Characteristics of a pan-Canadian National Rare Disease Strategy

Addressing barriers to appropriate rare disease treatments

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1. Executive Summary

RAREi believes that a compassionate health care system should be organized in such a way as to ensure timely and reasonable access to needed therapies. As such, it is very encouraged by the federal government’s efforts to develop a national rare disease treatment strategy for Canadians.

In this submission, RAREi outlines a series of elements it believes are crucial to an effective national rare disease treatment strategy in Canada. They include: timely and equitable access to rare disease medicines, reliance on models that already exist in Canada and internationally, clear definitions and timelines, improvements in the research environment in Canada, separate, customized and distinct pathways for the review and approval of rare disease medicines and recognition that provinces are responsible for delivery of rare disease treatments to patients and their overall care.

In addition, RAREi believes that two factors are crucial in the process of developing a federal rare disease treatment strategy. First, the federal government must play a facilitating role in building and supporting a true pan-Canadian rare disease framework. And second, all stakeholders – governments, industry, the research community and, above all, patients and families – must feel legitimately engaged with the process and heard in a meaningful way to co-create a strategy that they accept, support and will work actively to implement effectively.

Fortunately, this process does not have to start from a base of nothing. The new Canadian framework should be built from and based on the strategy developed by the entire rare disease community and presented in 2015 by the Canadian Organization for Rare Disorders (CORD).
RAREi, and its members, stand ready to contribute constructively to the process that is currently underway and the programs that emerge from the effort. We look forward to engaging with other stakeholders in the creation and implementation of a national program that meets the needs of rare disease patients across the country.

2. Introduction

The Canadian Forum for Rare Disease Innovators (RAREi) is a group of innovators of rare disease treatments in Canada. Its members are biopharmaceutical companies that are committed to improving the lives of patients around the world living with rare disorders by researching, developing and commercializing rare disease treatments. The RAREi forum includes:

- Akcea Therapeutics Canada
- Alexion Pharma Canada Corp.
- Amicus Therapeutics Canada Inc.
- Biogen Canada Inc.
- Biomarin Pharmaceutical Inc.
- Horizon Therapeutics Canada
- Ipsen Biopharmaceuticals Canada Inc.
- Mitsubishi Tanabe Pharma Canada Inc.
- Recordati Rare Diseases Canada Inc.
- Sanofi Genzyme
- Sobi Canada Inc.
- Ultragenyx Pharmaceutical
- Vertex Pharmaceuticals (Canada) Inc.

Canadians experience numerous challenges in obtaining access to treatments for rare conditions. It is estimated that there are around 7,000 rare diseases, but there are only effective treatments for a fraction of these conditions. And, even when an effective treatment has been developed, patients must still endure lengthy waits and great uncertainty when trying to access those medicines in this country or in their own province.

Rare diseases are often severely debilitating or life-threatening and the affected patients and their families (since two-thirds of patients are children) face many challenges living with these conditions. RAREi believes that a compassionate health care system should be organized in such a way as to ensure timely and reasonable access to needed therapies.

Affordability and access are important challenges for patients and health systems. However, overcoming these barriers should not focus exclusively on public or list prices. The federal government has too often focused on prices for some of these treatments without considering that they are for a very low number of patients, therefore the

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2 Canadian Organization for Rare Disorders, About CORD, Key Facts. https://www.raredisorders.ca/about-cord/.
The overall budgetary impact is low. Even if Canada finds a way to do a better job of extending public coverage for rare disease treatments, their total cost is expected to remain a very small percentage of public drug plan and broader health care budgets.

A recent analysis found that non-oncology-related orphan medicines represented only 1.9% of total public medication expenditure (and a much lower proportion of total health care expenditure) in Canada in 2019. Even if all rare disease treatments available were funded publicly, their share of national medication spending are projected to increase to only 6.5% by 2025 for a total estimated spend of $1.39 billion. Moreover, that estimate is likely far above actual spending, given that savings to public payers via product listing agreements are not accounted for in the analysis.3

The cost of treating rare diseases is even less when one considers the avoided costs in other areas, such as reduced hospitalization, supportive care, other costly interventions or the challenges associated with early deaths and patient suffering. For example, despite the relatively high price tag for new spinal muscular atrophy (SMA) therapeutics, a recent systematic review of the economic burden of SMA confirmed the substantial cost burden of standard of care for SMA patients and the high cost-effectiveness ratios of the approved medicines when delivered in post-symptomatic patients.4 Another good example is the use of nitisinone to treat a rare, but severe genetic metabolic disorder tyrosinemia type I. A Canadian study found that nitisinone treatment was associated with significant reductions in the number and duration of hospital admissions, the number of admissions to a pediatric intensive care unit, and the number of liver transplants. It decreased the costs associated with those interventions significantly and improved the outcomes of patients.5

RAREi is very encouraged by the Canadian government’s intention to develop a national strategy for access by Canadians to rare disease treatments. However, as we have stated before, RAREi vociferously objects to the use of the term “high-cost drugs” in the name of the strategy. That terminology immediately prejudices patients with rare diseases and suggests a cost-containment focus rather than a patient-oriented approach. It also limits and undermines any opportunity for governments to leverage the new strategy to support their innovation goals. Finally, in order to meet the needs of all Canadians with rare diseases, the strategy must pertain to ALL drugs for such conditions, not just those subjectively referred to as “high cost.”

In this submission, RAREi outlines 10 elements we believe are crucial to an effective national rare disease treatment strategy in Canada. For each, we present in detail below why it is needed and the elements we believe should be included:

1. Adoption of a framework approach that ensures more timely and equitable access to rare disease medicines across the provinces, building on models that have worked in other federations, such as the United Kingdom (UK) and elsewhere (i.e., Germany), and that already exist in Canada, such as Canada’s Rare Disease Strategy endorsed by the Canadian Organization for Rare Disorders (CORD)

2. Principles, measurable objectives and an independent external evaluation process

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3. Clear definitions for orphan medicines and rare diseases that are fit-for-purpose and aligned with international best practices

4. Improvements to Canada’s research environment to promote the development and adoption of new rare disease treatments

5. A separate specialized regulatory pathway aligned and in cooperation with international comparators, including incentives such as market exclusivity enhancements, as well as data protection similar to that offered in other jurisdictions.

6. Clear and predictable timeframes for funding decisions across all jurisdictions

7. A fair and internationally compatible pricing regulation process

8. A predictable and efficient health technology assessment and price negotiation process using rare disease-specific parameters

9. The development of comprehensive infrastructure to capture and evaluate real-world evidence to drive evidence-based decision-making

Before exploring what would be required in each of these elements, however, it is useful to begin with a proposed process for reaching agreement on the strategy followed by a review of the unique challenges that exist for any researcher or company developing and commercializing rare disease treatments in any jurisdiction. These special conditions must be kept in mind when developing the policies and procedures of any national rare disease treatment strategy.

While this paper addresses the issues involved in this manner, specific direct responses to the four questions asked in the discussion paper *Building a National Strategy for High-Cost Drugs for Rare Disorders* are presented as an appendix to this document.

### 3. Recommendations to improve patient access to rare disease therapies

The development of a federal rare disease treatment strategy is important not just for Canadians affected by rare diseases now and in the future, but also for the future of our health care system and, in particular, to provide key learnings for any future development of a universal national pharmacare program in Canada. It is vital that the process to achieve the strategy is thorough, transparent and meets the needs of Canadian patients now and into the foreseeable future. The current consultation is an excellent start to achieving these objectives.

As with many aspects of developing national policies for Canada, the framework of the Canadian constitution and federation can make this process challenging, but it must be respected. The provinces have sole responsibility for delivering health care to Canadians; that is unequivocally clear and a federal rare disease treatment strategy must respect this jurisdiction. However, it is also crucial that an effective strategy be consistent and consistently applied across the country. Indeed, one of the key objectives must be to ensure that coverage for treatments for rare diseases is equitable everywhere in Canada.
Two factors are crucial in the process of developing a federal rare disease treatment strategy to ensure these challenging goals are met:

1. The federal government must play a facilitating role in building and supporting a true pan-Canadian rare disease framework.

2. All stakeholders – governments, industry, the research community and, above all, patients and families – must feel legitimately engaged with the process and heard in a meaningful way to co-create a strategy that they accept, support and will work actively to implement effectively.

For the first objective, it is encouraging to see how the federal government is approaching the task to date of developing the strategy and its commitment to significant funding in the coming years. A mechanism will be required in the strategy to ensure that adequate funding levels persist beyond that of the current commitment by the federal government, and that it not be subject to significant change by whim of different governments or fluctuating financial circumstances.

The federal government will also have a vital ongoing role to ensure all jurisdictions live up to the commitments made to patients under the strategy by delivering the needed services and treatments or ensuring that citizens have access to them in some way (recognizing that it may not be practical for patients with certain very rare diseases to be treated within their jurisdiction due to lack of necessary resources and/or expertise).

For the second objective, it is vital that the results of this consultation create a fair and prompt way for all stakeholders to become co-creators of the ultimate strategy. This is not to say that any one stakeholder group will get everything they might want in the ultimate strategy, but it does set a bar that all stakeholders should accept the strategy as being the best result for the overall well-being of Canadians. This challenging objective can only be achieved with an ongoing constructive process of dialogue, debate and compromise, over a reasonable period of time.

RAREi sincerely hopes that the current consultation will result in the development of just such a process and, in the end, a true pan-Canadian strategy for rare diseases. It is fortunate that this process does not start from a base of nothing. The new Canadian framework should be built from and based on the strategy developed by the entire rare disease community and presented in 2015 by CORD.

Canada’s Rare Disease Strategy, available here is based on a five-point action plan:

1. Improving early detection and prevention
2. Providing timely, equitable and evidence-informed care
3. Enhancing community support
4. Providing sustainable access to promising therapies
5. Promoting innovative research

RAREi endorses the CORD strategy as the foundational element of the new Canadian rare diseases strategy. In the further recommendations outlined below, additional details for such a strategy are presented.
4. Challenges in developing and commercializing rare disease treatments

Developing and commercializing rare disease treatments is more challenging than for more common diseases for many reasons, including:

- **Knowledge of rare diseases is limited.** At the beginning of research and development into potential treatments, there is little to no previous scientific or technical knowledge on which to rely given the rarity of the disease. This means that research into rare disease treatments often begins at square one. Further, long-term disease progression data is also difficult to locate or develop. There can also be significant genetic diversity within a single rare disease, further challenging scientists’ understanding of the disease itself, which is needed before beginning to develop a potentially successful treatment.

- **Rare diseases affect a small number of people.** The fact that rare diseases affect few patients presents specific challenges from a research and development perspective. In particular, the low prevalence makes it difficult to locate and recruit patients for clinical trials. Consequently, many clinical trials are global in scope by necessity, and conducted via numerous clinical trial sites.

- **Few clinicians are familiar with rare diseases.** While also affecting patient care, clinicians’ lack of familiarity with rare diseases (because they don’t see them) makes it challenging to recruit knowledgeable physicians to administer clinical trials. This makes it unlikely that the necessary expertise would be available in one given country. If such expertise exists in Canada at all, it is likely that it would be limited to a very small number of clinicians.

- **Gold standard clinical trials are often infeasible or unethical.** Evaluations of new treatments, such as health technology assessments (HTAs) conducted by the Canadian Agency for Drugs and Technologies in Health (CADTH), are designed with the expectation that a clinical trial will be a randomized, controlled trial (RCT). However, this type of trial design is often infeasible given the low prevalence, or unethical given the disease severity and lack of other treatment options. When innovators cannot implement RCTs, they rely on other suitable methodologies in order to understand whether a potential treatment is effective in treating patients. An example of an alternative methodology is an adaptive clinical trial where participants are monitored to test the effect of the potential treatment on a defined schedule and specific parameters of the study change based on the observations.

- **Greater clinical and economic uncertainty.** Limited understanding of rare diseases and the small patient populations create greater uncertainty. More specifically, the nascent scientific understanding of many rare diseases results in limited understanding or consensus about clinically validated endpoints for studies of potential treatments. Smaller and shorter studies designed to expedite access to treatments in the face of very severe diseases result in less clinical trial data. In fact, sometimes only unpublished proprietary data is available at the time of submission. As well, the lack of clinician knowledge and of expert reference centres on which to rely means that the development of rare disease treatments fails more often than common disease treatments. Alternative clinical trial design methodologies that enable the study of rare disease treatments create greater uncertainty for regulators, HTA evaluators and those involved in the reimbursement process. While regulators have made great strides in understanding these data, innovators routinely face challenges when presenting study results in the context of HTAs due to the rigid evaluation framework.

Because of these challenges, the risk and cost involved in developing and commercializing treatments for rare diseases is often much greater compared to more common conditions. It is for all of these reasons that a comprehensive national strategy for rare disease treatments is needed in Canada. Such a strategy should include the following key elements.
5. Elements vital for an effective national strategy for rare disease treatments

1) Adoption of a framework approach that ensures more timely and equitable access to rare disease medicines across the provinces, building on models that have worked in other federations, such as the United Kingdom and elsewhere (i.e., Germany), and that already exist in Canada, such as Canada’s Rare Disease Strategy endorsed by CORD.

Why this element is needed in the strategy:
• This is the overarching key element of the strategy and the first priority to address since all other elements are dependent on the provision of access. As a federation with clear roles for the federal and provincial governments, a framework approach to a national rare diseases medicines strategy needs to facilitate and enhance the capacity for all stakeholders in Canada’s rare disease community to achieve their varied objectives – including provinces, research and clinical networks, medicine developers, caregivers and, most importantly, patients.

What needs to be in this element:
• A framework approach that works for Canada’s diverse patient populations and health systems across the country. The UK’s four-country approach to rare diseases tackles this challenge by leveraging and enhancing the different capacities, needs and powers of each country. The Canadian government can build on this approach, and the approach that is largely found in Canada’s Rare Diseases Strategy. A national framework strategy provides clear direction to all players in the rare diseases community regarding how they can adopt and implement specific actions, many of which are further elaborated in this submission, as well as other input that is sure to be heard from Canada’s diverse stakeholder community and health system partners.

2) Principles, measurable objectives and an independent external evaluation process

Why this element is needed in the strategy:
• In order to know if a strategy is effective, it is crucial to have objectively measurable goals and a tracking process to capture those measurements and evaluate performance.
• Clear guiding principles are required to give the foundation of how the strategy will be developed and implemented over time.
• The principles that guided the development of the pan-Canadian Oncology Drug Review (pCODR), which were largely adopted by the pan-Canadian Pharmaceutical Alliance (pCPA) when it was created, are still valid and should be incorporated into the national framework strategy, specifically they included:
  – Accountable governance
  – Collaborative and representative
  – Efficient and effective
  – Continuous evaluation
  – Health system focused
In addition, setting out objectives and how they will be measured in the strategy itself makes it clear and unambiguous what is intended to be achieved.

This process will make it easier to identify any deficiencies in the implementation of the strategy at an early stage so adjustments can be made promptly.

What needs to be in this element:

- Clear-language guiding principles for the strategy developed with the input of all stakeholders and guaranteeing that the input of patients and their families will be sought and recognized at every stage of the development and implementation of the strategy.

- Clear objectives for the strategy, clarity about how they will be measured and the levels of those measurements that are being sought to declare the objective as achieved. For example, an objective could be that Canada approves and reimburses a certain (high) percentage of rare disease treatments publicly within a certain timeframe from their availability in key comparator jurisdictions such as the US, UK and EU.

- Measurable objectives should be included for each key element of the strategy.

- A timeline and process to ensure regular and meaningful evaluation and review of the strategy over time with the input of all stakeholders, particularly patients and their families.

3) **Clear definitions for orphan medicines and rare diseases that are fit-for-purpose and aligned with international best practices**

Why this element is needed in the strategy:

- Other jurisdictions – including all of Canada’s developed-country counterparts – have adopted a clear definition for regulatory designations of orphan medicines, which have been critical in providing and defining intellectual property and regulatory enhancements for innovative medicines.

- Additional definitions or prevalence ratios may also be considered in terms of access to enhanced or tailored evaluation and funding processes, however, given the significant heterogeneity of rare diseases and treatments, these definitions should be fit-for-purpose and forward-looking.

What needs to be in this element:

- A clear national definition of the conditions for which therapeutic products will be designated as rare disease treatments or orphan medicines. RAREi recommends using the CORD definition which is “a condition affecting fewer than 1 person in 2,000 in their lifetime.” RAREi also strongly recommends that the criteria for application of the strategy should not involve reference to the treatment’s price (i.e., Health Canada should refrain from

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6 Canadian Organization for Rare Disorders, About CORD, Key Facts, [https://www.raredisorders.ca/about-cord/](https://www.raredisorders.ca/about-cord/).
describing medicines as “high-cost” or “expensive” as part of the strategy, which may stigmatize patients and reduce access to the medicines).

4) Improvements to Canada’s research environment to promote the development and adoption of new rare disease treatments

Why this element is needed in the strategy:

- The field of treatments for rare diseases is rapidly evolving and progressing on many fronts, particularly with exciting new genetic knowledge and technology. Canada has the expertise and infrastructure to play a vital global role in these developments and thereby also offer help to Canadian patients as early as possible in the process. However, the right educational, institutional and policy framework needs to be in place and maintained to ensure this important contribution to the Canadian economy and Canadian patients and families.

- Rare diseases, because of the small patient populations involved, do not lend themselves to clinical research being conducted in the same manner as for more prevalent conditions. Special rules and procedures are needed to allow different types of clinical research on rare diseases to be conducted, and the results of such research accepted for regulatory, HTA and patient access purposes.

What needs to be in this element:

- Canada’s research institutions should be supported to increase research on rare diseases in Canada.

- Regulatory authorities should be mandated to develop new criteria and processes for evaluating the benefits of new treatments and technologies for treating rare diseases

5) A separate specialized regulatory pathway aligned and in cooperation with international comparators, including incentives such as market exclusivity enhancements, as well as data protection similar to that offered in other jurisdictions.

Why this element is needed in the strategy:

- Most developed countries, but not Canada, have distinct regulatory frameworks to incent the development and commercialization of rare disease therapies. This is vital for such medicines for which many of the normal regulatory hurdles are difficult if not impossible to clear, such as providing efficacy and safety information from randomized clinical trials. This is perhaps the most essential element of a rare disease treatment strategy for Canada.

- Because many rare disease treatments are, by definition, for a small number of patients in any one jurisdiction, collaboration, including recognition of decisions, among international regulators is vital to speed processes and make them more efficient for all.

- Appropriate incentives such as regulatory review fees waivers, market exclusivity, data protection and/or increased patent protection are needed to continue to promote the research investments necessary to ensure ongoing discovery and development of new therapies.

What needs to be in this element:
• A clear definition that supports an orphan medication designation

• A mandate for Health Canada to promptly develop and implement a separate regulatory pathway for eligible rare disease treatments consistent and in collaboration with regulators in the US, European Union (EU), UK and Australia.

• Inclusion in the new regulatory pathway of clear objectives for timelines to be met and a requirement for regular (at least annual) reporting of performance against these objectives.

• The reliance on rolling reviews and other regulatory accommodations building on the experience that Health Canada has developed in the context of the COVID-19 pandemic response

• Greater use of conditional regulatory decisions pending use of the treatment and collection of real-world evidence (RWE) related to its safety and efficacy (see also #9 below).

• The waiving or significant lowering of user fees for regulatory applications under the new rare disease treatment pathway, especially for ultra-rare diseases that have limited commercial potential.

• Increased and improved intellectual property protection for rare disease medicines as has been implemented in other jurisdictions, such as the US and EU.

6) Clear and predictable timeframes for funding decisions across all jurisdictions

Why this element is needed in the strategy:

• At present there is no way for a company contemplating introducing a rare disease medicine in Canada to know when it might expect commercial patient access to be granted, (i.e., when all Canadian patients would have access to the new treatment through public drug programs). This unpredictability leads many companies to choose not to launch products in Canada which leads, as noted above, to increasing and inappropriate use of the SAP as a means for Canadian patients to access needed treatments.

• Clarity about when publicly-funded access can be expected following application for regulatory approval in Canada (under the proposed new pathway) would encourage companies to launch more needed treatments for Canadians with rare diseases.

• As already demonstrated in other jurisdictions such as France and Germany, timely access for patients need not be tied to price negotiations; access should be provided first on a predictable basis at a pre-determined milestone (such as regulatory approval) with price negotiations following (and payment adjustments as needed for usage that has already occurred).

What needs to be in this element:

• The Canadian rare disease strategy should aim for access for all eligible patients to treatments from the time of regulatory approval of a treatment by Health Canada (under the new separate regulatory pathway).

• Manufacturers would submit an internationally comparable price with their regulatory application which they would be paid by Canadian drug plans immediately upon regulatory approval for use of the treatment by Canadian patients while HTA evaluations and permanent pricing negotiations are in progress.
• Adjustments in payments already disbursed will be made either by drug plans or the company upon the successful completion of pricing and performance negotiations (under a new separate rare disease treatment process outlined further in #9 below).

7) A fair and internationally compatible pricing regulation process

Why this element is needed in the strategy:

• Developers of innovative rare disease treatments need to know they can achieve an appropriate and fair return if they invest in bringing their treatments to Canada and for that they need a fair and internationally compatible price.

• The planned implementation of the federal pharmaceutical price review changes provide very little predictability in terms of price compliance for developers of rare diseases medicines. The range of mandatory regulatory price decreases, compared to current levels, is very concerning and makes it almost impossible, in many cases, to develop a business case for the deployment of new rare diseases medicines in Canada.

What needs to be in this element:

• Repeal the new economic factors from the Patented Medicines Regulations until their impact on rare disease treatments and clinical trials have been appropriately assessed and that this data has been shared with health system stakeholders.

• Conduct meaningful consultations with stakeholders until the implementation date of the regulations and provide more clarity on key issues that have drastic effects on rare disease treatments.

8) A predictable and efficient health technology assessment and price negotiation process using rare disease-specific parameters

Why this element is needed in the strategy:

• As with clinical studies for safety and efficacy, the normal parameters used in HTA evaluations are not appropriate for rare disease treatments; therefore, separate standards and processes are required.

• RAREi notes that Quebec’s HTA agency, the Institut national d’excellence en santé et services sociaux (INESSS) has already committed to considering the concept of “promise of therapeutic value” as part of its reviews which is a great start in demonstrating an understanding of rare diseases and the level of evidence available at the time of launch. This approach presupposes the collection of RWE over time to support continued reimbursement.

• While prices for individual products per patient might be considered high in some cases, the overall cost must be considered in light of the low number of patients who will need the medication, usually resulting in low total budget impact.

• The federal government is the largest funder of the CADTH and also contributes to the financial stability of INESSS in Quebec through the Canada Health Transfer and other asymmetrical funding programs. Health Canada should leverage these investments to help develop specific HTA evaluation programs for rare diseases.

What needs to be in this element:
• Replacement of the common HTA assessment measures that are used to assess treatments for large and broad populations in recognition of the fact that those methodologies, which rely on determinations of quality adjusted life years (QALYs) and incremental cost effectiveness ratios (ICERs) are not appropriate for rare disease treatments.

• Adopt other cost comparators such as cost of lifetime care without treatment, loss of earning potential by patients without treatment, etc. and give greater weight to quality-of-life improvements for patients and caregivers.

• Introduce the potential to pursue novel reimbursement models such as pay-for-performance (pay only if the treatment is effective to an agreed upon level) and other risk-sharing models between payers and the company (see more under #10 below).

• Waive the requirement for HTA assessments for products with low market potential because of small patient numbers similar to how this is handled in France and Germany.

• Adopt a process that permits early reimbursement of new rare disease treatments in areas where there is unmet clinical need with post market assessment of value that relies on RWE.

9) The development of comprehensive infrastructure to capture and evaluate real-world evidence to drive evidence-based decision-making

Why this element is needed in the strategy:

• Given the challenges of generating data on efficacy and safety of most rare disease treatments from randomized controlled studies, it is crucial that as much data as possible be collected and analyzed about real-world use of rare disease treatments to inform approval and ongoing use of treatments.

• Technology now makes the collection and analysis of such RWE feasible and cost-effective, making it imperative it be used to inform both treatment and payer decisions to ensure a good return on investments in treatments.

What needs to be in this element:

• A process and mandate to collect RWE related to all patients using all treatments that fall under the rare disease strategy and to analyze that data in real time to inform ongoing and future treatment decisions as well as to be used as a tool to determine pricing/performance milestones.

• Creation of a separate body as part of the Canadian rare disease treatment strategy to evaluate the collected RWE from Canada and elsewhere – and to contribute Canadian data to international data collection programs – and to report regularly to clinicians and payer decision-makers to inform future treatment regulatory decisions.
6. Recommendations for development and implementation of the strategy

In order to effectively develop and implement such a comprehensive rare disease strategy in a timely manner and to implement it effectively, RAREi also recommends the following:

1. Make use of international best practices as much as possible rather than “reinventing the wheel.” Most of these recommended elements are already in place in other jurisdictions and could be transferred easily to Canada.

2. These recommendations build on the federal model and jurisdictional responsibilities related to health care in Canada. Provinces would remain responsible for delivery of the rare disease treatments to patients and their overall care. The provincial and federal participation in the pan-Canadian Pharmaceutical Alliance (pCPA) is a model for such united activity. However, the pCPA can be enhanced to provide faster and timely implementation of funding term agreements across the country.

3. As occurs already with the treatment of certain rare diseases for which specialists are not available in all provinces, agreements should be reached among provinces to ensure out-of-province patients get treatments and other required services promptly and with minimal administrative challenges or roadblocks.

7. Conclusion

RAREi appreciates the opportunity to participate in the strategy development process underway and acknowledges the open-minded approach elicited by Health Canada in moving it forward. However, Canadian rare disease patients have been waiting for a long time for a program of this nature to be constructed, so we look forward with anticipation to the results of the dialogue.

As it develops, RAREi, and its members, stand ready to contribute constructively to the process that is currently underway and the programs that emerge from the effort. We look forward to engaging with other stakeholders in the creation and implementation of a national program that meets the needs of rare disease patients across the country.

8. Appendix – Responses to questions from discussion paper

RAREi is pleased to provide the following responses to the four specific questions on three issues asked in the discussion paper Building a National Strategy for High-Cost Drugs for Rare Disorders.

Note that, as explained in the Introduction, RAREi vociferously objects to the use of the term “high-cost drugs” in the name of the strategy.

**Issue 1:** How to improve patient access to high-cost drugs for rare diseases and ensure that access is consistent across the country.

**Q1.** How can access to high-cost drugs for rare diseases be made consistent in order to improve patient access to these treatments?

**Answer:** Access to rare disease treatments can be made more consistent by implementing the elements outlined in the proposals presented in this brief. Consistent access by patients will only be achieved by having a fair and predictable framework applicable everywhere in Canada for every stage of the process, from the research environment, through regulatory approval, pricing negotiations and prompt and uniform access by patients in all jurisdictions.
Q2. Which of the proposed options, or combination of options, would be the most effective for improving access and improving consistency? (Options: A single framework for decision-making on high-cost drugs; A transparent coordinating body; Patient and clinician engagement; Co-ordinate support for research on rare diseases in Canada)

Answer: As noted in the ideas presented in this brief, a combination of all the proposed options in varying degrees is necessary to ensure an effective framework for rare disease treatments is developed for Canadians.

Q3. Please explain the option(s) that you selected above

Answer: The recommended elements of a Canadian rare disease strategy are explained in detail in the brief. No one option listed under this issue will on its own create the necessary environment for the many elements required to ensure prompt access by Canadians to rare disease treatments — a strong research environment, a medical system adapted to be responsive to rare diseases, an adapted and responsive regulatory system and prompt and equitable access to new treatments immediately following regulatory approval.

Issue 2: How to ensure decisions on covering high-cost drugs for rare diseases are informed by the best evidence available.

Q1. How can decisions on covering high-cost drugs for rare diseases be made when the evidence is limited?

Answer: First, it is important to acknowledge that it is usually not evidence about treatment effectiveness that is limited for rare disease treatments, but rather evidence in the form that current regulatory and HTA systems require as the only acceptable type of evidence, (i.e., randomized controlled clinical studies). Canada must learn and adopt processes to manage limited evidence that have been accepted in other jurisdictions. There are numerous innovative methods available which should be incorporated in the Canadian strategy. Importantly, no one method should be chosen to apply for all rare diseases and treatments because different diseases, types of treatments and patient populations will require different approaches due to different types of evidence being available in different circumstances.

Q2. Which of the proposed options, or combination of options, would be most effective for strengthening the evidence base? (Options: Innovative approval and coverage models; A national expert panel; A national data system; Independent national and international networks)

Answer: All of the above as appropriate in different circumstances for different diseases and treatments. They vital key must be flexibility.

Q3. Please explain the option(s) that you selected above.

Answer: Rare diseases cover a very broad spectrum of illnesses with vastly different causes, symptoms and impacts on patients. The all-important key will be to have a flexible model that can be adapted quickly and efficiently to meet the needs of the particular disease and/or treatment. The system must not be created so that all treatments are forced to fit into or be evaluated by the same criteria or regulatory or HTA structure; that simply will not work effectively.

Issue 3: How to ensure spending on high-cost drugs for rare diseases does not put pressure on the sustainability of the Canadian health care system.

Q1. Which of the proposed options, or combination of options, would be most effective for getting rare-disease treatments to patients? (Options: Sharing of costs and pooling of risks; Investments up front to reduce the risk in early development; Pay for performance; Supports for “made in Canada” innovation; International collaboration)
Answer: All of the above in appropriate circumstances. However, it is important to recognize that the cost of rare
disease treatments is very unlikely to even put pressure on, let alone threaten, the sustainability of the Canadian
health care system. Even if Canada finds a way to do a better job of extending public coverage for rare disease
treatments, their total cost is expected to remain a very small percentage of public drug plan and broader health care
budgets. Other elements of health care costs, such as costs for health professionals or of long-term care, are far more
likely to exert more pressure on the sustainability of the Canadian health care system.
A recent analysis RAREi found that non-oncology-related orphan medicines represented only 1.9% of total public
medication expenditure (and a much lower proportion of total health care expenditure) in Canada in 2019. Even if all
rare disease treatments available were funded publicly, their share of national medication spending is projected to
increase to only 6.5% by 2025 for a total estimated spend of $1.39 billion. This estimate is likely far above actual
spending, given that savings to public payers via product listing agreements are not accounted for in the analysis.7

Q2. Please explain the option(s) that you selected above.

Answer: The new Canadian rare diseases framework must be open to different cost management options depending
on the circumstances of the disease, the size of the patient population, the nature and cost of the treatment and the
expected benefit. As with the regulatory environment and evidence base, it will be vital for the framework to be open
to flexibility and a willingness to consider the most appropriate options in the given circumstances, rather than
creating a one-size-fits-all solution that would not be appropriate for any.

General question for discussion:

Q1. Do you have other ideas that might help improve access and lower costs for drugs for rare diseases?

Answer: RAREi’s other ideas are detailed in the main sections of this document.

7 Forte L et al., The Current and Future Costs of Orphan Drugs in Canada - A Public Payer Budget Impact Analysis, Patient Access Solutions, 2019