The Empire Club Presents

MR. ROB MCEWEN IN CONVERSATION WITH DR. MICHAEL LAFLAMME

Welcome Address, by Barbara Jesson President of Jesson + Company Communications Inc. and President of the Empire Club of Canada

November 27, 2017

From the One King Street West Hotel in downtown Toronto, welcome, to the Empire Club of Canada.

Before our distinguished speakers are introduced today, it gives me great pleasure to introduce our Head Table.

I would ask each guest to rise for a brief moment and be seated as your name is called. I would ask the audience to refrain from applause until all of the Head Table Guests have been introduced.

HEAD TABLE

Distinguished Guest Speakers:

Dr. Michael Laflamme, Robert R. McEwen Chair in Cardiac Regenerative Medicine; Principal Investigator, McEwen Centre for Regenerative Medicine
Mr. Rob McEwen, Chairman and Chief Owner, McEwen Mining Inc.; Co-Founder, Goldcorp Inc. and the McEwen Centre for Regenerative Medicine

Guests:

Mr. Ron Aiello, Head of Institutional Equity Trading, Haywood Securities Inc.; Registered Representative, Haywood Securities (U.S.A.) Inc.
Ms. Vivien Clubb, Head, Marketing and Communications, IBK Capital Corp.
Mr. Alok Kanti, President and Chief Executive Officer, Bayer Inc.
Mr. Don Linsdell, Partner, Assurance Services, Ernst & Young LLP
Ms. Cheryl McEwen, Co-Founder, McEwen Centre for Regenerative Medicine
Mr. Michael Melanson, Partner, Bennett Jones LLP
Mr. Graham Moylan, Head, Canadian Investment Banking, Cantor Fitzgerald Canada
Corporation
Mr. Derrick Rozdeba, Vice President, Communications and Public and Government Affairs, Bayer Inc
Mr. William White, Chairman, IBK Capital Corp.; Director, Empire Club of Canada

My name is Barbara Jesson. I am the President of Jesson + Company Communications and the President of the Empire Club of Canada. Ladies and gentlemen, your Head Table.

We are pleased to welcome students from Centennial College. Thank you, IBK Capital Corp., for sponsoring our student table today. Students, please, rise and be recognized.

I was catching up on some reading on a flight last month, and I came across an interesting story about Canada in The Economist. Apparently, we are the world leaders in artificial intelligence. Who knew? The article began by asking how this breakthrough emerged in the land of moose and maple syrup and went on to describe the culmination of factors that have given us this edge in a field that has captured public interest.

The Economist could well have a similar reflection about our leadership in stem cell research. I share Stephen Hawking's watchfulness with regard to AI: HAL filled me with enough terror for two lifetimes with 'I'm sorry, Dave; I can't do that." But I have no such qualms about stem cell research. In Canada, it began with biophysicist James Till and cellular biologist, Ernest McCulloch, who published their studies on the incredible potential of stem cells in 1961. Together, they opened the door to a flood of research into regenerative medicine and invigorated the biomedical industry in Canada.

With stem cells, Canada finds itself on the cusp of innovation. Through both industry regulation and legislation, Canada has created an environment where research can flourish. Stem cell research was revolutionized in 2006 with the development of a technique to transform a normal, adult skin cell into a stem cell. The discovery of this method, called 'induced pluripotent stem cells'—say that twice—vastly expanded the opportunities for stem cell therapies.

The McEwen Centre for Regenerative Medicine, part of UHN in Toronto, has become a leader in the field. Today, stem cell research at the McEwen Centre is based on the work with embryonic stem cells, iPS cells as well as adult stem cells.

The really wonderful thing about the McEwen Centre is

that it is applying bench-to-bedside science to medical solutions today for patients with diabetes, heart disease, disorders of the blood and neurodegenerative disease. McEwen scientists were first in the world to pioneer the use of gene therapy to recondition donor lungs for transplant. They were the first in the world to identify heart progenitor cells from human embryonic stem cells, and they have become world leaders in the creation of beating heart cells for research worldwide.

Several years ago, I had the privilege of touring the McEwen lab and there is no way to describe for you the awe of seeing beating cells in a petri dish. I say fie to those touting the miracle of artificial intelligence. The real mysteries of life are being discovered right here at the McEwen Centre. All of this science is bringing us closer to new treatments for the most pressing medical challenges of our time, including heart disease, Alzheimer's, Parkinson's, diabetes and cancer.

Our three guests today are from the frontiers of this exciting push into research and treatment. We are honoured to be joined in conversation this afternoon by Mr. Rob McEwen, Dr. Michael Laflamme and Cheryl McEwen as well.

Mr. McEwen is the Chairman and chief owner of McEwen Mining Inc., a recipient of the Order of Canada and a member of the Global Advisory Counsel for the International Society for Stem Cell Research. Together with his wife, Cheryl, Rob has donated more than $50 million to encourage excellence and innovation in healthcare and education. Their donations have funded the establishment of the McEwen Centre for Regenerative Medicine and the McEwen Leadership Program at St. Andrew's College, among other schools and programs.

Cheryl McEwen is the Vice Chair of the Toronto General Hospital Foundation, the President and CEO of Make My Day Foods Inc., and the Co-Founder of the McEwen Centre for Regenerative Medicine. We are very grateful to both of them for being with us.

Dr. Laflamme is the Robert McEwen Chair in Cardiac Regenerative Medicine at the University Health Network and a Senior Scientist in the Toronto General Hospital Research Institute.

Dr. Laflamme completed a postdoctoral fellowship in the laboratory of Dr. Charles Murry, investigating the role of exogenous and endogenous stem cells in myocardial repair. His independent research career has been largely focused on the development of cell therapies based on human embryonic stem cells, and his laboratory has made many important contributions in their work with pluripotent stem cells.

Dr. Laflamme has been the recipient of honours, including the Society for Cardiovascular Pathology Young Investigator Award, the Perkins Coie Award for Discovery and the American Society of Gene & Cell Therapy Outstanding New Investigator Award.

Please, join me in welcoming Mr. Rob McEwen, Ms. Cheryl McEwen, and Dr. Laflamme to our stage.

Mr. Rob McEwen and Ms. Cheryl McEwen with Dr. Laflamme

RM: Good afternoon. Waiting times are a big issue—waiting times to see healthcare professionals, waiting times for operations. Raise your hand if you want shorter waiting times. Almost everyone. It is important to understand that waiting times are just a symptom; they are not the cause. The root cause of the strain that our healthcare system is under is money. It is money that the government does not have. It is money that in the future with soaring healthcare costs and other priorities. Unless we do something about it, unless we demand a change and look for other answers, we could have rationing of healthcare in this country, meaning there are certain things you will not get done or you will have to go somewhere else and pay for it.

In 2002, Cheryl and I spent a lot of time in the hospital. Early in the year, one of my sisters died. She was three years younger than I was. Four months later, my mother died. We saw a lot of the problems and the strain firsthand. It was really a wake-up moment. We decided that we would like to contribute to see if we could find a cure, a solution to some of these problems to improve healthcare for all Canadians. That was going to need something to address this growing problem. At that point, we decided to invest in regenerative medicine and stem cell research, and we funded the McEwen Centre for Regenerative Medicine.

In 2007—in January of that year—we attracted Gordon Keller, from New York, to join as a Director. He is a superstar in the field of regenerative medicine. New York Magazine, at the time, named him as one of the six people, one of the six doctors that New York City could not afford to lose. As Toronto, we benefited getting that talent here. Since Gordon has arrived, he has attracted strong talent from around the world, and we have many superstars in our organization now, and they are doing great things advancing the frontier of medicine.

Last December, there was a very exciting moment for the entire stem cell world. One of the largest commitments ever made to stem cell research was made by the German pharmaceutical company giant Bayer AG. They and their partner, Versant Ventures, formed a company called BlueRock Therapeutics that has an office here in Toronto in the MaRS Tower. They committed $225 million (US) for stem cell research because they believe that commercialization of this research is near at hand, and it will be an endeavour they want to be very strong in. Their objective was to fund the best research in the world. Their first stops were Toronto, New York and Boston.

I am delighted to say that of the two people that are key in their program, Dr. Laflamme and Gordon Keller, we are going to hear from one today: Founding investigator Dr. Mike Laflamme.

You are also going to hear, today, about regenerative

medicine, that it holds out the promise to profoundly change the delivery of healthcare. It is now my pleasure to introduce my wife to tell you more about regenerative medicine.

CM: Thank you, Rob. Good afternoon, everyone. I have a question, just like Rob had a question. I have a question: Why cannot Canada lead in stem cell therapies around the world? As Rob has stated, we have a healthcare crisis. The baby boomers are about to descend upon our hospital at an alarming rate. We need solutions. We cannot change medicine or provide new therapies without research. We need to understand the body at a cellular level. We need to replicate conditions of disease, models in order to stop, reverse, repair, or even cure those conditions or diseases. We need to develop less invasive ways to treat or regenerate our organs without actually having to replace them.

The good news is all of that is happening at the McEwen Centre. You will hear, today, about an exciting journey to provide new therapy to treat heart disease and how it can be commercialized, which means the entire world can benefit. The path to commercialization requires special ingredients. It requires a successful centre with a very bold vision alongside a clinical hospital. It requires a world-leading research magnet, like Dr. Keller, who attracts the best scientists in the world, like Dr. Laflamme. It requires secure funding, largely from private philanthropy that can accelerate 10–15 years of research into 3–5 years to produce results quickly.

You will hear, today, about the work of Drs. Laflamme and Keller. This is something to be proud of. Over $40 million of philanthropy has supported this advancement. We are very excited about the investment from Bayer to establish BlueRock. They are providing the next leg of capital now required to take this breakthrough to the patient. This demonstrates the path to new medical therapies. Early, private funding that produces results and then attracts industry—that is how it works. We have three other major success stories that are in transition to where venture capital would likely invest, but they still need help. If you are wondering about what you can do to help, there are opportunities.

We have pacemaker cells in development to create a biological pacemaker. That is going to be the next big breakthrough. We have pancreatic beta cells that produce insulin to eliminate the need for insulin injections for type 1 diabetics. We have the Harry Rosen Chair [in Diabetes and Regenerative Medicine Research], Dr. Cristina Nostro, who is now ready to work alongside a clinician scientist to take her research to the patient.

If I could do a shoutout to Harry Rosen, who is here today. Nice to see you, Harry, and thank you for your early support, and also to my mom, Joyce Mason, who is also here and has been an early supporter of this research.

We also have functional liver cells and tissue to pro-

vide new therapies for liver disease, like cystic fibrosis. These projects are ready to move.

Now, back to my question. Why cannot Canada lead in stem cell therapies? We actually can. Let us work together to fund the talented scientists who will make it happen. When we do, we can create a biotech industry right here in Canada. Thank you.

[VIDEO]

BJ: Please, join me in welcoming Dr. Laflamme to the podium.

ML: Good afternoon. Let me begin by thanking the Empire Club for the invitation and Rob and Cheryl for their support over the years and the great introduction to the topic of regenerative medicine.

I thought, in my presentation, I would go into a little more detail and give you an example about how we are trying to harness stem cells to treat a particular disease, a disease that I am interested in, which is heart disease. We are trying to regenerate hearts after somebody suffers a heart attack.

Before going into that, I should tell you a little bit about the type of stem cell that we are working with. These are so-called 'pluripotent' stem cells, which is the stem cell type that most of the investigators in the McEwen Centre are interested in. They are defined by this unique property in that they can differentiate or give rise

to all of the cell types that are present in the adult body. There are two flavours or types of pluripotent stem cells, if you will. The one that probably most of you are familiar with are embryonic stem cells. These are isolated from embryos that are left over from in vitro fertilization and are otherwise slated for discard as medical waste. It turns out we can isolate those cells. They are essentially immortal, so my lab has historically mostly used human embryonic stem cells that are from the original 1998 paper that described their discovery. They can go through many hundreds of population doublings and still retain the properties that they had at the beginning.

Again, the unique property of these cells is that they can differentiate into useful cell types. To do this, we use lessons from developmental biology, and so some of the signaling molecules that we know normally tells tissues to develop into the right cell type. And we capitulate that in the dish, and so we can very efficiently guide these cells to become useful cell types, like neurons that you might imagine would be useful for Parkinson's or Alzheimer's disease, blood to replace all the circulating cell types that are lost in diseases like lymphoma or leukemia, the beta pancreatic cells that are lost in type 1 diabetes that normally release insulin, and the cell type that we are mostly interested in, which are cardiomyocytes or heart muscle cells, which are the cells that are damaged during a heart attack.

The type of pluripotent stem cell that maybe not all

of you have heard about but that was alluded to in the introduction are ‘induced pluripotent stem cells’. These are even easier to access. It turns out you can either isolate blood or take a simple skin biopsy or even isolate cells from voided urine; expand those cells in the dish; and then we treat them with what are called ‘reprogramming factors’. These are molecules that are normally present in embryonic stem cells, but not present in these easy-to-access cells. By forcing their expression, we reprogram these cells to become the equivalent of embryonic stem cells. Those are the so-called induced pluripotent stem cells or iPS cells that actually won a scientist in Japan the Nobel Prize in 2012 for this discovery that was made just about a decade ago.

Once you get IPS cells, they are essentially equivalent to embryonic stem cells, so again, we can use these molecules to guide them into the useful cell types. That has generated a tremendous amount of excitement in the regenerative medicine field because now we have a cell source by which we can generate replacement cells for a variety of different disease types. We can isolate the beta pancreatic islets cells that, again, are responsible for release of insulin. We can talk about regenerating the cartilage that is lost in regenerative joint disease or osteoarthritis; replacing circulating blood cell types; replacing the liver cells that are lost in diseases like cirrhosis; and, of course, trying to repair a heart after a heart attack experienced by those with heart disease, the

disease that I am most interested in.

This is what the cells actually look like. Some of you who have maybe come down to the McEwen Centre have seen this, and certainly all of you have seen the video with the exciting thing about these cells, which is that they do what heart muscle cells are supposed to do, to actually beat. With the very best of plates, you can actually see the beating activity just by the naked eye and what I call the most expensive lava lamp on the planet. These are the cells, again, you lose during a heart attack.

Scientists, including Gordon Keller, the Director of the McEwen Centre, have figured out methods, protocols, by which we can very efficiently guide these cells into heart muscle cells. More recently, progress that Gordon, other scientists at the University of Toronto, Peter Zandstra and scientists at a facility called the Centre for Commercialization of Regenerative Medicine have made is they have upscaled this further. Instead of doing this in small scale in petri dishes like you saw in the video a moment ago, they are now able to do this in what are called ‘stirred-tank bioreactors’, which is just fancy language for a vat. The way I sort of think of it is you are taking technology from the brewing industry, so now we are growing the cells in small aggregates and small clusters, and it turns out that in one 5-ml reactor, you can generate on the order of one billion cardiomyocytes, which is, coincidentally, the number of cells that you lose during a typical human infarct.

We are really excited because, as you heard with the launch of BlueRock Therapeutics, now we have a commercialization partner with whom we can hand off these technologies, and they can further upscale this to talk about generating the billions and tens of billions of heart muscle cells that we would need to treat heart failure patients at large.

Let us talk a little bit about the disease that we are trying to focus on. Probably in this room knows what happens during a myocardial infarction, also known as an MI or heart attack, and that is you have a blockage in one of the major coronary arteries that supply your heart. If that blockage lasts for more than a few minutes, all the muscle downstream that blockage very rapidly starts to die.

The good news is that, with improvements in modern medical management, with improved emergency respond times, we are much better at getting folks past the acute phase of an event like this, but then we run into a new problem, which is the heart is probably the least regenerative organ in the body. Over time, the muscle that is damaged during the infarct is replaced by non-contractile scar tissue, so the heart immediately loses force generating units and puts the heart at a progressive mechanical disadvantage and over time can lead to the development of a disease called heart failure, a situation where the heart can no longer meet the demands of the body.

Why is that important? A lot of people do not realize that a diagnosis of heart failure is really dire. On average, about 50% of the people that receive that diagnosis will be dead within a five-year time span. Currently, we have no clinically approved method to replace the muscle that is lost to an event like this, other than to give somebody a whole new heart. As you know, there is nowhere near enough donor hearts to meet demand. That is what has led to our idea, which is that we might be able to remuscularize these hearts instead by implanting these cardiomyocytes that are derived from pluripotent stem cells, and we might be able to do that initially surgically, and, perhaps, down the road, we might be able to do it via minimally invasive catheter-based delivery.

Where are we in the process of developing this into a real therapy? Right now, today, we can take these stem cells, and we can generate a couple billion cardiomyocytes as we would need for pre-clinical animal studies to prove their safety and efficacy. We are really excited about this new partnership, as you heard, with BlueRock Therapeutics that can further expand this. One of the important goals that they have is to convert this to an entirely clinical-grade process, a process that Health Canada or the Food and Drug Administration would be willing to approve.

Then, in parallel, we are going to do the pre-clinical studies to demonstrate safety and efficacy. If all of that goes well, our goal is to get this into clinical trials in

something like a three- to five-year time horizon. This has been a big project that has involved lots of people—obviously, scientists, including myself at the McEwen Centre, the Peter Munk Cardiac Centre at UHN, the Centre for Commercialization of Regenerative Medicine that I already alluded to, and now this new partner, BlueRock Therapeutics. It is also in our international operations, so we collaborate closely with scientists at the Technion Institute in Israel.

What is the evidence that this might work? What is the pre-clinical work that we have done today? Those studies began over—I am embarrassed to say—a dozen years ago with transplantation studies, with sort of proof of conduct studies in a rat model of myocardial infarction. That study showed that you could take ten million of these cardiomyocytes, implant them into injured rat hearts and get remuscularization within the infarct scar of the recipient animal. That transplantation mediated beneficial effects on contractile function. To demonstrate that, we used imaging modalities, just like you would use in a human patient, things like echocardiography and MRI. We actually went on to show that we saw greater benefits with this cell type than some other competing therapies.

A few years ago, we took one step further. My former colleagues, my predecessors, Chuck Murry, and others and I for the first time, tried transplanting these cells in a large animal model. In a non-human primate model of myocardial infarction, we transplanted one billion human

ES cardiomyocytes. What you are actually looking at here in this image is a slice through one of the recipient hearts. The red stain here is heart muscle; the dotted area shows you the infarct scar, so that is the damaged tissue. And the green tissue you see within that is the replacement human heart muscle that we formed both at delivery of these cells. For the study, on average, we muscularized about one-half of the total footprint of the infarct scar. We showed that over time, the grafts became structurally mature. Early on, they looked like heart muscle cells in the early developing heart, but, by three months later, they were structurally equivalent to the host cardiomyocytes, so they very rapidly assumed sort of adult-like properties.

We actually went on to do an experiment where we had heart muscle cells that flash every time they fire, so we were actually able to image these hearts and we showed that the flashes were occurring in synchrony with the electrocardiogram of the recipient. We showed, by that technique, that this was not just dead tissue we were forming, but this new heart muscle was actually electrically integrated and firing in synchrony with the host muscle as would be necessary for it to generate functionally meaningful new force-generating units.

We also showed that over time, there is remodeling of the vascular supply of these hearts, so blood vessels remodel and extend into the tissue to keep it alive. It is almost like there is an endogenous coronary bypass graft

going on to keep these grafts alive long term.

Let me summarize what we have shown so far and reported in pre-clinical models with these cells. We have historically done experiments where we have transplanted these cells in rats, in guinea pigs and non-human primates. In all these models, we have shown that the cells will ingraft, actually, ingraft probably best in the larger hearts. They do not form tumours, which is one of the things you worry about with the pluripotent stem cell–based therapy. These cells can become anything, so we do not want them becoming the wrong cell type in the heart, but we do not see that. In fact, we do not see any persistent noncardiac cells.

We have shown that there are improvements in contractile function in the small animal models. We still need to do that in the large animal model. The primate experiment I told you about was not designed or funded or intended to look at that. We have shown that these cells will couple. Again, that is something we have shown in both guinea pigs and primates, but that ability to couple is a bit of a double-edged sword. On the one hand, it is going to be necessary for it to contribute new force. On the other hand, if there are differences in the electrical property between the cells we are putting in and the recipient heart, you might worry about arrhythmias, and that is actually one of the hurdles we are still working to overcome. We think we know what is going on here, but in this primate model, we saw transient

arrhythmias for a couple of weeks post-transplantation. We think we know what is going on there, and we think we have the solution.

While we have learned a tremendous amount from these different animal models, they all have sort of a major limitation: They are all relatively small organisms. Even in the case of the primates, these were sort of 7-kg macaques with sort of plum-sized hearts that are firing at a much more rapid heart rate than you or I. That is concerning. We really would like to test these cells in a more relevant, a more human-like heart, so what we have just been doing in the last year or two is transplanting these cells in a pig model with myocardial infarction. It turns out the pig is really the model that if you have a novel cardiac therapy, you typically will get the safety and efficacy data to go to Health Canada or the Food and Drug Administration to show that it should be tested in humans. The idea there is that the size, structure and function of a pig heart is almost identical to a human heart.

I am happy to report to you, again—and the work is just really getting underway— that we have been able to show that we can transplant these cells, human cardiomyocytes, in injured pig hearts and that they will stably ingraft. I draw your attention to this upper image here.

What you are looking at, the blue area, is the scar tissue; the red is the heart muscle; and then I have dotted the new heart muscle that has been formed within the scar

tissue. I will draw your attention to the scale bar there. In this experiment, we are creating cubic centimetres of new human heart muscle, which I would submit is the degree, the sort of scale of remuscularization we would need to think about for repairing something like a human heart. We are excited because this is the big step that we think we need to do to push this forward to the clinic.

Let me summarize what I have told you here this afternoon. First of all, pluripotent stem cells represent an inexhaustible source of replacement cells for regenerative medicine application. I told you about that in the context of the heart, but, as you have heard, chronic diseases, these degenerative diseases that cause so much human suffering and expense to the healthcare system, are almost all diseases where we have lost the useful functional cell type. While we are interested in cardiomyocytes, there are other scientists at the McEwen Centre, like Cristina Nostro, trying to generate the pancreatic cells that you lose in type 1 diabetes. Stephanie Protze, who you saw in the video, is trying to make the pacemaker cells, and this same strategy could apply essentially for any cell type that you might imagine.

With our application, we are really excited because we have demonstrated the feasibility of large scale remuscularization of injured hearts using these heart muscle cells. We have still got some hurdles, some of which I highlighted. We need to establish scalable and economically viable cardiomyocyte manufacturing. That is why we are really excited about this new industrial partner that can help shoulder some of that work. We are going to have to deal with this phenomenon of graft-related arrhythmias that I told you about.

One thing I did not have time to talk about is whether we will have strategies to deal with the immune system. We do not want these cells to get rejected.

Finally, we are going to need to demonstrate efficacy in a large animal model. That is where we really think that the pig is the right species in which to test this with the goal of eventually moving on to a first-in-humans clinical trial that will be based here in Ontario. And, again, the hope, the expectation is to get there in something like three to five years.

With that, I will thank the many folks that contributed to this study. It is always a little sobering to summarize about 15 years of work in 15 minutes, but a lot of folks have contributed to this work. Of course, we would like to thank our various funding agencies that supported this work and the McEwens for the support of the McEwen Centre. Thank you. I think if there is a little bit of time, we would be happy to answer some questions. Please, let me know if you want to address the question to myself or to Rob and Cheryl, who will, obviously, be available as well.

Questions & Answers

Q: Hi, Dr. Laflamme. Thank you for your presentation today. With all your work on stem cell research, I was reading today that the average life expectancy for Canadians is about 82 years of age. What do you think that will be in the future with all this work you are doing?

ML: That is a great question. It is a tough question. I could speak for myself. I will be delighted, as I told you, if the life expectancy for these folks with heart failure, which is a large population of patients, is something we can improve from five years to something more like a normal expectancy. Just for those folks, I will be ecstatic.

Going forward, that is what is really exciting about regenerative medicine: We kind of have the building blocks, the replacement tissue, so I do not think this is something that is going to happen tomorrow, but you can think about really pushing the envelope beyond the 80 years we live now. I would expect that it will be an incremental process as we chip away and figure out how we fix someone's heart; then, we are going to have to deal with their brain for Parkinson's disease and Alzheimer's and the like, but, in principle, the sky is the limit. Rob, Cheryl do you have anything to add?

RM: Well, there is a book out called Singularity is Near, written by Ray Kurzweil. He is saying that if you can live to 2025, then your life is going to get much longer. It will be the confluence of nanotechnology, artificial intelligence and cellular biology that will extend life well beyond the range we know today.

Q: First of all, thank you all for your tremendous levels of intelligence and research. I think we should all rush out and have an MRI. My questions are simple. First of all, how are we going to reach the general public to show them how important lifestyle is because many of these conditions are preventable?

The other question is you are educated at a very high level. Education is expensive. How are young people going to afford to carry on with their education, so they can even contemplate what is available, and how they can study, and how they can become wonderful doctors?

RM: Two questions. One, about general fitness. I think all Canadians should look upon it as their responsibility, and they should be accountable for keeping their health in good condition. When you look at our healthcare system, we do not pay a penny. We should be looking at it, and the government should charge us something for healthcare. You get good marks for being in good health. You get bad marks or you get encouragement to get into good health, to eat the right foods, to exercise, to keep active.

In terms of education, I think that is part of the educational system. There should be more courses on how to stay healthy, how to stay fit, how to go beyond where

we are today because I see a really looming crisis that is coming at us, and we saw it in the hospitals, that there is enormous pressure on the healthcare system.

When I said I think there may be rationing in the future, I was not kidding. If you think of someone like a freestyle skier who is 22 years old and had six knee operations already, do we get to a day where they say you are going to have one hip operation? Or you are going to have one heart operation? Or you are going to have this many times in the hospital? Right now, in terms of the budget in Ontario, 43% of the budget goes to healthcare. The baby boom represents 29% of the population. Eighty percent of healthcare costs occur after you are 60 years old; 29% of the population is moving into that space, and healthcare costs are going up. We cannot scale up the healthcare system fast enough, and there is a whole lot of money that is retiring, and there are going to be fewer people supporting it. It is going to be the electorate that causes the rationalization of healthcare.

So, get out there, walk a little further, have some more vegetables. Cheryl can help you there, and you just keep going, but that is something that is—I think everybody should focus on and ask the politicians, "What are you going to do about this?"

Stem cells is one of those areas. It is not the only area, but it could be a very important area to improving healthcare as we go forward. Thank you.

ML: I would agree with that. Certainly, preventing a disease is

better than having to cure it once it is already established. On the other hand, keep in mind that these diseases are affected by the choices we make, lifestyle, environment, but also by hereditary. Even in the case of heart disease, we sort of think it is because of bad behaviour, but that is not entirely true. It is about 50–50 with most of these diseases and what influences do to our genetics, which we cannot control versus the choices we make.

Q: Hi. Thank you very much for your presentation. That was very enlightening. I always believed in stem cell research. My question is let us say it is a success—and I really hope it is—how are you going to get it to the common populace? Have you guys thought—even barely thought—about any pricing structure, or is it going to be a luxury thing or any common man can get that treatment? What do you think about it? How do you think it should be available?

ML: That is a great question. The short answer is that cell therapies, particularly, in the heart, are going to tend to be relatively expensive. On the other hand, the treatment that we are trying to replace, which is a heart transplant, is also tremendously expensive. There is another therapy that we will use for some of these end-stage patients where they will put in a pump that can keep somebody alive until they get a heart transplant.

That pump alone—not talking about the expensive surgery and care and so forth afterwards—is on the order of about $100,000 Canadian just for the pump. Obvious-

ly, if you are talking about all these other expenses, it is going to go up multifold. That is the benchmark that I think we have got to compete with. I think we can beat it, but we will see.

Q: There was a remark earlier in terms of private equity and in raising dollars. Where are you with that now?

ML: Specifically with the heart program or just globally overall?

Q: You can address both questions, I guess.

ML: With the heart program, as you heard, there was this large investment in BlueRock Therapeutics between Bayer and Versant. I think with regard to that specific application, we are pretty financially secure. That was $225 million U.S. That will carry us a long way. That is not true for the other applications, the other programs that you have heard in the McEwen Centre, which are at an earlier stage of development, but also need that sort of seed money to, what our expectation would be, would attract the same eventual investment from the private sector to carry them over that final hump through expensive clinical trials and scale of the manufacturing and the like.

Q: [Inaudible.]

ML: I am not sure I understand the question.

CM: I think to address that, BlueRock is specifically focusing on this particular heart program that Dr. Laflamme has presented on. I would like to remind everyone to

think about the focus of stem cell therapy, which is about quality of life and empowering the body to perform at its best. I think that while life extension might be a side benefit, I think what you want is to perform to your best ability to be able to not worry that your heart will fail or that your insulin injections are not working properly or whatever. There are so many other variables in life. If we can empower the body through stem cell therapy to perform at its best, that is really what we are excited about.

Q: Thank you. I will be brief. Looking at the management of healthcare in the future, there are many parts of Canada that do not have healthcare. Consequently, in the future, I think there is going to be a tremendous rush to the major centres like Toronto that are so blessed. Are you going to have enough trained medical people to cope with the immigration and the movement around the country to medical centres?

ML: That is probably a question that is for a higher pay grade than myself. I guess I would say one of the exciting things about regenerative medicine is, and I will use the specific example of the cell therapy, cell product that we are making that can be shipped elsewhere. What we are generating is heart muscle cells that we freeze in a vial and then can be stored for an indefinite length of time. It could be shipped somewhere. It could be shipped to the hinterland, delivered there on the site.

Probably this therapy would first be offered, if it is

successful, in tertiary or quaternary centres like we have here in Toronto, but the vision would be long term that it could be something that you could ship. My dream is that Toronto becomes sort of the Detroit of cell manufacturing, that we are shipping cells everywhere.

RM: If I could just add to that, we are going to be isolated. There are areas of specialty for operations up and down University Avenue, as they have the most complicated cases in the province, and maybe even in the country, that come to Toronto for treatment. You might want to go out to the politicians and attack some of the assumptions that we have in our healthcare system and say, "Why does Canada not become a centre for healthcare for the world? Turn it into an industry; double the size of our hospitals, so it can attract the best, like Michael, Cristina, Stephanie and others, so that there is a world price for healthcare and there is a Canadian price. The world price is higher."

I will give you an example. If you want a double lung transplant, you go to the Mayo Clinic, and it is $400,000. The cost here is about $100,000. You do not get an invoice when you go into the hospital when you have a treatment. Maybe we should start that, so everybody knows when you get on that dialysis machine, it costs $120,000 a year for the rest of your life. That is where the costs are coming from. No one realizes, but we should be looking and saying this is an industry that cannot be taken away because of a manufacturing plant.

If we double the size of our healthcare system, we invite the world to come here not so that we are crowded off, but so that we get the best service here from the best physicians. That is where we need to go.

I think for the outlying communities, there is telecommuting and medicine that way, through communications and robotic surgery that can be conducted at a distance. All of those are coming and one day may address some of those outlying communities. There is also—if you ever saw the film Avatar, where someone gets into a body—a firm Nippon Airways, which is working on a prize for an Avatar, so you could be here, but you could be a surgeon operating up by Hudson Bay with that body there. It is a little science fiction, but it is coming.

ML: Thank you, again, for your interest and your questions.

BJ: Thank you Dr. Laflamme and to Cheryl and Rob for this incredible contribution that you have made to Canada. It makes you very proud that we have an environment that nurtures this kind of research in our country.

In celebration of Canada's 150th birthday and our ninth event in our sesquicentennial series, I would like to ask our series sponsor, IBK Capital, represented by Bill White, as well as our guests of honour to join me at the podium and blow out the birthday candles.

[All in unison: Happy Birthday, Canada!]

Note of Appreciation, by William White, Chairman, IBK Capital Corp.; Director, Empire club of Canada

The cake is delicious, by the way. This is our ninth cake, and anyone who has not tried this cake, I strongly recommend you hang around until you get your piece of cake after the presentation here.

Madam President, distinguished Head Table Guests, fellow members and guests of the Empire Club of Canada, I have the pleasure to express our formal thanks to our three key speakers, Rob, Cheryl and Michael.

I first met Rob and Cheryl in 1985, with the financing and creation of Goldcorp. And Rob and Cheryl made that the most successful corporation that I have been involved in, in the last 32 years. Rob and his wife went on to found the McEwen Centre for Regenerative Medicine, which opened its doors in the MaRS Discovery District in 2007. In ten years, this Centre has accomplished all these wonderful things that we have heard of, but not without the assistance of doctors like Michael Laflamme, who is their principal investigator. He really had my attention because, 15 years ago, I had bypass surgery for a heart issue at the McEwen facility there with Peter Munk's help. That is an inside joke, by the way. The focus on developing stem cells based on therapies to treat heart disease, to me, is just amazing.

Now, you have heard that the Empire Club, of course, has celebrated its 150th birthday with Canada, with a series of ten special high-profile addresses from leaders of some of the Canadian institutions and organizations that have shaped Canada's history. Today, we have celebrated a topic, which is significantly going to influence the future, probably more so than all of the other nine institutions that we celebrated Canada's birthday with so far.

You have seen how forging partnerships between medicine and business, especially, in this topic of regenerative medicine has helped make Canada, I believe, to become the world leader in stem cells. Stem cell research is expected to shape Canada's future fighting degenerative diseases. We are definitely proud of how stem cells are transforming Canada's healthcare, and of, especially, the role of the McEwen Centre for Regenerative Medicine and how it is playing a role in global development of stem cell therapies.

Now, the real promise here, as we have been told today, is the ability for stem cell therapies to provide physicians and surgeons with new solutions to repair and regenerate tissues and organs in our body that are compromised currently by either disease, trauma or, in my case, simply old age.

I ask that you just join me now in a warm and special thank you to Rob and Cheryl McEwen and to Dr. Michael Laflamme, who are using stem cells to fight disease, which, ultimately, will enable all of us to live longer and much healthier lives. Thank you.

Concluding Remarks, by Barbara Jesson

The Empire Club could not host lunches like this without wonderful support from sponsors. I particularly want to commend our sesquicentennial sponsor, IBK Capital Corp. Every board should have a Bill White. I cannot tell you what a pleasure it is to work with him on the board of the Empire Club. He is just a tremendous supporter and incessant in his support for the Club. Thank you so much, Bill.

I also want to thank our presenting sponsor, Bayer. Mr. Kanti, thank you so much. Thank you for this lunch, but, more importantly, thank you for this remarkable gift that you have given to this country in terms of your support for bringing stem cell research forward along with the McEwen Centre.

Derrick, thank you for taking my call when I reached out. I am very, very grateful. As well, I want to thank our gold sponsors, Cantor Fitzgerald Canada Corp., Bennett Jones, Haywood Securities Inc., Ernst & Young, and H.C. Wainwright & Co. Without sponsors like these great companies, the Empire Club lunches would not be possible. Thank you all so much.

I also would like to thank mediaevents.ca, Canada's online event space, for recording today's event. Although our club has been around since 1903, we have moved onto the 21st century and are active on social media. Please, follow us on Twitter at @Empire_Club and visit us online at www.empireclub.org.

You can also follow us on Facebook, LinkedIn and Instagram. Finally, please, join us again at our next event on November 28th, with Minister Chiarelli, Minister of Infrastructure, at the Royal York Hotel. Thank you for your attendance, today.

This meeting is now adjourned.