LIFE SCIENCES ONTARIO

CAST OUR PEBBLE INTO THE POND

HOW ADOPTING A PROVINCIAL RARE DISEASES STRATEGY WOULD SAVE LIVES AND BOOST ONTARIO'S ECONOMY

A blueprint for an exciting, healthy and prosperous future

Life Sciences Ontario
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I. Prologue: One city council vote

Kendall Square, Cambridge, Massachusetts: "The most innovative square mile on the planet."

On January 10, 2020, two American virus vaccine experts received the DNA sequence of a new coronavirus after it was posted online by Chinese scientists investigating a strange new flu-like illness in the city of Wuhan. Amazingly, thanks to the Americans' experience with other coronaviruses, by the following day they had designed the modified proteins that could be used in a vaccine to fight it.

Just two more days later, on January 13, they turned their work over to their partner Moderna, a biotechnology company headquartered in Cambridge, Massachusetts, that had developed a potent platform to encode such proteins on genetic material known as messenger RNA. Six weeks later, Moderna had manufactured a vaccine ready for clinical trials – all before most Canadians realized in mid-March that COVID-19 would become a big thing. That vaccine is now being used around the world to protect people from COVID-19.[1]

Moderna is part of the greater Boston hub of biotechnology companies, the largest in the world with more than 400 companies and almost 40,000 people working in research and development alone and 75,000 in total. The hub generates more than US$12 billion in total wages annually to employees. Hundreds of millions of people have been treated by the life-saving therapies developed there, even before the COVID-19 vaccine.[2]

That hub exists because of one foresighted vote on February 7, 1977 – a city council zoning decision.[3] On such prosaic events, whole societies can advance.

It was the proverbial pebble thrown into a pond whose ripples 40 years later have created a scientific and economic tsunami that benefits people around the world.

In 1977, the idea of conducting research on recombinant DNA was considered dangerous and very controversial. It was playing with the building blocks of life with unknown consequences – perhaps unleashing a new life form that would destroy humankind, some warned – and few wanted anything to do with it.[4] The small city of Cambridge, MA, is home to two of the world's leading centres of learning – Harvard University and the Massachusetts Institute of Technology (MIT). Their scientists wanted to be able to conduct such research and went to the Cambridge City Council to get permission to do so.

Cambridge Mayor Alfred Vellucci had vowed he would never agree to it, saying "recombinant DNA is hazardous to the citizens of Cambridge." On the night of Feb. 7, 1977, however, he joined all eight city councillors to vote unanimously to permit the research, as long as new regulations from the National Institute of Health were followed. "I will vote for the proposed ordinance as it regulates DNA research," Mayor Vellucci said that evening. "There is no way to protect citizens without it."[5]

The decision to allow universities in the area to conduct DNA research instantly made Cambridge a magnet for new genetic-based biomedical research activity and companies quickly took advantage

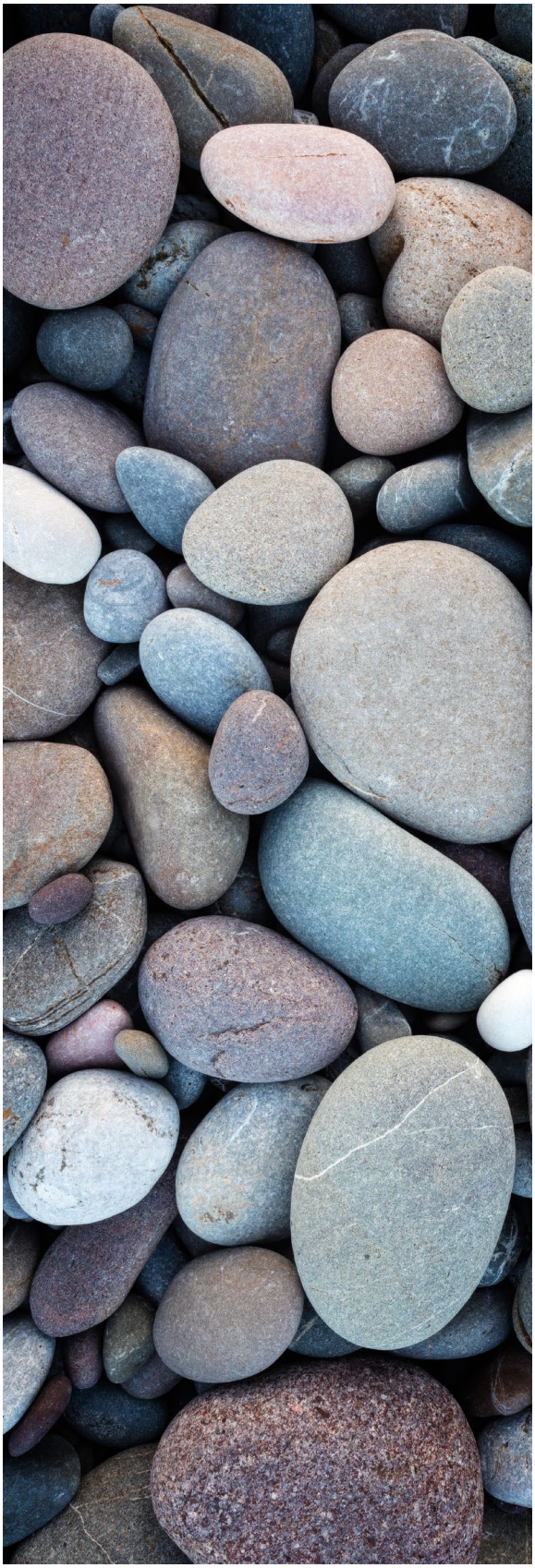
of being able to do their ground-breaking research there. The greater Boston biotechnology hub was born.

It centred itself around Cambridge's Kendall Square, which has since been labeled as "the most innovative square mile on the planet." It is home for biotech and life sciences research centres for companies including Amgen, Pfizer, Novartis and Biogen plus, of course, Moderna.[6]

As there was for Cambridge City Council in 1977, there is another unique confluence of events now, in the year 2021, for the province of Ontario to cast its biotechnology pebble into the pond to create a tsunami of benefit for Ontarians with rare diseases, for our already-strong life sciences ecosystem, for our economy, and for our future.

This paper provides a vision for how it can, and should, be done.

There is another unique confluence of events now, in the year 2021, for the province of Ontario to cast its biotechnology pebble into the pond to create a tsunami of benefit for Ontarians with rare diseases, for our already-strong life sciences ecosystem, for our economy, and for our future.



II. Introduction

The life sciences industry in Ontario has the potential to expand its already formidable economic and scientific footprint by implementing a provincial rare diseases strategy. We are entering what promises to be a new golden age for medical research and advancement. Our understanding of the human genome and the genetic basis of disease has exploded, reaching a crucial tipping point of being able to generate the types of health benefits of which we could previously only dream.

This offers huge potential for the millions of Canadians and Ontarians whose lives are impacted by rare diseases, most of which have a genetic cause.

Ontario is facing a crucial choice. It can ignore or fight these technological advances by shutting the door to healthcare innovation and concluding that what we do now is "good enough." Many, unfortunately, promote this approach, insisting we "can't afford" to do more and that new technology is "too expensive." These would be the same people who, a generation ago, said our system couldn't afford high-cost scanning equipment or new treatments for HIV/AIDS and cancer, or to develop ways to use computers or the newly created internet in healthcare.

The other option is to embrace the dramatic changes in science and healthcare and harness them for the benefit of both patients and our economic development. That's what happened in Boston and can happen in Ontario by having an integrated strategy for managing rare diseases in the province that provides both better and cutting-edge diagnosis and care for patients while building our life sciences sector as a vital pillar of a prosperous and growing economy.

This paper outlines the five key strategic pillars that are necessary now to make this happen. Together, they provide a roadmap for showing that Ontario is not just "Open for Business," but also open to healthcare, scientific innovation and better health for all, particularly those too long neglected – those with rare diseases.

It is time to make it happen. It is time to throw our pebble into the pond and create the waves of better health and prosperity that will benefit us all.

Dr. Jason Field
President & CEO,
Life Sciences Ontario

III. Executive Summary

The treatment of rare diseases is at a crucial tipping point, thanks primarily to great advances in recent years in medicine's understanding of the human genome and how to treat and even cure diseases at the genetic level. These new treatments are unlike older drugs that mostly alleviated symptoms or tried to slow the progress of a disease.

We need to stop thinking of them in the same way we think of the pills and infusions of traditional drug therapy. They should be thought of instead as being more like surgical interventions, though instead of involving, say, a lung or kidney transplant, many of the newer therapies are closer to microscopic "genetic" transplants to fundamentally alter or stop the disease. This mode of thinking puts both their cost and how the health system should manage them into a different perspective, which is why a whole new separate strategy is vitally need for managing treatments for rare diseases in Ontario and, indeed, in all of Canada.

Along with this genetic therapy revolution, there are four other key forces that make 2021 a crucial period for Canadians with rare diseases and their governments, but particularly that of Ontario:

- **The COVID-19 pandemic** which has heightened awareness of all Canadians of the importance of their health and having a strong healthcare system as well as the great value of innovative therapies and vaccines.
- **The strengths and vulnerabilities of the Ontario life sciences sector**, which has developed significantly over the past 20 years but is threatened by global pressures that require the right policies and environment to be in place in order to attract and maintain investments.
- **The new significant federal funding for drugs for rare diseases** which will come into effect in 2022-23 which provides a significant opportunity, but also a great need, for a comprehensive rare diseases strategy.
- **The new federal patented drug pricing policy** scheduled to come into effect on January 1, 2022, which is already causing delays in new therapies being brought to Canada, particularly for rare diseases, and threatens to undermine any of the other potential positive factors.

However, with the right policies and a comprehensive strategy coordinated nationally, Ontario has the potential to lead the way in helping its citizens who are impacted by rare diseases while also stimulating a vital sector of the province's economy – the life sciences. This can be achieved by focusing on five strategic pillars:

1. Build a workable system for patients that is driven by facts and data.

The system for rare disease treatments needs to be attuned to the needs of and workable for all the players – patients, governments, the health system, researchers and their institutions, and industry.

2. A clear, efficient and patient-friendly health regulatory system.

Treatments for rare diseases require separate and tailored systems and rules for clinical evaluation, regulatory approval, emergency drug access, health technology assessment and access processes that put prompt but safe access to patients as the top priority. Rare disease treatments need their own rules rather than being forced to fit into a system not created or suitable for them.

3. Accelerated funding for rare diseases diagnosis, treatments and care.

The health system must be structured and resourced to provide patients with better access to testing and diagnosis services, the best treatments that might help them and supportive care and services that can alleviate suffering and uncertainty.

4. Make managing rare diseases an economic development strategy.

Spending on healthcare, and rare diseases in particular, needs to be reconsidered not just as a cost to be borne grudgingly and restricted, but as an investment that is a key tool for economic development, contributing to prosperity as well as to better health.

5. Integrate Ontario's rare disease strategy with other health initiatives and the Canadian Rare Disease Strategy.

Ontario cannot act alone or in isolation. Its rare diseases strategy must fit seamlessly into and for greater economic benefit with national programs, as well as initiatives to address other major health challenges such as cancer and public health protection measures.

To achieve this for Ontario residents and, indeed, for all Canadians, Ontario should take a leadership role in the urgent development of a comprehensive strategy for rare diseases for Ontario that could act as a template for other jurisdictions in Canada.

IV. Opportunities and challenges – Why 2021 is a life sciences and rare diseases tipping point for Ontario

Several major health, economic and political developments are interacting in 2021 to make this a pivotal moment in shaping the future for the life sciences and the treatment of rare diseases in Ontario. It is an unprecedented confluence of events and policy decisions that has huge power to shape the province's future in many ways, making it vital that the right decisions are taken to ensure this unique opportunity is not wasted.

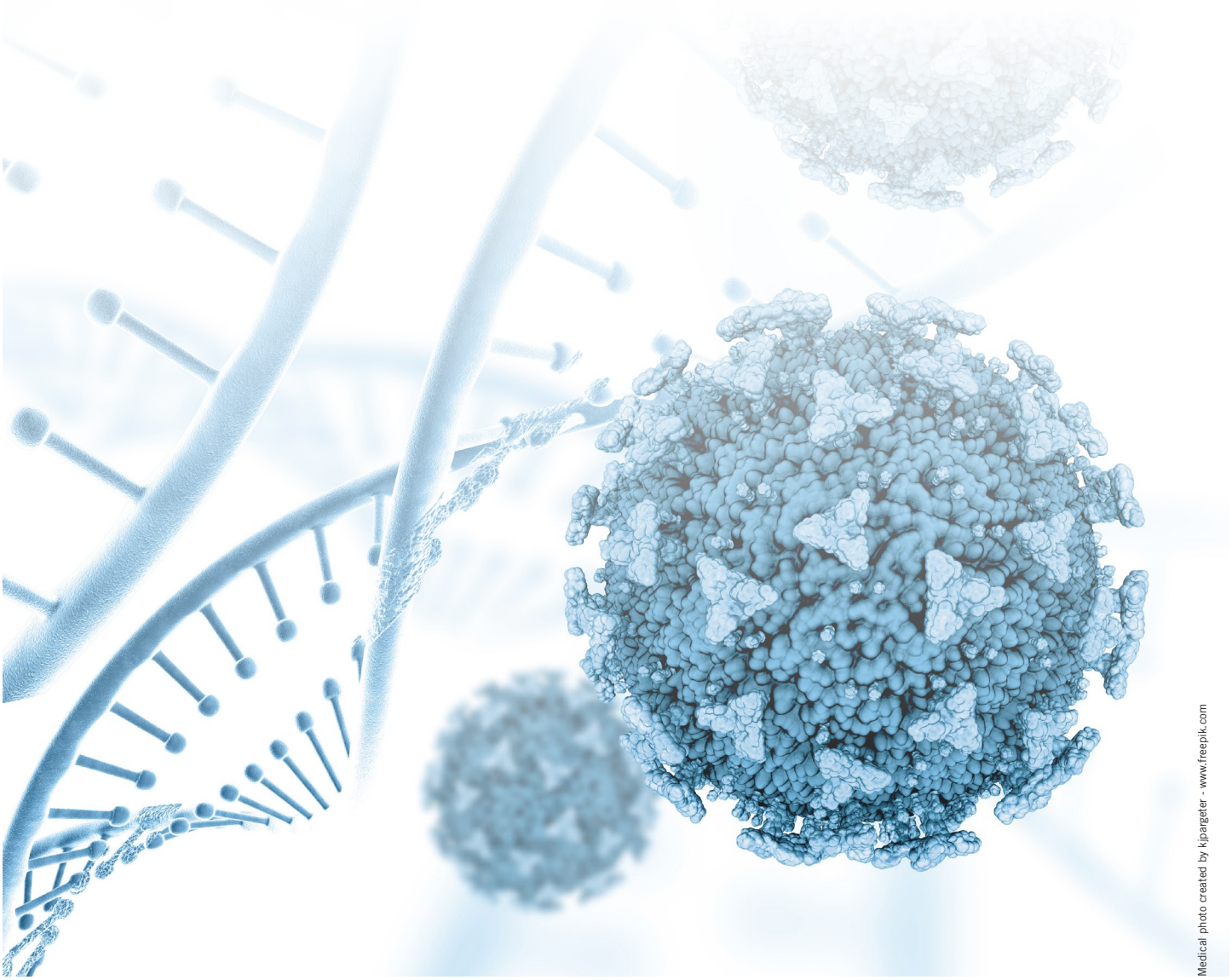
Five key forces and events are at play:

1) The COVID-19 pandemic

The pandemic events of 2020-21 suddenly taught everyone what people and families dealing with many rare diseases have always known – what it's like to live with or fear a disease for which there is no treatment or cure. The experience should open people's minds to the greater needs in our health system so that that visceral fear is eliminated as much as we possibly can, no matter the illness that someone faces.

The pandemic has also highlighted the weak points of our health system. This not only shows us where change is needed in the case of infectious diseases, but should open Canadians more to the need for other changes in how healthcare is viewed and delivered. The pandemic has shown us all too clearly how a strong, efficient and effective healthcare system for all is crucial to us having a strong and efficient economy.

Just as the Second World War made necessary the need for new ways for the nations of the world to interact and cooperate – and led directly to the development of the systems of universal medicare which dominate in most industrialized countries to this day – the pandemic creates a golden opportunity for fundamental change to how we deliver healthcare in our new scientific age.



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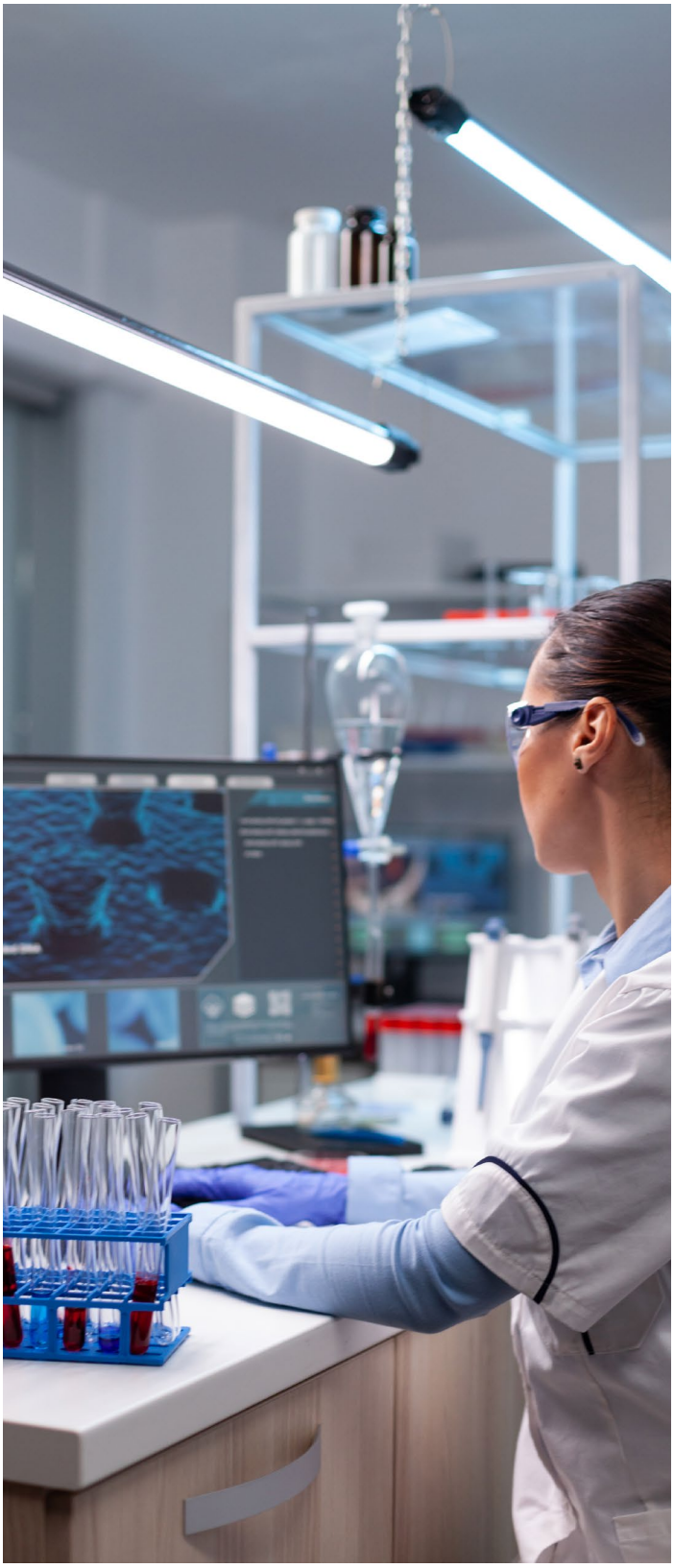


2) The revolution in new genetic medicines

The decoding of the human genome, a huge project started in 1990, was completed in April 2003, now 18 years ago.[7] Today, new discoveries and technologies are being unleashed by that landmark scientific accomplishment. We are understanding the genetic basis of many diseases and developing the technology to fix them.

It is not by what is traditionally thought of as "drug" treatment but more akin to being able to fix a faulty part in a car or other piece of equipment. It does not involve treating or alleviating symptoms but eliminating the disease at its very source. We need to stop thinking of them in the same way we think of the pills and infusions of traditional drug therapy. They should be thought of instead as being more like surgical interventions, though instead of involving, say, a lung or kidney transplant, many of the newer therapies are closer to microscopic "genetic" transplants to fundamentally alter or stop the disease.

This mode of thinking puts both their cost and how the health system should manage them into a different perspective. There are no debates about cost when a child is born with a defective heart and receives a heart transplant (the first of which was performed in Canada in 1989)[8] or a teenager with cystic fibrosis (CF) receives a double lung transplant, but when another infant needs a new genetic therapy – in effect a "gene transplant" – or a patient with CF seeks a promising new genetic therapy, the "high cost of drugs" is derided and access often delayed.[9]

We are already seeing the dramatic results that are possible in rare diseases thanks to new genetic therapies. Chimeric antigen receptor T-cell (CAR-T) therapies, for example, are effectively curing some childhood cancers by removing the patient's own immune system T-cells, manipulating them genetically and then giving them back to the patient so normal functioning can occur[10]. Other new genetic therapies treat the underlying genetic causes of diseases such as cystic fibrosis[11] and spinal muscular atrophy[12], both sources of untold illness, disability and untimely death in children.

And, of course, this new technology has been on dazzling display for the whole world with the development in record time of the first vaccines to prevent COVID-19, including those from Pfizer/BioNTech and Moderna.

There are thousands more medicine and vaccine developments either already in progress or soon to come. They herald an era of medical progress not seen since the first age of modern pharmaceuticals and vaccines starting a century ago, which allowed us to treat and prevent infections and other diseases. Ironically, this year, 2021, we are celebrating the centennial of the greatest medical discovery in Ontario and Canada that heralded that earlier age of innovation – insulin to treat diabetes.

However, this new genetic medical revolution needs new systems and procedures to manage it and deliver its benefits to patients. We can't rely on the old system – medical, regulatory, financial and political – to do the job anymore.

3) The strengths of the Ontario life sciences sector – and its vulnerabilities

The life sciences sector is an important part of the Ontario economy while also playing a strong role in contributing to scientific advance and to the overall global life sciences ecosystem as a significant sized cluster with leading expertise in many fields.

With the right policies in place, the life sciences sector has enormous potential in Ontario, given the strong foundation already existing both in terms of existing companies as well as the ready availability of skilled talent in all relevant fields. All the parts are in place to create huge growth in the right policy environment.

Ontario has done this before in other areas. It is recognized across Canada for its leadership in key policy areas, particularly ones related to economic growth and success, such as its significant reform of pension plans in 2018. Ontario has also already taken a leadership role in acting to help those with rare diseases, including the December 2017 report of the Ontario government's Rare Diseases Working Group and the creation of its Rare Disease Implementation Plan Steering Committee. This group was mandated, specifically, to create a plan for centralized management of rare disease patients, more genetic testing and to create an Ontario-specific rare disease registry to, as the government stated at the time, "help foster research and innovation in the discovery, management and treatment of rare diseases.[13]"

In addition, in the context of the current federal government's commitments on national pharmacare, the current Ontario government indicated its interest in focussing first on drugs for rare diseases. "I think that we should start with where we see a real problem, and Ontario sees a real problem with the rare and orphan disease drugs," Health Minister Christine Elliott was quoted in media in December 2019.[14]

However, there are vulnerabilities and dangers. Life sciences is very much a global industry that will locate and invest in the areas that offer the best overall potential. A crucial element of that is having the policies in place that promote and value health innovation and the huge investments that are needed to create it. It is in this area that Canada has often fallen short, and risks doing so again.

4) Federal rare diseases funding

In its 2019 budget, the Canadian federal government proposed an investment of up to $1 billion over two years, starting in 2022-23, with up to $500 million per year ongoing, to fund access by Canadians to treatments for rare diseases[15]. While this is an important and welcome development for Canadians with rare diseases, the exact form of the funding and its delivery is not clear as it is dependent on negotiation with the provinces and territories to determine how to structure the system to receive the funding.

Despite this uncertainty, there seems to be a positive recognition that increased funding is necessary to make new treatments for Canadians with rare diseases more readily available. As well, given that the parameters for the funding are not yet set, there is an opportunity to shape the policy that will accompany that funding so it can have the maximum possible benefit for patients and for Canada's and Ontario's economic development.

5) Federal patented drug pricing policy

The federal government in 2019 approved new regulations to change the way the Patented Medicine Prices Review Board (PMPRB) assesses the prices of patented medicines. These regulations are now set to come into effect on January 1, 2022. The complex and untried new rules will force manufacturers to reduce the prices of their new medicines by significant amounts, making Canada a far less attractive place in which to both launch new treatments and to conduct clinical and other research.

Surveys of the industry conducted for Life Sciences Ontario have already indicated that companies are delaying planned launches of new medicines in Canada and that they expect this to continue as long as this new policy is in effect or remains a threat to come into effect. The policy impact will be especially felt in the area of treatments for rare diseases because of the nature of the market, the small patient populations involved and resulting lack of traditional efficacy and pharmacoeconomic data on which the new planned pricing regulations unduly rely[16].

This policy threatens to undermine any of the potential positive factors outlined above that would provide great stimulus to the development of the life sciences sector in Ontario. It is not too late, however, for the policy to be revised to alleviate the worst of its effects. In particular, the country's experience with the COVID-19 pandemic may help contribute to a change in policy.

On the other hand, policies related to rare disease treatments in areas under the Canadian federal government's control can make a big difference in a positive way. In the United States, the passage in 1983 of the Orphan Drug Act is said to have "completely changed the face of therapeutics for rare disorders." The legislation provided financial incentives to attract industry's interest by providing a seven-year period of market exclusivity for a drug approved to treat an orphan disease, even if the drug was not under patent – that is, proving a new use in rare diseases for an existing medicine – and tax credits of up to 50% for research and development expenses. In addition, the legislation authorized the Food and Drug Administration (FDA) to provide grants for clinical testing of such treatments and to offer assistance in how to frame protocols for investigations. In other words, having the drug regulator become an active player in helping companies develop such treatments.

The American results were impressive. By 1990, the FDA had designated 370 products for orphan status, and of these 49 were approved for orphan indications. By 2002, these numbers grew to almost 1,100 and 232, respectively, providing treatment to an estimated 11 million patients[17].

V. What the future could hold: A vision for Ontario 2040

With our vision and realistic hope for the future, in the Ontario of 2040:

- The life sciences sector is a fundamental pillar of the Ontario economy and a huge source of international pride and prestige.
- The sector attracts even more global experts than at present to work in an environment where innovation is valued and ideas can be quickly developed into value for patients and society.
- Ontario residents from birth have access to a wide range of genetic services to diagnose and predict rare diseases and have access to services and treatments to prevent their development before they cause major health or impairment issues.
- Ontario is a world leader in the use of innovative health technology of all types and makes it available to patients universally and promptly.

VI. How do we get there? Five strategic pillars

To achieve the future we want for Ontarians with rare diseases and for our economy, there are five key strategic pillars, which are outlined in more detail in the sections that follow:

1) Build a workable system for patients that is driven by facts and data

The foundation for a comprehensive approach and system to manage rare diseases in Ontario begins with a clear understanding of the current situation and the reality of the companies and institutions that are working to address those needs so that the new system is achievable and effective at meeting patients' needs.

2) A clear, efficient and patient-friendly health regulatory system

We need a safe and well-regulated health and drug system, but one that provides a stable, clear and predictable pathway for prompt patient access to the world's leading health innovations and services. We must avoid short-term blunt instruments, such as the proposed changes to the PMPRB, but instead look to the longer term and where Canada needs to go. Solving this problem now will give a more meaningful solution to the future.

3) Accelerated funding for rare diseases diagnosis, treatments and care

We need to ensure our health system is structured and resourced to provide patients with better access to testing and diagnosis services, the best treatments that might help them, and supportive care and services that can alleviate suffering and uncertainty. With regard to treatments, there is no need to conduct economic reviews for all of them. For medicines that are reviewed, patients should be given access first, then the value reviewed for systems to finance appropriately. There should also be greater use of innovative funding models such as leasing technologies and pay-for-performance as well as more evidence-building programs for oncology medicines.

4) Make managing rare diseases an economic development strategy

We need to recognize and exploit our health care needs, particularly those in rare diseases, not as a cost to be borne grudgingly and restricted, but as an investment that is a key tool for economic development, holding a key to future prosperity as well as better health.

5) Integrate Ontario's rare diseases strategy with other health initiatives and the Canadian Rare Disease Strategy

We need to make Ontario's rare diseases strategy fit seamlessly into and for greater economic benefit with national programs for rare diseases as well as with initiatives to address other major health challenges such as cancer care and public health protection measures.

VII. Strategic Pillar #1:

Build a workable system for patients that is driven by facts and data

The foundation for a comprehensive approach and system to manage rare diseases in Ontario begins with a clear understanding of the current situation and the different realities of its key players. This includes understanding the scientific and economic underpinnings of the industry, companies and institutions that are working to address those needs so that the new system is realistic, achievable and meets patients' needs. Government policy in such a complex and important area cannot be created in a vacuum.

First, a common **recognition of the facts** is crucial, including the large number of conditions involved, the impact of them on patients and their families, as well as the existing serious shortfalls in their ability to access prompt diagnosis, effective new treatments and other needed care and support services.

A further crucial element to ensure the right policies are developed is understanding **the global economic realities** of the life sciences industry and what it takes to invest in developing new medicines, particularly ones for the small patient populations with rare diseases. Drug development is a global enterprise for all treatments, but it is even more so for rare diseases because of the need to access sufficient numbers of patients from different countries to assist in the clinical development of new treatments, often in innovative ways given that randomized controlled clinical studies are often not feasible (as discussed further in the next section).

It is also important for all involved in developing a rare diseases strategy for Ontario to understand both **the economic and medical realities** involved for life sciences companies in this field. The medical reality of new drug development is that most new treatments fail. Outside of the companies and medical specialists involved, these failures are seldom heard about or discussed, but they are real, and costly. This adds to the economic realities because successful treatments must not only pay for their own research and development, but also for the cost of all the failures that went before and will occur in the future.

Fortunately, new genetic therapies have a greater likelihood of being successful because, unlike most earlier drug development programs which often didn't have a clear understanding of how a new treatment might impact a disease, the pathway for a genetic therapy to act as a treatment is usually very clear. The costly challenge, however, is in developing the technology to deliver the desired genetic change safely and effectively. Sometimes, such as with the new CAR-T therapies, this is achieved, literally, on a patient-by-patient basis. All of these factors have a great bearing on the ultimate cost of the developed therapy.

It is also crucial to understand the impact of rare diseases on patients and their families, and thus the urgency of developing a comprehensive strategy and system to address their needs. While some rare conditions are now diagnosed thanks to genetic testing of newborns, many go undiagnosed correctly for years, with patients enduring several incorrect diagnoses and unnecessary treatments that do not work, all at significant cost to them personally (emotionally, physically and often financially) and to the health system. In a survey of Canadian patients with rare diseases conducted by the Canadian Organization for Rare Disorders (CORD), one-third said it took more than three years to get a correct diagnosis and one-fifth said it took more than six years, receiving several incorrect diagnoses in the interim.[18]

In the descriptions of the other proposed strategic pillars for a rare diseases strategy for Ontario, this paper outlines the different elements that are all needed to create an effective way to diagnose, treat and manage rare diseases in a way that works first for patients, but also for the other stakeholders – health professionals, health institutions, governments and the life sciences industry. The key is to ensure that this new system is not based on guesses and hunches but is driven instead by data, needs and technology to help patients and their families and, also importantly as explained further below, the province's economy.

Once in place, this new system must continue to be driven by data so that it can evolve continuously at the speed of new technology to meet new and changing needs of patients, institutions and industry for years to come.

In summary, the key requirements to achieve this Strategic Pillar are:

- A clear and common understanding by all stakeholders of the facts and challenges involved in effectively treating rare diseases
- An understanding by all stakeholders of the economic and scientific realities of the companies investing in developing treatments for rare diseases and the impact this has on how the system must be structured and managed
- Develop and implement a data-based system to ensure the most efficient and cost-effective management of the comprehensive needs of patients with rare diseases and their families
- Ensure the new system is driven by data to direct prompt evolution and changes as required going forward

VIII. Strategic Pillar #2:

A clear, efficient and patient-friendly health regulatory system

The current drug regulatory, pricing and access mechanism in Canada was not created for and is very ill suited to address the characteristics of new treatments for rare diseases. The system simply wasn't created for that purpose. Instead, it is tailored for new treatments for a large range of conditions affecting much larger patient populations and with potentially much larger impacts on total cost.

In addition, the system was not created to accommodate some of the new treatment technologies, as demonstrated recently when it was uncertain if Health Canada and the health technology assessment process would evaluate the first new CAR-T genetic therapy treatments as a pharmaceuticals or as medical devices/clinical interventions. The latter was chosen.[19]

In order for patients with rare diseases to have the timely access they need and deserve to new treatments, a distinct regulatory and access pathway for these treatments must be developed. It must be one that covers the special characteristics of these therapies from the beginning of development through regulatory approval to provision of treatment to patients.

While many of these processes are not under the jurisdiction of the provinces, Ontario can and should play a leadership role in driving their national development, as it did several years ago with the establishment of the pan-Canadian Pharmaceutical Alliance (pCPA), which united all provinces, territories and the federal government to negotiate public drug plan listings with companies for new approved treatments.

Clinical trials and regulatory approval

The normal standard data for efficacy and safety of new treatments for regulatory approval is from randomized controlled clinical studies. However, these studies simply are not possible for most rare conditions and new treatments due to ethical considerations and/or the small number of patients available for such studies. The special circumstances for new rare disease treatments need to be recognized by a regulatory framework that is flexible and adaptable to agree on customized approaches depending on the condition, the patient population and the type of new treatment. There is no one-size-fits-all approach, but there are creative means for regulators to be assured of adequate safety and efficacy in balance with both the risks involved and the patient need. An important source of data and experience that should be drawn upon is from comparable international partners such as regulatory bodies in the US, EU and Australia.

Federal pricing regulation

The federal drug pricing regime of the Patented Medicine Prices Review Board (PMPRB) is not appropriate or applicable for treatments for rare diseases, either in its current form or, particularly, under the proposed new regulations scheduled to come into effect on January 1, 2022. Under a proposed national strategy for drugs for rare diseases being discussed by the federal government, the PMPRB would duplicate the roles for and effectively prevent access to the Canadian market for many new rare disease treatments, undermining the entire purpose of a provincial rare disease strategy focused on improving access to improved care pathways and treatments for Ontarians.

Emergency and early drug access

Because of the current issues related to regulatory approval and pricing of treatments for rare diseases in Canada, the Health Canada Special Access Program (SAP) has acted on many occasions as an alternate pathway for drugs for rare diseases in Canada. With a comprehensive strategy for such treatments as outlined here, treatments for rare diseases will be needed in fewer cases. That said, the SAP pathways can continue to be improved, and the province can support this with programs to implement protocols that transition patients into the normal system for publicly-funded access once the treatment has been made commercially available.

Investments in clinical studies

As noted above, traditional randomized clinical studies of drugs for rare diseases are most often not possible. However, there are other ways that the efficacy and safety of new treatments can be evaluated and it is important that these are not just permitted but actually encouraged as an important way for Canadians to have access to the newest rare disease treatments. Investments by companies in innovative forms of drug treatment studies should be encouraged via grants and tax credits similar to those permitted for investment in randomized clinical studies and other research activities.

Making access to patients a priority

With traditional drug development, approval and access regulations, too often the process is the priority, not the objective of getting new treatments to patients. This is not necessarily inappropriate for evaluating new treatments for common conditions for which adequate existing treatments already exist. However, for drugs for rare conditions, many of which are the first and only treatments available for patients, access to patients must be the top priority, while also, of course, maintaining adequate risk safeguards, but also recognizing the risk and cost of not getting treatment to patients. This change of priority should be reflected in all aspects of regulating the study, approval and access to new treatments for rare diseases. The federal government has already recognized the shortcomings of the current system in special circumstances when it created special processes to speed up approvals of vaccines and medicines related to the COVID-19 pandemic.

In summary, the key requirements to achieve this Strategic Pillar are:

- Changes to federal regulatory drug approval system for rare diseases and to better accommodate new technologies that don't fit existing categories
- Changes to the federal drug pricing regulation system
- Changes to emergency and early drug access programs
- Changes to regulations to further promote investments in clinical studies and alternate means of evaluating of rare disease treatments
- Innovation to speed all aspects of the regulatory system and make them more coordinated with the access and reimbursement process to speed access to patients

IX. Strategic Pillar #3:

Accelerated access to rare diseases diagnosis, treatments and care

The traditional approach to developing and introducing new drug treatments in Canada has been very sequential: clinical studies, regulatory approval, health technology assessment evaluation, pricing negotiations and, ultimately, availability to patients through public drug plans – at different times for different provinces and public plans. The overall process takes many years, including a very long and growing gap between regulatory approval and patients actually being able to access a treatment through government drug plans.

For example, a 2019 study confirmed that Canadian public reimbursement delays from drug approval to country-wide listing increased in just a two-year period (2013-14 to 2015-16) by 22% to 571 days (1.5 years).[20]

A patient-centric approach for Ontario, and for all of Canada, would adopt steps that have been taken by other jurisdictions which put patient needs first by providing automatic access to rare disease medications upon regulatory approval, pending the pricing and reimbursement negotiations. In France, this is done for all treatments for which the budget impact is expected to be €30 million (CAD$45 million) or less while Germany does so if the budget impact is €50 million (CAD$75 million) or less. Canadian patients deserve this as well so they are not caught in the middle of ongoing price discussions between companies and governments and so governments are not provided the incentive they have now to delay reimbursement of medicines as a means to save money.

Instead, they will be incentivized to provide access immediately once Health Canada has approved the products and, in some cases, negotiations can be undertaken even before Health Canada approval in order to improve the value for payers and ensure much faster patient access. For medicines that will have a higher market size than a given threshold, the health technology assessment (HTA) process can be streamlined and independent HTA evaluations can be applied. Negotiations can happen simultaneously with reimbursement contingent on a positive clinical HTA review.

We saw this happen with the approval and rollout of the first COVID-19 vaccines in late 2020, from Pfizer and BioNTech. Health Canada received the initial application for approval on October 9, 2020, and conducted a rolling review as new data became available before granting approval on December 9, 2020, just 61 days later.[21] The first vaccine was administered to a patient – paid for publicly – just five days after that. The whole process from first application by the company to Health Canada to patients getting paid access to the vaccine took just 66 days.[22]

There are also other innovative pricing and payment ideas that should be evaluated and used when appropriate such as pay-for-performance in which governments only pay for treatments that provide pre-defined successful results or acquiring new technology on a lease basis for evaluation before making large investments in purchasing it.

There is huge range in the types of rare diseases and the impact they have on patients, which means patient needs for many conditions are not met because they don't fit established program criteria or require more resources than certain programs permit (beyond prescribed limits). A patient-centric system for Ontarians with rare disorders would allow managers of services and systems the flexibility to expand certain programs on their own authority to meet the needs of a few patients with a particular disorder who have exceptional needs beyond the normal range of the program in question.

The new rare disease strategy must also embrace new technologies that already exist and be set up to easily adopt further technological changes that will inevitably follow. The new CAR-T treatment technology is a useful example that requires specialized knowledge and procedures. It makes sense that these be provided only at specialized centres, so systems need to be set up to ensure those centres can seamlessly handle out-of-province patients from regions where specialized centres do not exist and it is impractical to have them.

The new rare disease strategy must also embrace new technologies that already exist and be set up to easily adopt further technological changes that will inevitably follow.

Additionally, there are many new technologies available and in development that can provide different help and services to patients and their families, such as remote monitoring or devices that help with providing for patient needs. Many of these technologies at present fall through the cracks of the health system and payment programs because they are not easily categorized as either medicines or medical devices. Our broader health system simply wasn't set up for and hasn't adapted to how to best manage these new technologies, so they are often ignored. They can be vital, however, for helping to treat patients with certain rare disorders, in addition to pharmaceutical or biotechnology treatments.

Another important aspect to both help patients and their families and make the health system more efficient is to improve access to diagnostic tests and services as well as to specialist evaluation. In one survey conducted by CORD, one-third of patients said it took more than three years to get a correct diagnosis and one-fifth said it took more than six years, receiving (and being treated for) several incorrect diagnoses in the interim.[23]

Incorrect diagnoses not only waste healthcare resources but they can cause great harm and discomfort to patients, often exacerbating their illness which leads to use of even more care resources. Training is one element of improving diagnoses, but so is easy and ready access to different diagnostic tests. Another crucial element, given that many rare disorders are genetic-based and affect children, is genetic testing of newborns and young children if symptoms develop.

Technology can play an important role in helping with the diagnosis problem by establishing systems that provide family physicians ready access to specialists to consult with early on when they are seeing patients for whom accurate diagnosis is proving a challenge. For example, the Canadian Foundation for Healthcare Improvement has had a program in place that has allowed 2,200 family physicians to have access 800 specialists for speedier consultations rather than simply referring their patients.[24] More initiatives like this could be implemented to connect family doctors with services and specialists, as well as to improve education programs that allow them to consider possible rare disorders when they are faced with patients with unusual challenges.

In summary, the key requirements to achieve this Strategic Pillar are:

- Changes to how decisions are made, and the criteria used, to pay for rare disease therapies and their timing to make access available at the same time as regulatory approval
- Provide greater leeway to allow flexibility by health system leaders to adapt services and systems to specific needs of individual diseases and conditions
- Changes to health system structures and processes to better accommodate new technologies and processes involved with new treatments
- Investments in necessary services to speed diagnosis and to provide care to patients and support to families

X. Strategic Pillar #4:
Make managing rare diseases an economic development strategy

Ontario, and Canada as a whole, has for too long considered spending on healthcare only as an expense, not an investment that can reap returns not just for the better health of patients but for the economy as a whole. These returns come from two major sources: turning otherwise ill and unproductive citizens into ones able to work and contribute to society as well as the financial returns seen from creating jobs by providing healthcare services and spending on goods required to provide those services.

For example, healthcare spending is rarely considered a major driver of employment in Canada but there are 531,000 Canadians who are doctors or nurses,[25] let alone all the other jobs involved in healthcare and life sciences, from other health professionals to support personnel of many types. But consider that number – there are several times as many doctors and nurses in Canada as total workers in the oil and gas industry, which employs about 174,000 Canadians.[26]

In Ontario, there are 85% more doctors and nurses than there are direct workers in the automotive industry (186,500 vs 101,000), the latter of which is often held up as a key engine of economic activity in the province.[27] The largest employer in "Steel Town" – Hamilton, Ontario – is now not the steel industry but healthcare. In 2019, the city reported 42,000 employed in "healthcare and social assistance" compared to 28,854 in the whole "manufacturing" sector, including steel production, and 27,445 in the whole retail sector.[28]

Beyond the economic impact of direct healthcare delivery there is also the significant contribution of the life sciences industry. The industry in Ontario ranks among the top clusters in North America and has been a key economic sector for the province for decades. It is responsible for more than 82,000 jobs and contributes $21.6 billion to the province's GDP.[29]

A change in perspective by governments and healthcare system decision-makers is needed to recognize and encourage the economic contribution and potential of the whole research, life sciences and healthcare system. The opportunity to invest in the development and provision of better care and treatments for Canadians and Ontarians with rare diseases should be seen as that – an investment in creating positive economic activity and jobs while also helping those with the conditions.

Too often spending on healthcare initiatives is regarded simply as lost money – a cost to be borne to help individual patients almost out of charity, with no other return. Instead, it should be recognized as what it really is – an economic investment in job creation and economic development (from which helping patients is the very positive outcome) with the same positive potential as other government investments in other economic sectors such as the auto industry, manufacturing, resource extraction or digital technology.

As happens with government spending in other key economic sectors, such public investments in rare diseases would stimulate other private investments and economic activity, particularly in the life sciences sector. Helping Ontarians with rare diseases is therefore also good for helping Ontario to be open for business.

Governments are also realizing the need to make significant investments in much-needed new infrastructure, both because it is needed but also to stimulate the economy post-pandemic. While the roads, bridges and other facilities often first considered under such programs are important, investments in hospitals, clinics and technical medical infrastructure to help diagnose, treat and manage rare diseases is also greatly needed so that all Ontarians will be able to benefit from the major knowledge advances that are making effective treatment of many serious rare diseases possible.

In summary, the key requirements to achieve this Strategic Pillar are:

- Recognize investments in healthcare and treating rare diseases as economic development investments that create jobs and boost economic activity, rather than as lost expenses that need to be curtailed
- Public policy and health system investments and decisions that would encourage additional private investment in life sciences research and businesses in Ontario, contributing further to employment and prosperity
- Further investment in public health facilities (clinics, hospitals, etc.) to help them create the infrastructure and systems they need to conduct more rare disease clinical research with patients and to provide better diagnostic and care services

The opportunity to invest in the development and provision of better care and treatments for Canadians and Ontarians with rare diseases should be seen as that – an investment in creating positive economic activity and jobs while also helping those with the conditions.

XI. Strategic Pillar #5:

Integrate Ontario's rare diseases strategy with other health initiatives and the Canadian Rare Disease Strategy

While healthcare delivery clearly is a provincial responsibility under Canada's constitution, it is important that Ontario not act alone or out of step with the rest of the country in addressing the needs of those with rare diseases. However, as the largest province it can and must play an important leadership role in this crucial area.

For the diagnosis and treatment of rare diseases, inter-provincial cooperation and consistency is particularly important. It is simply not practical or feasible for every province to have the resources and specialized knowledge and care facilities to diagnose and treat all rare diseases. For ultra-rare conditions that impact just a few patients per year, having just one or two centres for the whole country is the sensible approach. As a result, systems must be in place that facilitate the seamless movement of patients and their files from one province to another for prompt diagnostic services, expert consultation and, ultimately, treatment. Therefore, a coordinated national approach is needed, as well as the technology to make potential national provision of services from one or two locations feasible and efficient.

Fortunately, we already have a national rare diseases strategy available to act as a blueprint for the federal government and all provinces to create what is needed to meet the needs of Canadians with rare diseases. This national strategy was developed by the entire rare diseases community in Canada and presented by CORD in 2015. It is crucial that any provincial strategies and initiatives for rare diseases be consistent with this broader national strategy.

While national and provincial strategies are important, we have to recognize and accommodate the needs of varied and diverse populations, particularly those living in more isolated areas so that they can also benefit from needed services, using technology to lessen distance as much as possible. Additionally, certain genetically based rare diseases are more prevalent in certain ethnic groups, so it makes sense to prioritize the location of services for those conditions closer to where these populations live.

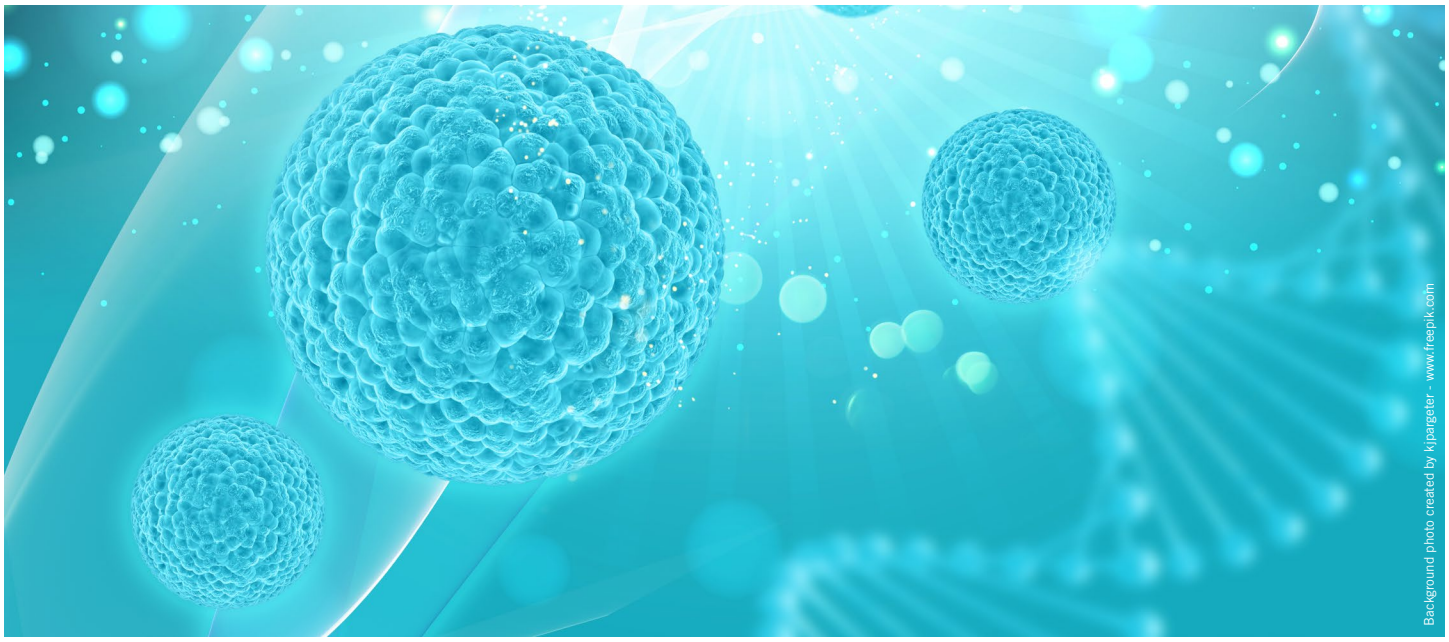
There are also possibilities to incorporate meeting the special needs of those with rare disorders into broader strategies for diagnosing and managing chronic conditions such as heart disease and diabetes, as well as cancer and other serious illnesses. One option would be the creation of specialized non-hospital clinics for meeting these needs, incorporating specialty care for rare diseases into such centres.

The broad community outreach that is important in diagnosing and treating rare diseases could also provide an opportunity for delivering enhanced public health messages and services that will be a crucial part of the new health system following the most acute phase of the COVID-19 pandemic. Enhanced recognition of the need to reach all citizens with important public health information provides an excellent opportunity to raise awareness of rare diseases and diagnostic services available for those who are facing challenges in getting a correct diagnosis and treatment for a condition.

Investing in the diagnosis and treatment of rare diseases in Ontario should be recognized as important not just to improve the health and lives of Ontarians but as a vital part of the province's economic activity and well-being. Healthier and more active residents make for a stronger economy and a stronger province.

In summary, the key requirements to achieve this Strategic Pillar are:

- Ensure it is consistent and supports the national rare diseases strategy led by CORD
- Ensure it is flexible enough to incorporate the many very different conditions that are considered rare diseases and their very different patient populations
- Ensure it fits with and supports needed progress to improve treatment of other chronic and serious conditions such as cancer and diabetes
- Ensure it supports enhanced public health preparedness measures that will come in the post-pandemic era
- Ensure it is consistent as a key element of Ontario's overall strategic economic development



XII. Where do we go from here?

As detailed in Section IV, there are urgent reasons and opportunities for immediate action to develop and implement a new strategy and program to deliver drugs for rare diseases to Ontario residents, and indeed to all Canadians.

It is important for action to be taken immediately to start the process of developing the necessary plans and programs which should be tied to the start of the new federal funding for drugs for rare diseases in 2022-23.

Fortunately, a roadmap for this already exists in *Canada's Rare Disease Strategy* put forward by the Canadian Organization for Rare Disorders (CORD) on behalf of the rare disease community in 2015. This should be used to create a system that takes into account the five strategic pillars proposed in this document.

To ensure movement towards the development and implementation of a comprehensive rare diseases strategy for Ontario in the very near future, the following steps are strongly suggested and recommended:

1. Ontario take a decision to play a leadership role among the provinces and territories on new programs and strategies for rare diseases and to lead by example, with a goal of ensuring new strategies and programs are in place by the start of the new federal rare disease drugs funding in 2022-23.

2. The Ontario Minister of Health start an urgent consultation with CORD to ensure alignment and agreement on next steps for a plan forward.

3. The Ontario Minister of Health conduct urgent consultations with the federal Minister of Innovation, Science and Economic Development (ISED) and ISED officials to align with federal plans regarding the announced rare disease drugs spending.

4. The Ontario Minister of Health engage in consultations with the federal Minister of Health on exempting drugs for rare diseases from the new economic evaluation provisions of the *Patented Medicines Regulations* governing the Patented Medicine Prices Review Board.

5. The Ontario Minister of Health engage in consultations with the federal Minister of Health and Health Canada on revisions to the regulatory pathway for rare disease drugs and changes to the health technology assessment process for rare disease drugs by the Canadian Agency for Drugs and Technology in Health (CADTH).

6. The Ontario government initiate and lead discussions with the pan-Canadian Pharmaceutical Alliance (pCPA) on a new approach to negotiating product listing agreements with pharmaceutical companies for drugs for rare diseases.

7. The Ontario government align with the federal government on a firm target date for implementation of a strategy and the start of new federal funding.

8. Based on the foregoing discussions, the Ontario government finalize its rare diseases strategy and plan in time for the start of the new federal spending.

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