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ANNUAL REPORT 2019



Commercializing Living Therapies **CCRM** is a Canadian, public-private partnership supporting the commercialization of cell and gene therapies with strategic funding, dedicated infrastructure and specialized business and scientific expertise. By partnering with leading research institutions to launch new ventures, enabling industry by providing innovative contract development manufacturing organization (CDMO) services, and scaling emerging companies by catalyzing investment, CCRM is accelerating the translation of promising technologies, processes and therapies into life-changing health outcomes for patients.

### **OUR PURPOSE**

CCRM is revolutionizing health care by solving the big problems in regenerative medicine.

Cell image credits: Cover - Malvin Jefri Left - Lilit Antonyan Right - Carole Doré

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### **OUR VISION**

To be the preferred global destination for the best people, technologies, clinical trials, companies and investments in regenerative medicine.

To be the premier global enabler of clinically-tested, revolutionary new medical therapies and foundational technologies.

#### **BOARD OF DIRECTORS**

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#### **EXECUTIVE MESSAGE**

# TOGETHER, WE ARE SOLVING THE BIG PROBLEMS IN REGENERATIVE MEDICINE

We now have more than 100 full-time highly qualified personnel employed at CCRM. Many of them work in purpose-built facilities supporting product and process development, scale-up and manufacturing for Phase I/II clinical trials. Across our six business units, we also have experts in technology evaluation, market research, investment, intellectual property management, regulatory affairs, company creation, procurement, quality control and quality assurance, all supported by operations and support teams that keep our organization thriving.

> To recognize the entire CCRM team, we have included a company-wide photo here - a change from prior annual reports to showcase the diverse group of individuals that fuels CCRM's success.

Looking back at 2019, three significant events stand out.

First, CCRM realized its first exit from an early-stage investment, achieving a key milestone in its mission to reach sustainability and re-invest the fruits of success back into the ecosystem. AVROBIO, a gene therapy company launched in Toronto in 2016, executed a successful initial public offering on the NASDAQ in 2018. By selling its stake in AVRO in 2019, CCRM hopes to seed an early-stage investment fund to further accelerate the commercialization of a growing pipeline of exciting advanced therapy discoveries. Second, we co-launched Notch Therapeutics – the first company that has gone end-to-end through CCRM's internal company incubation process. After two years of countless meetings, filings, budgets, pitches, and more recently identifying leadership and engaging with potential partners and investors, Notch has closed its first financing and is hiring aggresively to accelerate the development of a nextgeneration pipeline of off-the-shelf, universally compatible, genetically tailored T cell therapeutics derived from renewable stem cell sources. You can read more about the CCRM company incubation strategy on page 4.

Notch is the embodiment of 10 years of research from the labs of Drs. Juan Carlos Zúñiga- Pflücker at Sunnybrook Research Institute and Peter Zandstra at the University of Toronto. Additional



founders include the Toronto Innovation Acceleration Partners and Lumira Ventures.

Right out of the gate, Notch announced a significant collaboration and license agreement with Allogene Therapeutics to research and develop induced pluripotent stem cell (iPSC) AlloCAR<sup>™</sup> therapy products for blood cancers. We couldn't be more pleased.

Notch will be headquartered in Toronto, and for now is being set-up at CCRM, but it is also building a development team in Vancouver, British Columbia.

Third, we are excited to be leveraging three years of internal investment in viral vector process optimization through our FedDev-supported partnership with GE Healthcare into an advanced manufacturing process for lentiviral vectors (LVVs) as part of a consortium with iVexSol (intelligent **Ve**ctor **Sol**utions) Canada, a newly-formed vector manufacturing company.

LVVs are critical in manufacturing cell and gene therapies and because of expensive, inefficient and hard-to-scale methods, the world is facing a global shortage. The iVexSol consortium has received support from the Government of Canada through the Next Generation Manufacturing Canada (NGen) Supercluster, which is providing \$1.89M in funding to the \$4.25M project to establish Canada as a world leader in gene-editing tools and technology. The consortium also includes GE Healthcare and STEMCELL Technologies.

As always, we would like to acknowledge funding from the Government of Canada, through the Networks of Centres of Excellence program, to take the best of Canada's regenerative medicine-based technologies and therapies, and support their path to the market for the benefit of patients. Revolutioninizing health care through the promise of living therapies is a bold vision that requires us to tackle access to capital, the scalability of manufacturing, the development of specialialized talent and the launch and scaling of companies in a more capital-efficient and accelerated manner.

Read on to learn how we are solving these big probems in regenerative medicine....

tand U. May

Michael May President and CEO

# FROM CONCEPT TO CLINIC

In 2019, CCRM put a Notch (Therapeutics) on our belt by launching our first incubation company. The team responsible for identifying and developing promising technologies, and nurturing them to the company creation stage, is ready to work with you. We have illustrated the process here.





# 2019 HIGHLIGHTS

This section captures only a fraction of the noteworthy and memorable things that happened at CCRM in 2019. Read the following pages for more and, if you don't already, please subscribe to CCRM's newsletter at www.ccrm.ca for real-time updates.

### Notch soars when it leaves the nest

CCRM's first incubation company, Notch Therapeutics, makes its public debut and reveals that it is collaborating with Allogene Therapeutics to treat blood cancers. The partnership involves Allogene making an upfront payment of \$10M with the possibility of additional payments and royalties if specific milestones are achieved. The deal could be worth hundreds of millions.



#### Good Manufacturing Practices (GMP) facility now operational

The Centre for Cell and Vector Production has had an exciting year from welcoming its first clients, to manufacturing multiple cell banks, to creating its first batch of GMP-grade cells to conducting multiple engineering and aseptic process simulation studies. Get in touch to see how we can support your needs.

### New viral vector consortium announced

A consortium led by new Toronto-based iVexSol Canada, with CCRM, GE Healthcare and STEMCELL Technologies, is awarded \$1.89M by Next Generation Manufacturing Canada to develop a new advanced manufacturing process for viral vectors as part of a \$4.25M project. The group will address current manufacturing barriers in viral vector production.



HERAPEUTICS

#### **CELLS I SEE**

Our favourite contest crowns another winner. Congratulations to Joshua Dierolf, from Western University, for "The View from Eris" – voted this year's Grand Prize winner at the 2019 Till & McCulloch Meetings.



### New technical resource is live

CCRM launches the CDMO Education Centre on our website to provide free expert technical information from a contract development manufacturing organization perspective. The blog posts cover the development and manufacturing of cell and gene therapies, the latest advancements in product and process development for immunotherapies, viral vectors, pluripotent stem cells, and much more.



### Laying the foundation for Israeli hub

CCRM hosts a networking event in Tel Aviv, Israel, to advance Israeli start-ups and promote international collaboration in the commercialization of regenerative medicine advanced therapies (RMAT) and to publicly sign an MOU between CCRM and INACA. We will work together to accelerate the translation and commercialization of RMAT in Israel, Canada and internationally.



### Taking home the hardware – again!

For the second year in a row, a video we created with our partners at Big Red Oak has won an industry award. Our GMP facility video won the 2019 Videographer Award of Excellence from the dotCOMM Awards, as judged by the International Association of Marketing and Communication Professionals. Visit our website to watch it.

# MORPHOCELL BREAKS NEW GROUND IN THE TREATMENT OF LIVER DISEASE

According to the Canadian Liver Foundation, a quarter of Canadians are affected by liver diseases, owing to a variety of factors. At this time, no available treatment for acute or chronic liver disease can fully restore liver function; therefore, a liver transplant is the closest thing to a cure. Each year, only 400 livers are available for transplantation, at a cost of roughly \$800,000 per procedure, and over 5,000 Canadians succumb to liver disease.

> Canadian company Morphocell Technologies has taken on the challenge of transforming how liver disease is treated.

Morphocell was founded by three physicians in Montreal, Quebec: Massimiliano Paganelli, MD PhD, pediatric transplant hepatologist at the Centre hospitalier universitaire Sainte-Justine (CHU Sainte-Justine); Claudia Raggi, MD, research associate in the hospital's Hepatology and Cell Therapy Lab; and Margaret Bywater Ekegärd, MD MSc, a serial entrepreneur and expert in building biotechnology and life science-related businesses. In 2016, Drs. Paganelli and Raggi set out to investigate the feasibility of using an engineered liver tissue, which performs like the human liver, to treat people suffering from liver failure. This work was funded by the Canadian Institutes of Health Research and the Stem Cell Network.

"We began to see results soon after starting the project," says Dr. Paganelli. "The initial experiments were successful, which gave us the confidence to explore the approach further. We progressed from an idea to meaningful pre-clinical data in less than two years."



Morphocell was created in 2018 to enable the founders to secure the private funding and other resources required to move its product forward.

Morphocell's cell-based product, ReLiver<sup>™</sup>, is a unique, allogeneic stem cell-derived technology capable of immediately replacing liver function when it is implanted. The tissue is fully matured in the lab prior to implantation and does not need weeks or months to take effect. Further, immunosuppression is not required thanks to an innovative encapsulation approach.

ReLiver<sup>™</sup> is the foundation of Morphocell's current treatment pipeline, which is focused on acute and acute-onchronic liver failure.

Dr. Paganelli reflects on what the treatments could mean once they are available. "If treatments work as we

expect, we might avoid liver transplants in up to 80 per cent of patients with acute liver failure, saving lives and also significantly reducing costs for health systems." Then the team will move on to focus on treating chronic liver disease, which is the cause of two million deaths worldwide annually.

2019 was a good year for Morphocell: It closed a round of seed funding in July, raising more than \$1M, opened its own lab within the research centre of the CHU Sainte-Justine and expanded its leadership team by hiring Dr. Jennifer Moody as Chief Operating Officer.

Morphocell engaged CCRM to support the completion of one of the year's key milestones. Executing on tech transfer and process development, we de-risked a key manufacturing hurdle required for clinical trials, and advanced the company towards a valuable inflection point. CCRM also provided regulatory expertise to support the company's interactions with Health Canada.

Although Morphocell is enthusiastic about its research results and optimistic as it embarks on clinical trials, Dr. Paganelli reminds us that it could take five to seven years before Morphocell's treatments are available to patients. But, if proven effective, ReLiver<sup>™</sup> will be a game changer for millions of people around the world.

# TRANSLATING DISCOVERIES INTO TREATMENTS FOR INTRACTABLE BRAIN CANCERS

As a child reading books in the library of her father, a psychiatrist, Dr. Sheila Singh became enthralled with the works of Sigmund Freud and dream interpretation. She found what she read about the brain fascinating and was surprised to learn that it was only the tip of the iceberg.

> Dr. Singh, now a pediatric neurosurgeon, was motivated to further the understanding of the brain and how it connects to humanity. Traversing into this uncharted territory has led Dr. Singh to her current roles: Scientist at the McMaster Stem Cell and Cancer Research Institute; Professor at the Department of Surgery, Division of Neurosurgery, Faculty of Health Sciences, McMaster University; Canada Research Chair in Human Cancer Stem Cell Biology; and, CEO and Co-Founder of Empirica Therapeutics.

The Singh Lab was established in 2007 to investigate challenging types of brain cancers: adult glioblastoma (GBM), pediatric medulloblastoma and brain metastasis (BM). The team aims to uncover new targets, information to inform patient prognoses, and therapeutic modalities.

The first focus of the Singh Lab, adult GBM, robs people of their neurological function. The public's awareness of GBM has grown as high-profile individuals have been diagnosed with it in recent years. Median survivorship is just 14 months, and no major breakthroughs have increased the survival rate above four per cent.

After being awarded the largest teambased cancer research grant from the Terry Fox Research Institute in 2016 (a Terry Fox New Frontiers Program



Project Grant), Dr. Singh worked with researchers and clinicians to foster a translational pipeline of new antibodies and immunotherapy-based treatments for GBM.

Once promising therapeutics were discovered through this pipeline and were ready for translation to clinical trials, a spin-out company called Empirca Therapeutics was formed.

"As a classically-trained neurosurgeon and scientist, and being very academic, I'm the last person who I would have thought would be driven to commercialize discoveries," says Dr. Singh. "The creation of Empirica was by necessity because treatments for brain cancer are an underperforming area for industry. I realized I had to engage the right people to help me create much-needed new therapies." Established in 2018, Empirica Therapeutics creates new therapeutics emerging from understanding the biology of intractable brain tumours. Dr. Singh founded Empirica with Dr. Jason Moffat, an expert in functional genomics and gene-editing platforms at the Donnelly Centre at the University of Toronto.

GBM is the target of Empirica's first product in its preclinical pipeline. Called eCAR-133, the therapy targets treatmentrefractory disease reservoirs, showing preclinical efficacy against recurrence of the disease. eCAR-133 is based on genetically-engineered T cells with chimeric antigen receptors (CARs) that bind to CD133, which is an essential marker of the cancer stem cells present in therapy-resistant GBMs, recognizing and killing the cancer cells. This product can be also tested in BM with high levels of the CD133 marker. Dr. Singh credits CCRM's support for Empirica's advancement. We provided expertise in regulatory affairs to aid successful liaisons with Health Canada, and in finance and investing to build financial models and attract other investors. CCRM was the second investor in the company. Empirica is our eighth portfolio company.

For scientists who are interested in following in her footsteps, Dr. Singh shares some advice. "Scientists make keen observations. Once observations are documented, they become data. If you follow the data, you will reveal truths about the world around you. This takes you out of your comfort zone, but that's good because it's how you discover new things."

#### FEATURED STAFF

## FROM THE SMALLEST DETAIL TO BIG THINKING, OUR EXPERTS HAVE YOU COVERED

#### HONG CHANG PhD, MD, Quality Control Manager

Hong leads the quality control team for client-based projects in CCRM's Centre for Cell and Vector Production (CCVP). Her team monitors the clean rooms of the facility and conducts analytical testing to ensure the quality of products is properly maintained during the manufacturing process. Before joining CCRM, Hong gained experience in the pharmaceutical industry and in clinical medicine and academic research in molecular and cellular biology.

#### JASON DOWD PhD, Vice President of Science and Technology

Jason has over 19 years of industry experience in regenerative medicine, research, development and Good Manufacturing Practices. He has successfully brought cuttingedge technologies and therapeutic products to European, Canadian and U.S. markets. Dedicated to innovation, Jason joined CCRM to advance technology translation and bridge the protocol and process development pipeline to the manufacturing stage of cell and gene therapies for clinical use.

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of CCRM employees have graduate level degrees and 85% come from STEM disciplines. We have 68 women and 48 men on staff.



72%



#### LORI ISEMAN MSc, Senior Project Manager

Lori manages the portfolio of projects executed in CCVP. She helps customers build strategic plans and timelines to create budgets for Phase I/II clinical work done in the clean rooms and viral vector suites. Lori studied neuroscience at the University of Toronto and began her professional career in regulatory affairs prior to moving to project and client management.

#### VANJA MISIC PhD, Development Scientist II

Vanja specializes in process development and scale-up of viral vector manufacturing. He is part of the team working in the Centre for Advanced Therapeutic Cell Technologies (CATCT). To help overcome challenges in the manufacturing of cell and gene therapies, Vanja brings leadership in technical expertise, strategy and planning, as well as a passion for innovation.

### TAILORING A TRAINING PROGRAM THAT OFFERS NEW, AND TRIED AND TRUE

If it ain't broke, don't fix it right? CCRM's training and education program is well established at this point, but there's always room for something original.

In April, CCRM hosted our first event dedicated to investing in cell and gene therapies. More than 130 local and international investors and entrepreneurs gathered inside JLABS @ Toronto to network and discuss what's on the horizon for the hottest sector in biotechnology. The event was held in partnership with TOHealth! and Johnson & Johnson Innovation during Toronto's Health Innovation Week. Planning is already underway for a repeat event in March 2020.



The following month, we launched an online resource for those seeking answers to technical questions pertinent to working with a contract development manufacturing organization (CDMO). The CDMO Education Centre, on our website, draws on the knowledge of our skilled technical teams to educate visitors about challenges and trends in process development and manufacturing of cell and gene therapy products for clinical use and therapeutic applications. New blog posts are published regularly and cover viral vector production, CAR T manufacturing, quality control, media development and more.

The Business of Regenerative Medicine was held in Boston, Massachusetts, with

the Harvard Stem Cell Institute hosting this repeat summer event for venture capitalists, entrepreneurs, ecosystem advocates, and scientific leaders. New in 2020, CCRM Australia and the NSW Stem Cell Network are hosting the Business of Regenerative Medicine Asia Pacific in April. Visit our website for details.



For graduate students, post-docs and early-career researchers, we've continued to build on the success of existing events. Here's a partial list of where we partnered to leverage our collective ability to train Canada's future leaders.

- CellCAN's second pan-Canadian Strategic Forum on Cell & Gene Therapy. The conference brought together national and international experts to explore the most recent technological innovations in cell and gene therapy manufacturing and commercialization strategies.
- Medicine by Design's third installment of its popular Summer by Design program invited local and international PhD candidates and postdoctoral fellows to participate in an intensive two-week commercialization program also intended to build a collaborative international network.



- The Clinical Translation Education Group (CTEG) hosted its third annual workshop highlighting new tools and current trends shaping and disrupting the biotherapeutics industry. CTEG is comprised of BioCanRx, CCRM, CellCAN, Ontario Institute for Cancer Research, Ontario Institute for Regenerative Medicine and Stem Cell Network.
- The Till & McCulloch Meetings, hosted in partnership with Stem Cell Network, saw the largest number of attendees in its eight-year history as Canada's premier stem cell conference. Next year we head west, to Vancouver, British Columbia.



### OIRM CATALYZES INVESTMENTS INTO CURES

The Ontario Institute for Regenerative Medicine (OIRM) is a non-profit stem cell institute dedicated to transforming discoveries into clinical trials and cures. Through its commitment to collaboration and partnerships, including its commercialization partnership with CCRM, OIRM leverages resources to support promising advances.

Since 2015, OIRM has invested \$7M into CCRM's business development and technology platforms. In return, our experts provide advice on patents, commercialization and regulatory affairs, and our scientists conduct development work in our lab to advance the projects of OIRM investigators. It's an important partnership that benefits both groups and especially OIRM's funded scientists.

For example, OIRM invested almost \$2.5M in the initial research for the

technologies that led to BlueRock Therapeutics and Notch Therapeutics, which were then supported through CCRM's commercialization platform.

Progress this year includes the following:

- conducting 25 commercialization consulting engagements with OIRM investigators;
- generating 39 iPSC lines for OIRM investigators; and,

• completing 12 gene editing projects for OIRM investigators.

OIRM and CCRM also partner on educational events for the next generation of Ontario's stem cell scientists (see page 14).

Together, we train, support and enable Ontario's stem cell leaders to turn yesterday's discoveries into tomorrow's cures.

#### MEDICINE BY DESIGN

### POSITIONING TORONTO'S REGENERATIVE MEDICINE ECOSYSTEM FOR GLOBAL IMPACT

Medicine by Design has launched the next phase in its mission to strengthen Canada's global leadership in regenerative medicine with a new \$20M investment in multi-disciplinary, multi-institutional research at the University of Toronto and its affiliated hospitals.

The portfolio of 11 projects spans stem cell-based therapies for the treatment of heart failure and other common and debilitating diseases, to technologies to enable large-scale cell manufacturing. It harnesses Toronto's world-class research excellence in life and physical sciences, engineering, computer science and medicine. A renewed partnership between Medicine by Design and CCRM will accelerate the breakthroughs and new technologies that emerge from this research toward impact for patients and the economy. In addition to a full range of consulting services, CCRM is providing strategic support to Medicine by Designfunded investigators focused on defining pathways for early-stage translation. Medicine by Design and CCRM are also working together to develop and promote Toronto's and Canada's regenerative medicine ecosystems and increase capacity to turn new regenerative medicine discoveries into better health outcomes and jobs.



### **KEY FUNDERS**





Agence fédérale de développement économique pour le Sud de l'Ontario



### **FOUNDING INSTITUTIONAL MEMBERS**









ASSOCIATE INSTITUTIONS











THE UNIVERSITY OF BRITISH COLUMBIA

### CURRENT AND FORMER\* PORTFOLIO COMPANIES





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• Mesentech





herapeutics

EMPIRI



### **COLLABORATIVE PARTNERS**













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1000 scientists. One goal. Discovering cures.









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### **INDUSTRY CONSORTIUM**

CCRM has established a consortium of more than 100 companies that represent key sectors of the regenerative medicine industry, including therapeutics, devices, reagents, and cells as tools. These companies range from multinational corporations, to small-medium enterprises, to emerging start-ups. They have been able to utilize the translational platforms developed by CCRM to enable new opportunities and address real-life bottlenecks in their businesses.

CCRM would like to acknowledge the valuable relationships that have been fostered with these companies. We believe all parties have benefited from the synergies created through the industry consortium.

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#### **CCRM**

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