Commercialization of Regenerative Medicine Science: The BlueRock Opportunity in Toronto[1]

It was October 15, 2016, and Michael May, CEO of CCRM, was excited about the prospect of his team playing a key role in BlueRock Therapeutics, a biotechnology company being formed by Versant Ventures and the Bayer Life Science Center (BLSC), a division of Bayer AG (Bayer). After six months of competitive market analyses, intellectual property landscaping exercises, and negotiation of numerous agreements amongst multiple parties, May hoped that the commercialization and cell manufacturing expertise of his team would be well placed to help the new company achieve its technical and strategic objectives.

At the same time, May recognized that supporting such a groundbreaking start-up would have real risks. This was because the size, scale and complexity of the venture was unprecedented, with the skills and resources required for success dependent upon a globally distributed ecosystem of partners who would need to work effectively and collaboratively for years to come.

Looking ahead to the November 30, 2016, provisional deadline for concluding a deal that would bring BlueRock to life, May wanted to make doubly sure that the strategic logic for CCRM's participation was sound, and that his organization was prepared to help the new venture succeed. This left him with several questions to consider. Was the BlueRock opportunity truly a strategic fit for CCRM? What rewards could CCRM earn from the deal, and what risks went along with these potential gains? How could May and his team develop a sufficient understanding of the other ecosystem partners to trust their intentions and capabilities, knowing CCRM was not party to all the agreements being negotiated?

CCRM BACKGROUND

CCRM (known legally as the Centre for Commercialization of Regenerative Medicine) was a not-for-profit, public-private consortium founded in 2011. During the creation of BlueRock, CCRM was preparing to relocate within the Medical and Related Sciences (MaRS) Discovery District, Canada's largest government-sponsored entrepreneurial support hub. MaRS itself was surrounded by Canada's largest hospital and research network, in the heart of downtown Toronto.

CCRM's vision was to accelerate the commercialization of cell and gene therapies and associated enabling technologies, while positioning itself as a value chain partner for regenerative medicine firms. To this end, CCRM was organized around five distinct sets of activities:

- *Build*: provided business development resources related to due diligence on intellectual property (IP), along with business planning and regulatory consulting services.
- *Advance*: offered scientific and technical expertise in support of cell reprogramming and engineering, cell differentiation and protocol development, and technical assessments.
- *BridGE*: strived to overcome gaps to industrial scale manufacturing by offering process development services and performing cost and risk analysis through the Centre for Advanced Therapeutic Cell Technologies (CATCT), which was established in 2016 in partnership with GE

[1] This case, which provides the basis for classroom discussion, was prepared by Tom Gleave and Will Mitchell, Anthony S. Fell Chair in New Technologies and Commercialization and Professor of Strategic Management at the Rotman School of Management, University of Toronto. Support for creating the case was provided by Medicine by Design, University of Toronto, an initiative funded in part by the Canada First Research Excellence Fund. Eric Soller of Versant Ventures provided invaluable suggestions. We greatly appreciate insightful input from multiple knowledgeable contributors.

Healthcare.[2]

- *Deliver*: planned to offer a Good Manufacturing Practices (GMP) facility that complied with regulatory best practices and procedures related to the conducting of clinical trials, expected to open in 2018 in partnership with the University Health Network (UHN).
- *Launch*: supported the establishment of new start-up companies with diligence, seed funding and interim management.

In the five years it had been operating, CCRM had grown to 70 employees and leveraged its initial government funding of CAD$15M to almost CAD$100M in public and private financial support. With the completion of the GMP facility, its staff would rise to 100. It had supported the launch of three portfolio companies — AVROBIO, KisoJi Biotechnology, and ExCellThera — which had all subsequently secured financing to support clinical trials. Meanwhile, CCRM had started to scale its commercialization model by establishing global partnerships in other regions with strengths in regenerative medicine, including Australia, Netherlands, Japan and Israel.

As a key value chain partner in the emerging BlueRock ecosystem, CCRM would be expected to serve as the new venture's manufacturing partner based on its ability to support scalable production of pluripotent stem cells and their differentiation into different types of therapeutic cells.

THE BLUEROCK ECOSYSTEM

The vision of BlueRock Therapeutics (BlueRock) was to become a leading regenerative medicine company that would develop best-in-class induced pluripotent stem cell therapies to address diseases associated with significant cell loss and diminished self-repair. With its headquarters in Toronto, the biotechnology company would leverage the expertise of local and international partners, including the McEwen Centre for Regenerative Medicine, UHN and CCRM, all based in Toronto, along with Memorial Sloan Kettering Cancer Center in New York City and iPS Academia Japan in Kyoto.

Versant Ventures from Silicon Valley and BLSC based in Leverkusen, Germany, were the two investors backing the new firm. The funding they expected to provide would include initial start-up payments as well as ongoing payments based on specified development milestones as products moved toward potential commercialization.

BlueRock planned two initial therapeutic programs. One focused on the regeneration of cardiac muscle in heart attack patients or those who suffered from chronic heart failure, both of which were leading causes of morbidity and mortality worldwide. The second was related to therapies being developed to help restore neurons that secrete dopamine in Parkinson's disease patients, another significant unsolved global health problem. The scientific foundations of the research streams would provide the basis for moving towards the downstream stages of clinical trials, regulatory approvals, commercial production, and market entry, whether within BlueRock or via other firms.

The foundational science behind the cardiac program was being led by Dr. Gordon Keller, Director of the McEwen Centre for Regenerative Medicine, based within UHN in Toronto. Established in 2003 following a CAD$10 million donation from local philanthropists Rob and Cheryl McEwen, the Centre coordinated research amongst 15 leading stem cell scientists working at five hospitals within UHN.[3]

Keller was widely considered one of the world's top stem cell scientists, most notably for his research that led to a process for converting embryonic stem cells into heart cells and other mesoderm cell types. After returning from New York City to his native Canada in 2007 to lead the Centre, his research activities

[2] CATCT was funded by the Government of Canada through FedDev Ontario and by GE Healthcare, each contributing CAD$20 million to the manufacturing facility.

[3] In 2007, the McEwens contributed a further CAD$10 million to support the Centre's research.

focused on restoring the electrical and contractile function of injured hearts through remuscularization using pluripotent stem cell-derived cardiomyocytes.

Keller knew that he would need to prepare for pre-clinical validation and clinical trials that would be needed to take his science to the next stage. In 2015, he persuaded Dr. Michael Laflamme to leave his position at the University of Washington in Seattle to join UHN. Laflamme is a world-leading translational stem cell scientist.

BlueRock's Parkinson's disease program originated from the lab of Dr. Lorenz Studer at Memorial Sloan Kettering in New York City, an institution that had earned a global reputation for supporting clinical research and trials that had the potential to develop therapies for a range of debilitating diseases. Based on research that showed the potential for directly treating Parkinson's through replacement therapy using stem cell-derived dopamine-producing neurons, Studer received US$14.9 million in funding from the Empire State Stem Cell Board (NYSTEM) in 2013, and in 2015 he was named a MacArthur Fellow (also known as "genius grants"). Given progress to date, Studer and his colleagues expected to start conducting their first-in-human trials in the near future.

The platform around which BlueRock was being established required a licensing agreement with iPS Academia Japan. The Kyoto-based organization controlled critical IP related to induced pluripotent stem cell protocols based on the research of Dr. Shinya Yamanaka, who discovered that mature cells can be reprogrammed to become pluripotent. For this discovery, Yamanaka won the 2012 Nobel Prize (in physiology or medicine), along with Sir John B. Gurdon, whose separate pioneering discoveries were developed at Oxford University in the 1960s.

Versant Ventures was a major investment firm with substantial experience with health sector entrepreneurs. The firm invested across the health-care sector and at all stages of company development, with an emphasis on the discovery and development of novel therapeutics. With US$2.3 billion under management and offices in North America and Europe, Versant had built a team with deep investment, operating, and scientific expertise that enabled a hands-on approach to company building. Since the firm's founding in 1999, more than 65 Versant companies had achieved successful acquisitions or initial public offerings (IPOs).

After establishing its Canadian operations in Vancouver in 2011, Versant became one of the most active biotechnology start-up investors in the country with significant series A rounds for Inception 4, Turnstone Biologics, Northern Biologics and Repare Therapeutics. Much of the background research and due diligence that went into making these investment decisions came from Blueline Bioscience, a biotechnology discovery engine that Versant established at MaRS in Toronto.

BLSC was established in 2015. Bayer, BLSC's parent, was as German-based player in health care and agriculture, with over 100,000 employees worldwide. The mandate of the strategic innovation unit was to make significant equity investments in promising, early-stage R&D technologies as well as participate in the building of companies and the creation of their IP.

BLSC's investment approach was based on the premise that a combination of leading technologies was necessary to develop therapeutic breakthroughs. Recognizing that the ability to operate across scientific domains was often constrained by scattered IP landscapes, it was able to call upon its sister Bayer business units to leverage internal IP and expertise to increase the probability of success of its invested companies.

ASSESSING THE OPPORTUNITY

Viable therapies for cardiac-related diseases and Parkinson's disease had "blockbuster" potential in the global health-care market. In the United States alone, approximately 1.5 million heart attacks and strokes occurred every year, with about 800,000 people dying from cardiovascular disease annually. At the same time, the annual cost of heart disease and

strokes was estimated to be US$317 billion, about one-sixth of all national health-care expenditures.[4]

In the case of Parkinson's, as many as one million Americans suffered from the disease, more than those diagnosed with multiple sclerosis, muscular dystrophy and Amyotrophic lateral sclerosis (commonly known as Lou Gehrig's disease) combined. Total direct and indirect costs, including treatments, social security payments and lost income due to the inability to work, were estimated to be nearly US$25 billion annually, with medication costs averaging US$2,500 per patient per year, and therapeutic surgeries costing up to US$100,000 dollars per patient.[5]

Historically there had been a lack of applied innovation in both major disease areas. Few approved bio-pharma products in the market addressed these conditions effectively.

Given the significant global market potential of the cardiac and Parkinson's-related therapies, Bayer and Versant were prepared to pool over US$200 million to fund BlueRock. This would make it one of the largest-ever series A financings for a biotechnology company.

New York-based Eric Soller was hired by Versant as an Entrepreneur-in-Residence with an immediate mandate to coordinate and finalize the various agreements needed to establish the company, with a view towards providing strategic management oversight and operations support if the start-up was launched. Soller had completed a PhD at the Massachusetts Institute of Technology focused on induced organ regeneration and had previously worked as junior partner at McKinsey & Company.

In sizing up the potential of the start-up, Soller outlined the horizons around which Bayer and Versant justified their investment interests:

> *Initially BlueRock would focus on the ability to develop and deliver an appropriate cell therapy to replace the lost cell type for patients suffering from cardiac tissue damage or Parkinson's disease. A breakthrough in either area, in and of itself, could be a blockbuster by normal industry standards given the high unmet need, lack of historical innovation, and size of the global addressable patient population for both therapies.*
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> *In the mid to long term there was the possibility to develop an industry-leading allogeneic platform for truly "off-the-shelf" therapies that could extend treatments originally intended for moderate to severe patients to patients who suffered from less severe but still debilitating forms of the diseases and to develop additional cell therapy products to target an even wider array of degenerative conditions affecting organs beyond the brain and the heart.* [6]

Apart from assessing the general global market potential and technical risk of the initial therapeutic programs, Bayer and Versant needed to consider competitive dynamics, as well as possible locations for forming the BlueRock ecosystem. Based on Versant's global competitive market and IP landscaping analyses, several academic and commercial regenerative medicine hubs had been identified that could potentially become BlueRock partners, including the California Institute for Regenerative Medicine and City of Hope (California), Wisconsin Alumni Research Foundation, the Cell and Gene Therapy Catapult in London, U.K., iPS Academia and numerous potential academic programs in Japan, and UHN and CCRM in Toronto.

During its analysis, Versant concluded that none of these centres was close to securing a dominant market position. Major uncertainties

[4] *Million Hearts. Costs and Consequences*. Accessed June 3, 2017 from: https://millionhearts.hhs.gov/learn-prevent/cost-consequences.html

[5] *Parkinson's Disease Foundation. Statistics on Parkinson's*. Accessed June 3, 2017 from: http://www.pdf.org/parkinson_statistics

[6] Allogeneic therapy aims to avoid rejection of the cell product by the patient's immune system and can take two general forms: the first matches donor cells to a patient and the second modifies the cell product to evade the patient's immune system. In contrast, autologous therapy avoids immune rejection by using stem cells derived from the patient's own body. Source: http://www.cancercenter.com/treatments/allogeneic-stem-cell-transplant/

about the science, technology, regulations, business models and general market acceptance underpinning the different efforts still existed. Consequently, Versant and Bayer both believed there was legitimate potential to be an early market leader in developing specific cardiac and Parkinson's disease therapies, provided that a complementary ecosystem of support partners could be assembled.

After discussing the global competitive market and IP landscapes at length, Bayer and Versant decided that Toronto was the best city for establishing BlueRock's primary R&D footprint. One reason for this decision was the quality of the stem cell research and regenerative medicine capabilities at the McEwen Centre and within UHN. The fact that Keller was director of the McEwen Centre and a proposed scientific co-founder of the start-up would give BlueRock a high degree of scientific credibility worldwide, with this reputation reinforced by having Laflamme as the translational partner. In addition, UHN's Office of Technology Development and Commercialization was readily positioned to help negotiate commercialization agreements for the scientists' work. Moreover, the foundational research would have ready access to CCRM's business, technical and manufacturing support services, all of which would be co-located in the same building at the MaRS Discovery District.

Apart from science-related considerations, Canada's regulatory environment and history of public and private support for stem cell research and development were viewed positively by both Bayer and Versant. For example, despite stem cell research being considered controversial in some other countries, in 2015 the federal government awarded the University of Toronto CAD$114 million, the largest single research award in its history, to support Medicine by Design. This initiative, which was co-located with CCRM in the MaRS Discovery District, brought together cross-disciplinary researchers from across the university and its affiliated hospitals to advance the design of cells, materials and therapeutics towards commercialization. This was followed within a year with a CAD$20 million contribution to support the establishment of the CATCT at CCRM, which was matched by GE Healthcare.

In rationalizing Toronto as the proposed base for BlueRock, Soller highlighted the merits of the location, while also pointing to potential limitations:

> *At first glance, some might not consider Canada or Toronto to be the most logical place to set up a category-leading stem cell and regenerative medicine company. Yes, there's an amazing research legacy, especially at UHN and the University of Toronto, but the leap to commercial viability has never been made. We (Versant) have a different thesis informed by what we have learned over the past five plus years since coming to Canada, our track record in forming leading, high-science companies here, and our ongoing efforts to build this cluster. We continue to believe there's great science coming out of Toronto and it's still woefully under-tapped.*
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> *For example, we soon came to appreciate the work of Gordon Keller and Michael Laflamme, whom we consider to be the cardiac cell therapy "dream team." Gordon is one of the very top foundational scientists in his field, with a demonstrated mastery of many different cell types, beyond cardiomyocytes. Michael provides exceptional translational capabilities that can help provide the necessary pre-clinical validation we will need before entering first-in-human trials.*
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> *Having them working together side by side at UHN on cardiac therapies is encouraging, and is especially appealing to Bayer as a strategic investor because of its deep history and desire to keep pushing the frontiers in this space, and its willingness to offer BlueRock cardiac expertise when and where it makes sense. Add to this the potential to extend Gordon's cells to other therapeutic areas and this makes the prospects even more appealing.*
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> *Gordon and Michael have also already shown a clear interest in commercializing their work by using their Ontario Institute*

for Regenerative Medicine (OIRM) funding to support the scale up of their cells at CCRM. That kind of foresight is rare for an academic team — it seems that they don't need to be educated or coached into participating. We believe the willingness is there.

Beyond this, UHN is one of the most respected hospital clusters in the world. The Princess Margaret Cancer Centre, for example, is one of the leading global centres when it comes to cancer treatments and research. So, over and above the cardiac research, we think there is potential for Versant and UHN to work together on sponsored research opportunities in other high impact areas.

Assuming success down the road with clinical trials, we would need capacity to significantly scale-up production of stem cell-derived products — the necessary cell dose can be quite high depending on the application — and we need to do it at a reasonable cost.

Some of this manufacturing expertise already exists elsewhere or could be built, but it would be a significant capital commitment for an early-stage venture. That's why we are looking to enter into a flexible and cost-effective arrangement with CCRM, one that won't lock up BlueRock's capital or commit us to contract manufacturing requirements before we are ready for large-scale production. It would be an added benefit to have a like-minded partner whose core mission includes commercialization and is part of a wider network and has the pulse of what's going on in regenerative medicine and stem cell science around the world.

There are a couple of potential drawbacks that we need to be mindful about in considering Toronto as BlueRock's R&D base. One is the limited availability of R&D management talent in the city relative to some of the more traditional clusters (Boston, San Francisco), meaning people who have the technical acumen, discipline, and proven track record to turn BlueRock's vision into reality. It's rare for traditional research-driven academics to gain this kind of industrial experience without relocating, especially in biotech clusters that are not as well-developed.

So we would likely need to attract top management talent from abroad to establish the company. The good news is that we have established a track record in recruiting talent to Canada to take leadership positions in our other portfolio companies, so this gives us some confidence we can do this with BlueRock, too.

There is also the issue of limited lab space. Can we find the right labs and the right amount of space in these labs? There is some space available at MaRS, but much of it has already been committed to other entities. The cooperation agreement between CCRM and GE Healthcare may increase on-demand contract capacity and consulting talent to balance this risk, although this is a new initiative and will need some time to get set up.

Finally, there have been some questions about the curious mismatch between the science being undertaken in Toronto and the dearth of private-sector investment supporting its commercialization. The federal and provincial governments are clearly willing to support the foundational science and, to some extent, manufacturing capabilities. But we would like to see more investment from other sources, and that hasn't happened yet. We're accustomed to doing the heavy lifting of building new biotechs, but it would be better for the ecosystem if Toronto could attract more commercial anchors and private investors — we think this would help grow the pie for everyone.

From the German perspective, Lucas Martin, Director of Early Licensing and the key person negotiating on behalf of Bayer based out of its West Coast Innovation Centre in San Francisco, identified additional benefits of having BlueRock based in Toronto, while acknowledging some potential risks:

The University and hospitals in Toronto have been supporting stem cell research for a long time, going back to the sixties.[7] There is clearly significant public, private and philanthropic support that has been driving things forward for decades. So, in addition to having access to world-class researchers, facilities and manufacturers, we think there are stable and supportive government partners who want the research to succeed. The risk that the government would change policies in a way that impedes the research seems low.

All of this said, it is still very important for Bayer that clinical guidelines meet international standards. If products were eventually approved for use in Canada, would this bode well for approvals in other markets? This remains an open question. There are no guarantees that the U.S., for example, will approve a cardiac therapy developed in Canada. There is still risk involved.

Bradly Wouters, UHN's executive vice president for science and research, also highlighted the strength — and challenges — of Toronto being BlueRock's R&D base:

The Toronto ecosystem is starting to pay off — it takes time to build. You need to get some big deals done to get the ball rolling. Some critical mass within the network is needed to get feedback from the parties involved.

The big gap for Toronto now is management talent and disciplined commercial acumen. It's an unnatural path for traditional research-driven academics to move into business. So we need to attract top management talent from abroad.

In the case of another life sciences company at MaRS, they were able to attract the former Chief Scientific Officer (CSO) for a major pharmaceutical company to move to Toronto, and she was able to attract six others from the States, even as far away as Texas. So far they are staying here — the question is will they do so over the longer term?

EVOLUTION OF A DEAL IN PROGRESS

According to CCRM's Michael May, two independent pathways converged to help bring together several of the parties involved in the BlueRock negotiations:

One path started back in 2012, with CCRM's board approving the CCRM's first project — the scale-up of Gordon Keller's cardiomyocyte production. Working with Gordon logically led to discussions about starting an induced pluripotent based therapeutics company based on Gordon Keller's reputation and scientific IP, and CCRM's manufacturing know-how.

The second path came about after Bayer tasked Versant with creating a strategic company that had the potential to make significant breakthroughs in iPS cell therapeutics. Dr. Stefan Larson, one of our [CCRM's] Investment Committee members at the time, was also the CEO of Northern Biologics, an antibody platform company founded by Versant based here at MaRS. Stefan (and likely others) pointed Versant towards Gordon Keller, and the circle was complete.

After the Versant and Keller connection was made, the venture capital company informed Bayer about its findings, with a view towards possibly co-investing in a new induced pluripotent stem cell company. As Bayer's Lucas Martin recalled:

Both companies have been very interested in stem cell research for many years. In fact, we had been incubating something like a BlueRock before the opportunity presented itself with a clearer view, as had Versant. Our relationship goes back several years, and our teams are very complementary. We have worked together on other investments

[7] In 1961, working at the Ontario Cancer Institute in Toronto, James Till and Ernest McCulloch demonstrated the existence of multipotent stem cells, based on studies of radiation on the bone marrow of mice.

already, most recently on Casebia.[8]

We are a very well established global company with long-standing capabilities related to drug discovery and we have a full pipeline of cardiology treatments. We also have enormous R&D resources that we are willing to use to back smart research investments. Versant is smaller, but is more nimble in many ways, and has a strong grip on what science is taking place around the world, and has deep experience building and supporting start-ups.

So it's no surprise that we converged on this opportunity. We are now looking to establish an independent biotech that will be given a high degree of operating autonomy as well as be able to compete for capital on the open market.

In mid-2015, after the two investors agreed to back the BlueRock venture in principle, Versant was tasked by Bayer to lead a global market opportunity and IP landscaping analysis. Based on the findings from these activities, in early 2016 Versant approached CCRM, the McEwen Centre, UHN, Memorial Sloan Kettering and iPS Academia Japan with the hope of securing each party's participation in the new company. In approaching the opportunity, Versant and Bayer shared a philosophy that ran counter to practices that were common in the venture capital industry. Eric Soller explained:

For many reasons we (Versant and Bayer) both feel the time is right to build an independent, category-leading pluripotent stem cell company. We are also well aware that our management team needs to get a lot of things right to build this company well — including perfecting the science for each cell product, recruiting a team of the best technical talent we can find, aggregating multiple technologies to build an industry-leading pluripotent stem cell technology platform, and scaling the production of our cell therapies for clinical and eventually for commercial use.

This is why we are all prepared to commit to a very substantial series A funding round, perhaps US$200 million or more. By contrast, many promising biotechs in this sector might secure $20 or $30 million for their first round of funding. That's substantial by many standards, although it might be insufficient to get to mid-stage clinical trials, particularly for a company with our strategic mandate (breadth of focus) that is working to develop relatively cost-intensive cell therapies.

We want our team to be able to focus on getting the science and scalability right without having to worry about going out to raise additional rounds of funding every 12 to 18 months. If we can pull this off that's a real advantage for our team and partners — and if we're successful we'll be validating a new model for the formation of next-generation biotech companies.

The person at CCRM mandated to lead its negotiations with Versant was Jennifer Moody, Vice President of Business Development, whom Michael May brought into the picture in March 2016. In characterizing her impressions of the negotiation process, Moody stated:

At the start, we were focused mainly on assessing the IP landscape. In my first meeting there were eight people, five of whom were lawyers from Bayer, plus Eric Soller and the lawyer from Versant, and myself. Everyone was focused on de-risking the investment by looking at IP umbrellas. We needed to make sure that we had the freedom to do what we hoped to do.

As the process has evolved, discussions have become more intense. At CCRM, our lawyer and I have been entirely devoted to coming to an agreement with Versant at the expense of our other work. One of the agreements we are working on involves the licensing of IP related to manufacturing.

[8] Casebia Therapeutics was a joint venture founded in Cambridge, MA, by Bayer and Basel-based CRISPR Therapeutics (a gene-editting venture). Casebia' mission was to discover, develop and commercialize therapeutics designed to cure blood disorders, blindness and congenital heart disease. Versant was an investor in CRISPR and provided investment and management advisory services in completing the Casebia deal in early 2016.

The other focuses on the ongoing enablement of manufacturing solutions in anticipation of BlueRock's evolving operations.

It has been a complicated process and a real learning curve for us at CCRM. Actually, for everyone, I believe. This is because of the complexity and nature of the organization that we are all trying to help create and support.

But as complicated as it has been for us, it must be amazingly complicated for Eric. He, more than anyone, has been driving the whole process. He has also had to simultaneously manage eight or ten different agreements amongst all the parties involved. CCRM only needs to finalize two agreements.

From his arms-length perspective, Michael May offered his view of the evolving deal-making process:

Bayer has significant resources that it is bringing to the table and Versant has the expertise needed to understand what is possible in terms of platform creation. From where I stand, Bayer seems to be acting like an oversight committee, something you would expect from a strategic investor. Meanwhile, Eric has been leading the charge, including the assessment of what IP exists and which scientists and organizations around the world should be part of BlueRock. This must be a complicated and demanding process.

Eric has a real sense of urgency in what he is doing. In my experience, he certainly has been moving the process forward much faster than would typically be the case if an investor was working with an academic alone. It can't be easy because there are probably 10 to 20 people involved at any given time, with multiple ongoing discussions that are not always transparent to all the parties. This requires that we have a substantial level of trust amongst each other to make this work.

After all, the platform being created is quite complex. It would bring together the foundational IP from a Nobel Prize-winning scientist, the IP from two scientific co-founders who are living in different cities researching different therapies, plus our own manufacturing IP at CCRM. And some of the IP that has been developed must reflect commitments that already exist.

Presuming all of this gets sorted out, Versant will still need to identify and propose the management team who would take things forward, and it is far from clear who those people would be or where they will come from. Nobody in Toronto comes to mind who might be able to weave all these pieces of the puzzle together, including knowing what cell developments should be supported, what scalability models should be used to convert lab IP into pre-clinical validation and clinical trials, what regulatory hoops to jump through and, ultimately, how to bring presumably successful R&D to market. We (at CCRM) can help those who are brought on board, although it will still take some heroic leadership to make all of this happen.

LOOKING AHEAD

With the provisional negotiation deadline of November 30, 2016, just six weeks away, Michael May pondered the enormous opportunity solidifying in front of him, a perfect example of what CCRM was established to achieve. Was the deal right for CCRM and could CCRM live up to the demands of such a bold, complex new enterprise?

May also recognized that, even as the big picture vision underlying the BlueRock venture was becoming clear, the work of keeping multiple parties engaged to transform vision into reality remained. Who would actually lead and manage the company? What specific science would be supported? How would it scale and commercialize its science and technologies? How would the company be governed? The success of BlueRock would be based not only on the merits of extensive and rigorous market opportunity, IP landscaping and negotiation processes, but also a leap of

faith in the company's execution.

Exhibit 1: Overview of Stem Cells and Regenerative Medicine [9]

Stem cells are undifferentiated (or unspecialized) cells capable of renewing themselves indefinitely. This undifferentiated state means that a single stem cell has a unique capability to grow and generate a wide variety of specialized cell types under the right physiological conditions (e.g. muscle cells, neurons, heart muscle cells). Thus, they have the potential to provide a renewable, and virtually unlimited, source of cells to repair or replace damaged or diseased cells and tissues for conditions such as Parkinson's disease, Alzheimer's disease, spinal cord injury, heart disease, and diabetes.

Embryonic stem cells are derived from a very early stage embryo known as a blastocyst, which is a cluster of cells that resemble a hollow, microscopic sphere. Unlike adult stem cells, which are restricted to producing limited cell types, embryonic stem cells are pluripotent, and thus have the potential to generate every cell type in the body. Induced pluripotent stem cells (iPCS) are derived from blood or skin cells that have reprogrammed back into an embryonic-like state.

Regenerative medicine harnesses stem cells to repair, regenerate or replace diseased cells, tissues and organs. This multidisciplinary field includes several research areas, including:

Stem cell biology: investigates basic mechanisms of stem cells.

Cellular therapy: seeks to address many disease conditions that are caused by the malfunction or death of specific cell types. For example, heart failure may occur because cardiac muscle cells die or cannot function properly. Scientists are developing cellular therapies that seek to transplant live cells to replace defective cells in an attempt to restore normal function across a wide range of organs.

Tissue engineering: combines the principles of material engineering and bio-medical sciences to develop bio-artificial tissues and organs that can be used as "replacement parts" to repair damaged or diseased organs. The process generally involves growing various cell types onto three-dimensional scaffolds, which are then implanted into the patient. These scaffolds are carefully designed to allow the cells to develop into tissues that mirror the natural structure and function of the damaged body part.

[9] McEwen Centre for Regenerative Medicine (adapted) http://www.mcewencentre.com/discoverandlearn/regenerativedetails.php