE IN CANADA, AND MY GREATEST WISH IS FOR ALL PATIENTS TO RECEIVE THE SAME GIFT OF LIFE, UNDER THE SAFEST POSSIBLE CONDITIONS.

One danger, however, is that enthusiasm may lead to publicly exaggerated hype and extravagant claims. This can lead to unrealistic expectations of both the benefits of these therapies and the speed at which they can be achieved. With unproven stem cell therapies growing here in our own country and worldwide, it is crucial now—more than ever—to establish strong guidelines regarding manufacturing practices.

As the global cell therapy and regenerative medicine industry undergoes exponential growth over the next decade, Canada is well positioned to lead the next wave of development. CellCAN can play a leadership role as a go-to resource. As a networked hub of scientists, clinicians, hospitals and cell & gene manufacturing facilities, CellCAN is uniquely positioned to galvanize cell-based therapy clinical trials in Canada.

We believe CellCAN will improve the quality, safety and feasibility of cell & gene therapy in Canada through optimal manufacturing practices, for the benefit of patients in Canada and around the world.

MESSAGE FROM THE CEO

DENIS CLAUDE ROY

CellCAN, a nonprofit organization that is part of the Government of Canada's Networks of Centres of Excellence, is pleased to present its First Mandate Report, which highlights our activities and impacts during the past four years. We have an urgent need to unite the strengths of all Canadian stakeholders in our field so that Canada can maintain its advantage in the face of strong competition from other countries while ensuring that Canadian patients have access to novel and life-changing cell, tissue and gene therapies. Our significant achievements so far have been in line with this need and are aimed at **building a strong Canadian network, advancing regulatory standards, positioning Canada as a world leader, and generating efficient outreach to all Canadians**.

THIS IS KEY BECAUSE CELL, TISSUE AND GENE THERAPY MANUFACTURING IN CANADA MUST OPERATE UNDER A COMMON SEAL OF QUALITY TO BOTH INCREASE CAPACITY AND RAPIDLY AND EFFECTIVELY MIGRATE INNOVATIVE AND LIFE-SAVING TREATMENT CONCEPTS INTO STANDARD CLINICAL PRACTICE.

CellCAN continues to work closely with Health Canada as the voice of the cell & gene manufacturing sector. Momentum is building, globally and locally, around regenerative medicine and cell therapy. Canada can build on this momentum to spearhead innovation and commercialization for revolutionizing therapies. We must intensify our efforts to mobilize knowledge and open a dialogue between stakeholders in our field not only to maintain and enhance Canada's leadership, but also to advance cell & gene therapies and let more and more patients benefit from the most innovative therapies.

By building on our impactful work so far, CellCAN is ready to meet this challenge and continue to bring together all stakeholders to focus on our vision that cell & gene therapy manufacturing in Canada must operate under a common seal of quality to increase capacity and rapidly and effectively migrate innovative treatment concepts into standard clinical practice.

UNDERSTANDING THE COMPLEXITY OF CELL MANUFACTURING

GOOD MANUFACTURING PRACTICE (GMP) CELL MANUFACTURING IS PERFORMED BY HIGHLY QUALIFIED PERSONNEL (HQP) UNDER STANDARD OPERATING PROCEDURES (SOPs).

Quality assurance and quality control mechanisms ensure that the entire process adheres to validated procedures that comply with stringent regulatory oversight.

DONOR

MEDICAL PRACTICE

Minimally manipulated/
Homologous use only

RECIPIENT
(Autologous)

More than minimally manipulated
Homologous or non-homologous use

GMP MANUFACTURING

VALIDATED PROCEDURES

REGULATORY OVERSIGHT

1. **PROCESSING BY HQP UNDER SOPs**
   - Dissociation/Separation/Purification
   - Washing/Media Optimization
   - Selection & Quantification
   - Viability & Functionality Assessment
2. **CELL CULTURE**
   - Expansion/Differentiation/Proliferation
3. **RELEASE TESTING**
   - Characterization
   - Microbiology Testing
4. **QUALITY ASSURANCE / QUALITY CONTROL**
   - GMP documentation
   - Packaging and Labelling
   - Storage

CELL THERAPY
Product Release

RECIPIENT
(Autologous or Allogeneic)

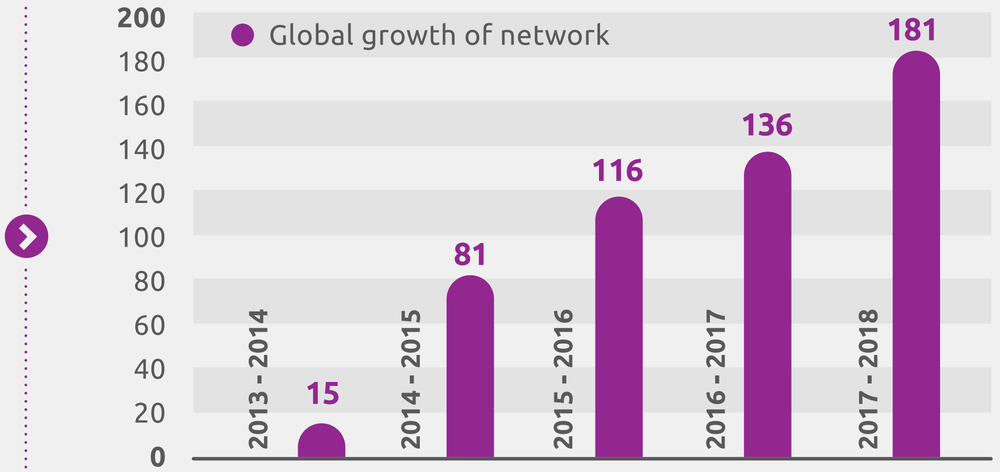
CellCAN AT A GLANCE

- **Mainly funded** by the Networks of Centres of Excellence (NCE) of Canada, by the Hôpital Maisonneuve- Rosemont Foundation (thanks to a donation from Ronald Black and Herbert Black), and by cash and in-kind contributions from several health and educational organizations across Canada
- **$2 million** funding for 2014-2018
- **$123,780** cash contributions
- **$244,865** in-kind contributions

7-FOLD LEVERAGING OF NCE FUNDS:

CellCAN was able to leverage its **$400K-a-year grant** into over **$11.2M in projects** by partnering with the right organizations, positioning Canada as a key player in cell & gene therapy, and fostering collaboration between its Network Affiliates.

Growth of our Network's key connections since our creation.



KEY CORPORATE METRICS

4	Full-time employees
13	Network Affiliates
181	Network collaborators
25	Partner organizations

DELIVERING WORLD-CLASS MANUFACTURING IN HIGHLY INNOVATIVE CELL, GENE &TISSUE PRODUCTS

- CellCAN Network Affiliates of cell, tissue and gene therapy manufacturing facilities
- CellCAN Network Affiliates transversal cores

BEFORE CellCAN

- Minimal collaboration amongst cell manufacturing facilities (CMF)
- Unclear vision and variable quality
- Manufacturing was a black box
- No coordinated regulatory interactions
- No single voice to represent manufacturing

- CMF worked in silos
- Lack of qualified technical personnel (HQP) for CMF
- Stakeholder knowledge of manufacturing best practices was limited
- Validation of new procedures: very expensive and time consuming

- Outdated regulatory policies with lengthy review periods
- Cumbersome applications filled with redundancies
- No official national accreditation for GMP
- Inconsistent manufacturing practices and quality standards

- Existing facilities operating under 50% capacity
- Prohibitive manufacturing operating costs
- Poor recognition of CMF importance to the regenerative medicine and cell therapy (RMCT) ecosystem

- Knowledge gaps as to what CMF have in their pipeline
- Limited lay-public knowledge of cell therapy: proven vs. unproven therapies

HOW WE OPTIMIZE THE DEVELOPMENT OF CELL & GENE THERAPIES IN CANADA

Unique networking opportunities: Connections through a **network of Canadian researchers, clinicians and HQP from coast to coast** through our platforms, workshops and events

Manufacturing-oriented HQP training in cell & gene therapy

Knowledge-sharing community (Extranet) in cell & gene therapy with **over 150 shared SOPs** across multiple cellular therapy platforms

Access to **concerted, open dialogue** between Canada's primary group of cell therapy stakeholders and **Canadian regulatory agencies**

Expertise to achieve the **highest standards of cellular production (GMP)**

Revisions to Canadian policies, like the New Substances Notification Regulations

No other organization in the RMCT sector brings together all stakeholders, especially CMF, around the need to standardize GMP, which is an essential step in bringing innovative cell-based therapies to more patients. In this role, CellCAN acts as the unified voice of CMF with regulatory authorities such as Health Canada.

BUSINESS PRIORITIES

BUILD A STRONG CANADIAN NETWORK

We are translating and mobilizing knowledge to build a strong cell & gene manufacturing sector.

ADVANCE REGULATORY STANDARDS

We are channelling information from all Canadian CMF and providing input to Health Canada to advance regulatory standards and help establish adequate regulatory oversight. We take into account new technologies and deliver knowledge back to our stakeholders.

GENERATE EFFECTIVE OUTREACH

We are empowering information multipliers and Canadians to make informed decisions about their safety regarding cell & gene therapies.

POSITION CANADA AS A WORLD LEADER

We are helping to drive Canada’s economy by creating business and networking opportunities with the cell & gene manufacturing community.

BUILD A STRONG CANADIAN NETWORK

EXTRANET

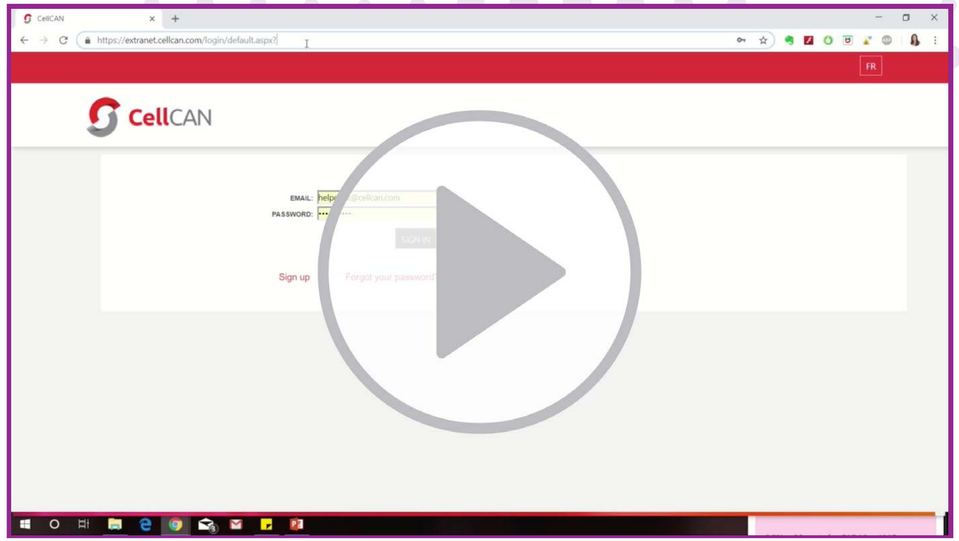
Over 150 shared SOPs

$4,5M worth of SOPs are available through CellCAN's Extranet

Global first

Point of reference to **validate procedures and review SOPs through the** Extranet

Representing **know-how** for **10 cell types** & **15 therapies**



CMF NOW **AIM FOR A COMMON SEAL OF QUALITY** TO IMPROVE PATIENT SAFETY.

The Extranet is a highly secure web-based platform that allows CellCAN's Network Affiliates and partners to share protocols, best practices and work collaboratively.

BUILD A STRONG CANADIAN NETWORK

TRAINING

Over **250** HQP trained

Unique **manufacturing-oriented** HQP training

Educating knowledge users on **why, when and how to engage manufacturing centres** in the process to create a clinical product

A FEW OF OUR WORKSHOPS

- Breaking the mould: flourishing multicentre clinical trials in Canada
- How to survive the valley of death
- Never underestimate the cost of cell and tissue manufacturing
- Hands-on GMP workshop

CellCAN offers multiple unique training opportunities every year.

Learn more

OUR TRAINING OFFER

BUILD A STRONG CANADIAN NETWORK

STRATEGIC FORUM

CellCAN hosted the first pan-Canadian Strategic Forum on Cell & Gene Therapy.

The forum was attended by **160 people** from various stakeholder groups: researchers, federal regulatory agencies, federal and provincial funding agencies, the industry, networks, etc.

96 % of attendees said they would participate again.

For the first time, all stakeholders came together over two days to have open discussions and help establish a national agenda to advance the cell & gene therapy field in Canada.

READ THE FULL REPORT FROM OUR **FIRST PAN-CANADIAN STRATEGIC FORUM**, HELD IN MONTREAL IN MARCH 2017, TO LEARN MORE ABOUT THIS EXCITING AND ONE-OF-A-KIND EVENT.

Read full report

BUILD A STRONG CANADIAN NETWORK

STRATEGIC FORUM

DURING THE STRATEGIC FORUM WE ASKED OUR PARTNERS WHAT MAKES CANADA A POWERHOUSE IN CELL & GENE THERAPY...

Watch what they had to say!

BUILD A STRONG CANADIAN NETWORK

CellCAN supported **7 collaborative knowledge mobilization projects** throughout Canada in 2017-2018 that contribute to **3 specific goals**:

1. Creating a database of SOPs on CellCAN's Extranet
2. Advancing regulatory standards for cell & gene therapies and for national and international multicentre clinical trials
3. Validating advanced and non-invasive product characterization

BELOW IS A SUMMARY TABLE OF THESE PROJECTS:

BUDGET **$70,000** · TARGET COMPLETION **DECEMBER 2018** · STARTED **SEPTEMBER 2017**

PROJECT LEAD	SITE	PROJECT TITLE • PROJECT DELIVERABLES
DAVID COURTMAN	Biotherapeutics Manufacturing Centre at Ottawa Hospital Research Institute	**SOP development & SAPPHIRE product shipping validation** CellCAN shipping protocol development
LUCIE GERMAIN	Centre multidisciplinaire du développement du génie tissulaire	**SOP development & validation of room temperature transport** CellCAN shipping protocol development
GREG KORBUTT	Alberta Cell Therapy Manufacturing	**SOP development & validation of cold chain transport** CellCAN shipping protocol development
MARTIN GIROUX	Centre d'Excellence en Thérapie Cellulaire	**Quality assurance, validation and C.A.R.E Trial SOP portfolio** Multicenter clinical trial SOPs portfolio
SOWMYA VISWANATHAN	Regulatory Cell Therapy Consultants	**Recommendations to the New Substances Notification Regulations (NSNR) for cell & gene therapies** Workshop in partnership with BIOTECanada, Whitepaper Publication
BARTHA M. KNOPPERS	Centre of Genomics and Policy, McGill University	**National and international multicentre clinical trials regulatory and ethical recommendations** Whitepaper Publication
JAMES PIRET	Michael Smith Laboratories	**Product characterization** Multi-site shipment of single cell product for characterization

ADVANCE REGULATORY STANDARDS

HEALTH CANADA CELL THERAPY STAKEHOLDER GROUP (CTSG)

9 Network Partner Organizations united in a harmonized CellCAN-led approach at the CTSG

Over **990** investigators from across Canada contribute to and receive knowledge disseminated at CellCAN-organized CTSG meetings (1012% increase since CTSG initialization in 2015)

Over **1300** additional international investigators and members from across 5 continents are reached by having the International Society for Cell Therapy (ISCT) on the CTSG

Concerted, open dialogue between Canada's primary group of cell therapy stakeholders and Canadian regulatory agencies

A voice for Health Canada to promote Canadian policies on the international stage for multicentre clinical trials

THE CTSG

Curious to learn more about the CTSG, its work and how it can benefit you?

Learn more

THE RMCT COMMUNITY NOW HAS A **UNIFIED VOICE TO ADDRESS REGULATORY CONCERNS** AND A **SINGLE ENTRY POINT TO ACCESS CRITICAL INFORMATION.**

ADVANCE REGULATORY STANDARDS

THE NEW SUBSTANCES NOTIFICATION REGULATIONS (ORGANISMS) **WORKSHOP**

ONE OF **OUR MAIN IMPACTS**

Modified policies and guidelines to reduce redundancies and favour streamlined clinical trial applications (CTA)

A need to reduce regulatory burden and regulatory overlap between *CEPA* and the *FDA* and related regulations to facilitate the manufacturing, clinical trials, and therapeutic use of gene, cell and viral therapies in Canada was identified by the RMCT community.

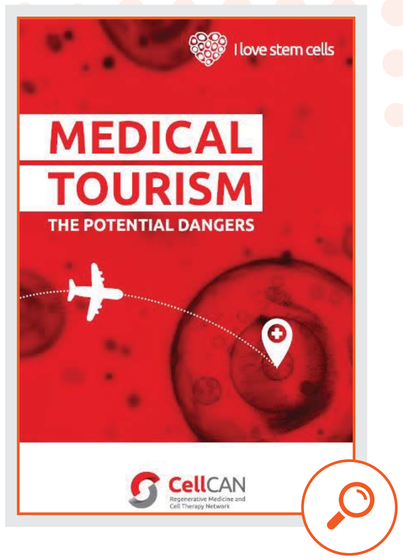
In collaboration with BIOTECanada, CellCAN organized a workshop at the Biologics and Genetics Therapeutic Directorate (BGTD) at HC to discuss overdue changes to the NSNR(O).

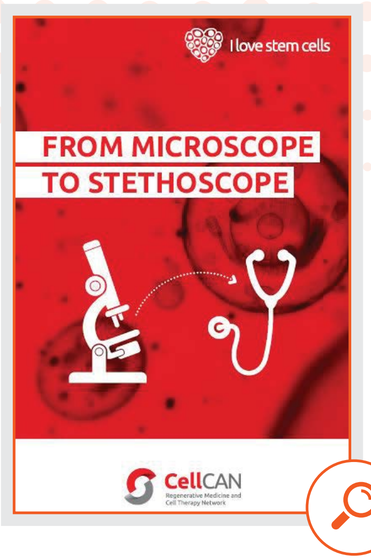
Want to know what type of work we do about the NSNR(O) ?

Learn more

GENERATE EFFICIENT OUTREACH

- Presence in media with a reach of over **2 million** Canadians
- Direct reach to over **5000** Canadian patients during our first mandate
- CellCAN's **website has over 47,000 pageviews from web users around the world**: 43% in Canada, 27% in the United States and 5% in France
- **Recognized as the nation's knowledge mobilization service for Health Canada** for fast and easy access to key regulatory information





All of our information flyers are available for distribution and can be used by patient groups or health professionals to give reliable comprehensible information to their patients.

View more

EMPOWERING INFORMATION MULTIPLIERS AND CANADIANS TO MAKE INFORMED DECISIONS FOR THEIR SAFETY REGARDING CELL & GENE THERAPIES.

GENERATE EFFICIENT OUTREACH


PERSONALHEALTHNEWS.CA — A SPECIAL INTEREST SECTION BY MEDIAPLANET

BLOOD HEALTH & ORGAN TRANSPLANTS

The Social's Lainey Lui turns caregiver for her mother and helps her deal with a rare blood disorder. p06

Research on Rare Blood Disorders Can Help Save Lives

We call blood the essential "life force" and blood donations the "gift of life." But could research on a rare blood disorder save your life? It may already have. People with hemophilia, a rare bleeding disorder, have led researchers to many medical discoveries. In the 1980s, when many hemophiliacs became infected with HIV, it helped confirm that the virus was transmissible through blood. In the 90s, hemophilia research proved that a bioengineered product with no viral risk could control bleeding as well as "blood-based" factor. Today, synthetic blood factors are successfully used in surgery and on battlefields to save lives.

Treatments for rare blood disorders help all

Knowledge about rare blood disorders has benefitted more common diseases. For example, sickle cell disease and thalassemia – both rare blood disorders – demonstrated that a single gene mutation offers a protective advantage against the malaria parasite, but two mutated genes lead to a life-threatening condition.

The identification of persons with (rare) inherited high cholesterol demonstrated a link between cholesterol and heart disease. The subsequent development of statins, a class of lipid-lowering medications, has saved millions of lives.

Revolutionary gene therapy: reality today

Canadian rare blood disease researchers and patients are involved in revolutionary gene therapies. In 2012, the European Medicines Agency approved the first medicine that delivers a gene into the body to correct a genetic deficiency. Patients with a rare lipid disorder were recently treated as part of a trial in Quebec. Last year, the EMA approved a gene therapy for children with an ultra-rare immune disorder caused by very low white blood cell counts. Canadian hemophilia patients participating in gene therapy trials are showing signs of a cure, which may allow them to avoid infusions altogether in the future. And Canadian researchers are participating in cellular therapy for acute lymphoblastic leukemia, which reprograms a patient's own T cells to increase their ability to fight cancer.

The Canadian Organization for Rare Disorders calls upon all governments, industry, and other stakeholders to support Canada's Rare Disease Strategy – a five-point comprehensive program for research, diagnosis, treatment, and support of all rare diseases.

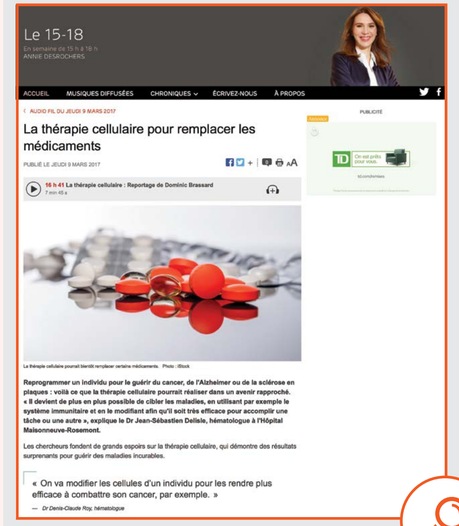
Durhane Wong-Rieger
President & CEO, Canadian Organization for Rare Disorders

Durhane Wong-Rieger

Our network of experts at your finger tips!

Want to know why there is a hype surrounding stem cells? Need help to navigate through the noise? Want to learn about the real potential of stem cells and what they can do for your health?

Consult CellCAN's Helpdesk ! www.cellcan.com/h



CellCAN HAS BEEN ACTIVE AND OFTEN CITED IN THE MEDIA TO ANSWER THE EMERGING QUESTIONS ABOUT CELL & GENE THERAPY AS WELL AS TO RAISE AWARENESS ABOUT THIS PROMISING FIELD.

Whether you are a health professional, a researcher, an HQP, a journalist or a member of the industry, if you have a question about the work that we do, cell manufacturing or more broadly about the cell & gene therapy field, CellCAN's Helpdesk was created to answer your questions. **Reach out today!**

POSITION CANADA AS A WORLD LEADER

CANADIAN PAVILION

- For the past 2 years, the CellCAN-led Canadian Pavilion was at the ISCT meetings, the largest conference in the field of RMCT, and the **Pavilion doubled its size and its number of participating organizations from year 1 to year 2**
- **New** national and international strategic connections
- **4500** participants learned about Canada's leadership
- Existing strategic relationships were **strengthened** and **reinforced**

INTERNATIONAL EVENT ATTENDANCE

- **6000** leading scientists reached globally
- The excellence of cell, tissue and gene therapy manufacturing centres is **now showcased** in the international RMCT community

At the occasion of the ISCT 2018 conference in Canada, CellCAN reunited key players from the Canadian RMCT field to showcase our expertise, know-how and infrastructure.

"Through CellCAN, our interactions with new stakeholders have been impactful and will lead to new collaborations and partnerships."
Eileen Raymond, Business Advisor,
National Research Council Canada

ENHANCED GLOBAL AWARENESS AND PERCEPTIONS OF CANADIAN KNOW-HOW, MARKET READINESS AND EXCELLENCE IN RMCT.

SINCE CellCAN WAS FOUNDED

CREATION OF A CMF COMMUNITY OF PRACTICE

SHARED PROCEDURES (SOPs) BY CMF

EMERGENCE OF A COMMON VISION

WORK TOWARDS HARMONIZED PROCEDURES

IMPACTFUL AND COORDINATED REGULATORY INTERACTIONS

ENHANCED GLOBAL AWARENESS OF CANADIAN EXCELLENCE IN RMCT

BETTER UNDERSTANDING OF THE CELL MANUFACTURING SECTOR IN CANADA.

PRIORITIES FOR THE COMING YEARS

2018

CONSOLIDATING
OUR BASE

- Increasing the number of CMF
- Harmonizing product labelling & shipping methods
- Advancing recommendations for NSNR(O) changes
- Increasing information multipliers
- Organizing a second edition of the hands-on GMP workshop
- Organizing a second edition of the Strategic Forum

2019

BUILDING
THE STANDARD

- Launching our HQP webinar training platform initiative for GMP
- Integrating manufacturing workflows for different disease indications in the CCMBOK
- Building awareness among health professionals

2020

ADAPTING TO
AN EVOLVING RMCT LANDSCAPE

- Contributing to and supporting the integration of next generation cell & gene therapies
- Facilitating optimization of CMF manufacturing processes
- Mobilizing knowledge in collaboration with regulatory agencies to promote safe and proven therapies

2021

ACHIEVING
SUSTAINABILITY

- Integrating common seal of quality throughout commercial and academic institutions
- Gaining recognition from government, health professionals, the general public, and patients

CONTRIBUTORS

BOARD OF DIRECTORS (AS OF MARCH 31, 2018)

- Pierre Duplessis, Chairman (2014-2017)
- William Brock, Vice-Chairman (2014-2017), Chairman (since 2017)
- Fiona Fitzgerald, Director (since 2017), Vice-Chairman (since 2017)
- Jean Picard, Treasurer (since 2015)
- Philip Welford, Secretary (2014-2018)
- Armand Keating, Director (since 2014)
- David Dolphin, Director (since 2014)
- David Phipps, Director (2014-2018)
- Denis Claude Roy, Ex-Officio Director and Chief Executive Officer (since 2014)

MANAGEMENT TEAM

- Denis Claude Roy, Chief Executive Officer
- Vanessa Laflamme, Chief Operating Officer
- Craig Hasilo, Chief Scientific Officer
- Marie-Ève Desormeaux, Project Manager and Communications Coordinator
- Ruth Yafali, Administrative Assistant

INTERNATIONAL SCIENTIFIC ADVISORY COMMITTEE

- Adrian Gee, Director, Clinical Applications Lab, Baylor College of Medicine
- Philippe Hénon, President and Scientific Director, CellProthera
- Geoffrey Lomax, Senior Officer, CIRM Strategic Infrastructure
- Jerome Ritz, Executive Director, Connell O'Reilly Cell Manipulation, Dana Farber Cancer Institute

CellCAN WOULD ALSO LIKE TO THANK THE NCE SECRETARIAT, NCE PARTNERS AND ALL OTHER COLLABORATORS

STEERING COMMITTEE

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- Greg Korbutt, Scientific Director, Alberta Cell Therapy Manufacturing, University of Alberta
- Gayle Piat, Project Manager, Alberta Cell Therapy Manufacturing, University of Alberta
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