Takeda

Better Health, Brighter Future

Enhancing Diagnosis, Access, Care and Treatment:

Recommendations for Health System Readiness for Rare Diseases in Canada

August 2024

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Executive Summary

A "rare" disease is any disease that affects a small number of individuals. It is often genetic, chronic throughout a patient's life and can be life-threatening.[1] In Canada, the impact of rare diseases on patients and the healthcare system is significant, often resulting in disability and the need for lifelong treatment for patients.[2] Although each of these rare diseases is individually uncommon, their collective impact is substantial, affecting approximately 1 in 12 Canadians.[3]

Novel drugs for rare diseases (DRDs) are innovative medications that address unmet medical needs and play a critical role in treating patients with these conditions. While the clinical development of novel DRDs is impactful for patients and their families, Canada's healthcare system must be prepared to provide these medications effectively, safely, timely and equitably to Canadians. The aim of this report is to assess active* DRDs in the current drug development pipeline and discuss the associated policy considerations for the Canadian healthcare system in terms of system readiness, which highlighted medical education, genetic testing, access to physicians, infrastructure, and the need for innovative funding models and collaboration.

In an analysis of the IQVIA™ Pipeline Intelligence database, this report found that over 1,100 DRDs are currently in development, with nearly 200 expected to launch in Canada within the next 10 years. There are several key factors that must be considered to ensure Canada's healthcare system is adequately prepared for this anticipated influx of DRDs:

1. **Physicians treating rare diseases must possess in-depth knowledge of these conditions and the treatments available.**
   Particular attention should be given to conditions where a first-in-class DRD is on the horizon, which offers new treatment opportunities, but may also require clinicians to develop new knowledge, resources and skills.

2. **Genetic testing plays a crucial role in diagnosing rare diseases and guiding treatment decisions.**
   One-quarter of DRDs treat genetic conditions, requiring prior genetic testing. However, the current administration of newborn screening programs across Canadian provinces leads to inequities and variation in the screening of rare diseases.

3. **Patients with a rare disease may encounter delays in diagnosis and access to treatment.**
   Access to knowledgeable healthcare providers is critical, especially for progressive diseases. In Canada, there is a shortage of physicians, further impacting the diagnosis and treatment of rare diseases.[4,5]

4. **One-third of DRDs in the pipeline are administered via intravenous infusion or are a specialized injection.**
   Clinical infrastructure is crucial for the administration of these treatments. Specialized injections and gene/cell therapies may necessitate access to an operating room or a dedicated treatment room.[6]

*Active status is applied to drugs where significant research and development activity has been reported within the last 3 years.

5 **Innovative funding models and collaboration can improve access to DRDs for patients with rare diseases.**

The adoption of novel healthcare financing strategies, inter-provincial, and inter-ministry collaboration play an important role in enhancing the availability and quality of patient care across Canada.

6 **Patient engagement and partnership are key to developing and planning healthcare services.**

The patient voice is a key component in ensuring that the correct care is reaching the right patient, at the right time in their healthcare journey. Greater involvement of patient groups and ongoing collaboration throughout the process of healthcare planning is essential to ensure that the needs of patients with rare diseases are met.

Canada's healthcare system needs to be equipped for the expected increase of DRDs to effectively identify and treat patients with rare diseases. These patients encounter unique obstacles due to the nature of their conditions, as well as the medications necessary for treatment. To effectively support specialized care, several resources within Canada's healthcare system are essential. These include investing in medical education, access to genetic testing, specialized treatment centres, infrastructure for the administration and storing of medications, and innovative funding models. Each of these components plays a pivotal role in ensuring optimal care and positive patient outcomes.

Introduction

Rare Diseases in Canada

Rare diseases include an array of clinical conditions that are often progressive, debilitating, and, in some cases, life-threatening.[3] There is no globally accepted definition of rare disease, however, most G20 nations define a rare disease as one that affects fewer than 1 in 2,000 people.[1] These conditions affect a relatively small proportion of the global population, yet their consequences are profound. Currently, researchers have identified between 6,000 and 8,000 rare diseases.[7]

In Canada, the impact of rare diseases are significant with approximately 1 in 12 Canadians – two-thirds of whom are children – affected by a rare disease.[3] The current landscape of medications for rare diseases in Canada presents both challenges and opportunities. As of 2019, 93 drugs with an annual cost of over $100,000 per patient have been approved in Canada for the treatment of rare diseases, with over 50% of these exceeding an annual cost of $200,000 per patient.[8]

1 in 12 Canadians are diagnosed with a rare disease. Two-thirds of rare disease patients are children.[1]

Given the diverse nature of these conditions, expertise and resources may be fragmented and limited across the country. To address these gaps in treatment, Canada's National Strategy for Drugs for Rare Diseases has allocated up to $1.5 billion, over three years, to enhance the affordability and accessibility of drugs for rare diseases (DRDs).[9] While challenges persist, these efforts signify progress towards increased access to treatments for patients with a rare disease. As a result, Canada's National Strategy for Drugs for Rare Diseases aims to address challenges such as delays in testing, limited treatment options, and barriers to accessing available treatments. The strategy focuses on early detection, equitable care, community support, access to promising therapies, and innovative research.[3] Furthermore, Canada's Drug Agency-L'Agence des médicaments du Canada (CDA-AMC) is actively involved in establishing a pan-Canadian Rare Disease-Based Registry.[10,11] These registries serve as centralized repositories, collecting standardized information about patients sharing specific rare conditions. The goal of these registries is to serve as real-world data (RWD) repositories to allow the generation of high-quality real-world evidence (RWE) that can inform regulatory decisions, health technology assessments (HTAs), and drug lifecycle management for rare diseases.[10,11] By recognizing rare diseases as a priority across the country, provinces and territories can work with the federal government to improve patient outcomes and advance healthcare initiatives on a broader scale.

Resources Required for Patients with Rare Diseases

Patients diagnosed with a rare disease face unique challenges due to the rarity and complexity of their condition. To address their specific needs, several critical resources are essential, such as ensuring clinicians have the appropriate knowledge and skills to treat patients with rare diseases,

access to genetic testing, specialized care and treatment centres, the appropriate infrastructure to store medications used to treat rare diseases, and innovative funding models. While each of these components will play a crucial role in ensuring optimal care and outcomes for individuals with rare and complex conditions, patient participation and collaboration with patient organizations at every step of future planning is vital to providing that the solutions that are appropriate for patients with rare diseases.

Objective

The objective of this report is to assess the DRDs expected to launch in Canada within the next decade and discuss the policy considerations for the Canadian healthcare system in terms of medical education, genetic testing, access to care, infrastructure, and funding models (**Figure 1**).

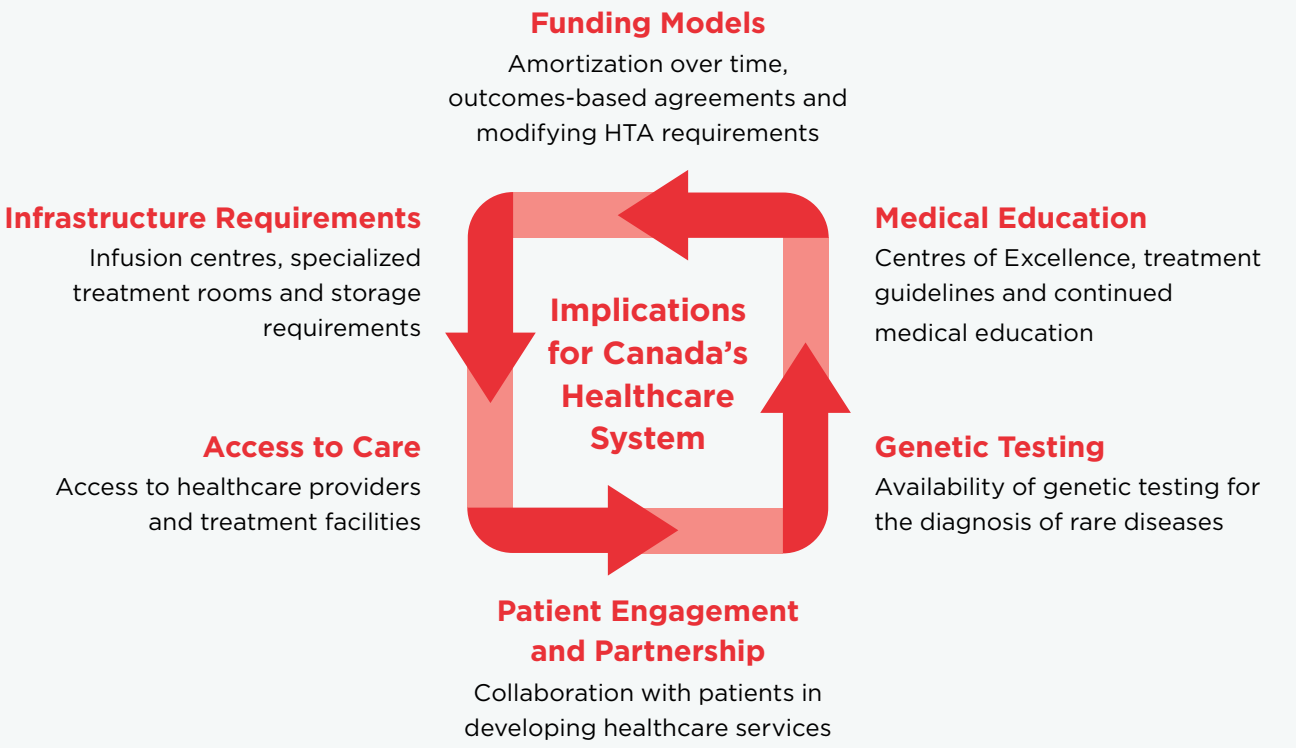


Figure 1: Impacts and considerations of incoming DRDs for Canada's Healthcare system

Methodology

IQVIA™ Pipeline Intelligence

IQVIA™ Pipeline Intelligence database was used to identify DRDs in the drug development pipeline. The Pipeline Intelligence database is a comprehensive source of drug information that provides the most up-to-date research and development insights across the entire drug development lifecycle, from early-stage research to commercialization. The database includes information on over 40,000 drug profiles from more than 170 countries worldwide. Pipeline Intelligence includes specific information on each drug product, such as phase of development (from discovery to marketed), indication, orphan drug status, mechanism of action, and therapeutic class.[12]

Selection of Drugs for Rare Diseases (DRDs)

DRDs from Pipeline Intelligence were initially identified based on orphan drug status (a drug that is intended for the treatment, diagnosis, or prevention of a life-threatening or chronic and serious rare disease), or those that had an indication for a rare disease.[13,14] DRDs that were not in active development, had only rare oncology indications, were duplicates, or are currently marketed in Canada for their rare disease indication were excluded (**Figure 2**). Overall, 1,147 DRDs were included in the pipeline analysis.

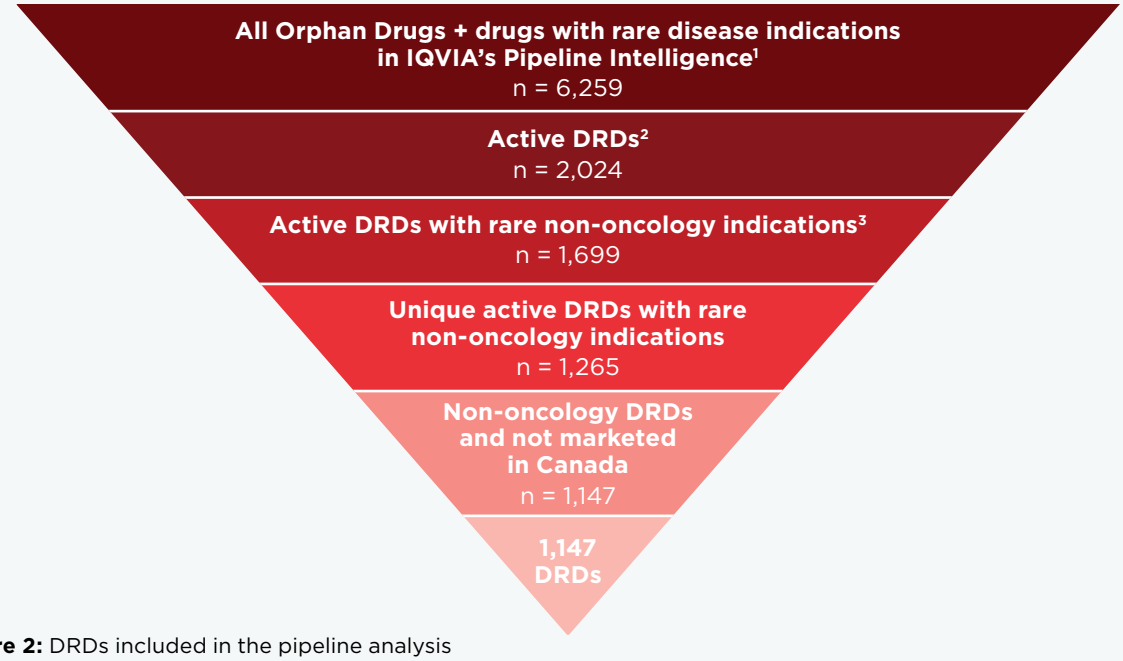


Figure 2: DRDs included in the pipeline analysis

1. Includes drugs being developed for rare diseases and/or have been granted orphan drug status.
2. Active status is applied to all drugs in Discovery phase to Registered where significant research and development activity has been reported within the last three years; Marketed drugs where the drug is still in a pre-marketed development somewhere in the world or for additional indications or the drug has been launched worldwide within the last three years.
3. Drugs with only oncology indications or drugs with oncology and non-oncology indications, but the non-oncology indication is not considered rare.

Data Source: IQVIA Pipeline Intelligence. 2023.

Data Segmentation and Estimation Methodology

The results of this report are presented using various stratifications to identify areas of Canada's healthcare system where additional future investments and policy developments may be required. Data are presented by phase of drug development, therapeutic area, route of administration, therapy type, rare versus ultra-rare disease status, pediatric indications, requirement for genetic testing, and first-in-class treatments. Detailed definitions of each of these segmentations are shown in **Figure 3**.

The DRDs identified in the pipeline in phase II, III, or pre-registration/registration were used to estimate the number of DRDs that may launch in Canada within the next decade. To arrive at this estimate, the number of DRDs likely to reach the global market was calculated based on historical trial progression rates for DRDs.[15] From this initial estimate, the proportion of DRDs launching specifically in Canada was calculated based on previous rates of medications launched in Canada following their global launch.[16] This estimate does not include Health Technology Assessment (HTA) recommendations or drug plan listings.

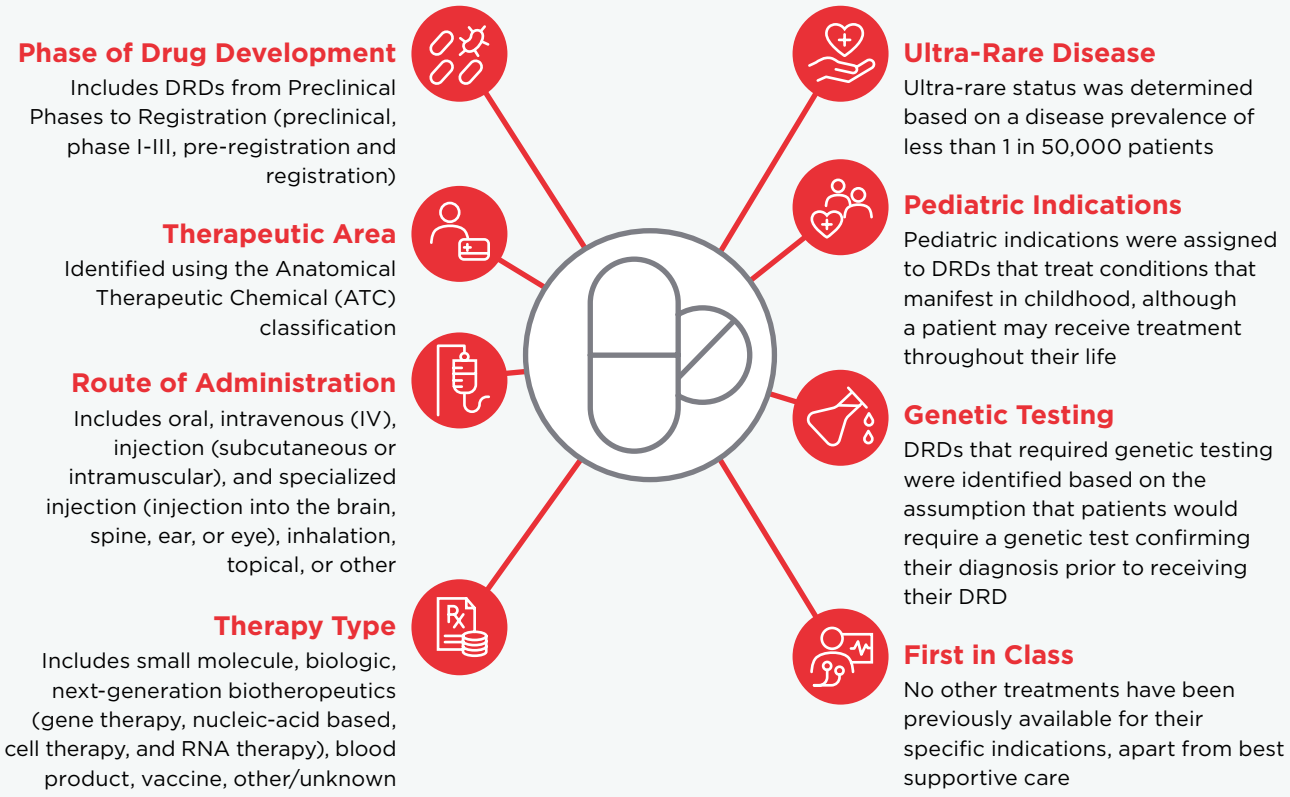


Figure 3: Study definitions used in the segmentation of DRDs

Results and Considerations for the Canadian Healthcare System

Impact of Growth in Volume in DRDs

Almost 200 DRDs are expected to launch in Canada within the next decade.

Globally, over 1,100 drugs are currently in development for the treatment of rare diseases. These include both novel or pre-existing molecules that are being investigated for rare indications (**Figure 4**). Approximately half (n=637) of these DRDs are currently in phase II/III and 10% (n = 109) in registration or pre-registration. The DRDs that progress through the phases of clinical trials are expected to become globally available in the next several years. From the Canadian standpoint, 46% of DRDs launched globally are expected to launch in Canada.[16] Thus, a total of 186 DRDs from Phase II to registration can be anticipated to launch in Canada within the next 10 years. This increase of medications within a relatively short timeframe necessitates strategic investments and focused policy work to circumvent potential challenges and ensure optimal patient benefit.

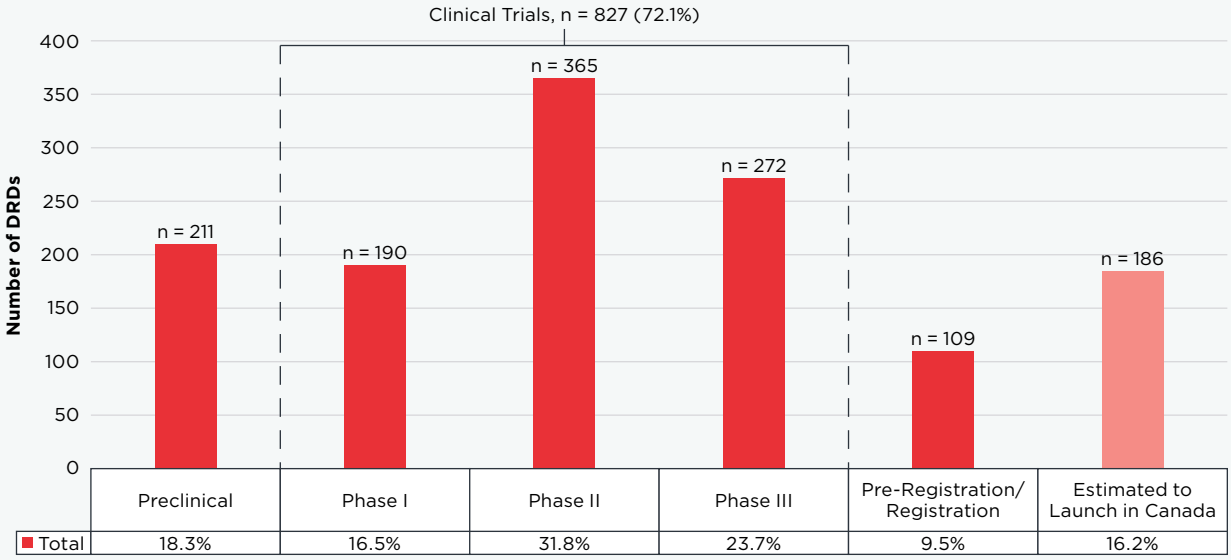


Figure 4: DRDs by phase, N = 1,147
Data Source: IQVIA Pipeline Intelligence. 2023.

Current Capacity to Deliver Drugs for Rare Diseases

In anticipation of the expected influx of DRDs into the Canadian market over the next decade, it is crucial for Canada's healthcare system to strategically allocate resources to be prepared. Overall, broad investment and policy work across the healthcare system, including in medical education, genetic testing, access to healthcare, infrastructure, and innovative funding models, will be necessary in preparing for the anticipated influx of DRDs.

Medical Education, Learning, and Awareness

Rare diseases are complex and require specialized care and treatment. As such, clinicians treating patients with rare diseases must also possess in-depth knowledge of these conditions and the available treatment options. Centres of excellence, such as Care4Rare, which is located in 20 sites across Canada, play a pivotal role in delivering healthcare services to rare disease patients.[2] Centres of excellence benefit the greater healthcare system by implementing rigorous standards of care, treatment guidelines, and algorithms that help ensure patients receive evidence-based care.[3,17] Additionally, centres of excellence serve as referral centres and participate extensively in clinical trials, which further the development of novel treatments for rare diseases.[18] In Canada, the geographical dispersion of both patients with rare diseases and clinical experts has led to the growing recognition of centres of excellence and virtual clinical networks as necessary components of high-quality care.

First-in-Class DRDs

While education should be provided for all rare diseases, particular attention should be directed towards first-in-class DRDs that are expected to enter the Canadian market. About 39% of all DRDs in phase III, pre-registration, or registration (N = 381) are first-in-class (**Figure 5**). DRDs that are first-in-class treat conditions that have not had treatments previously available, except for best supportive care. The influx of DRDs that are first-in-class presents an opportunity for patients, especially those with conditions that have no currently available treatment, but also present a challenge for Canada's overburdened medical system. Further medical education will be necessary to enhance education related to diagnosing and treating rare diseases.

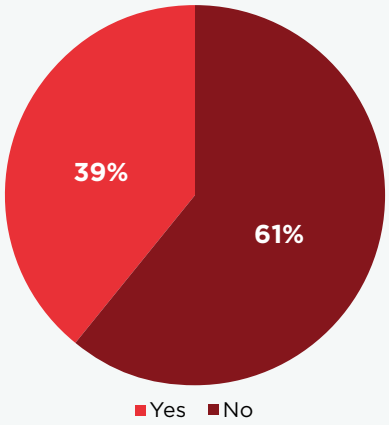


Figure 5: DRDs in phase III, pre-registration or registration, split by first in class, N = 381
Data Source: IQVIA Pipeline Intelligence. 2023.

Therapeutic Area

The DRDs currently in the pipeline are distributed across a diverse set of therapeutic areas, spanning different Anatomical Therapeutic Chemical (ATC) classifications. Notably, a substantial proportion of these DRDs target conditions related to the nervous system, immune system, and alimentary tract/metabolism. As a result, these specific therapeutic categories are expected to see an influx of DRDs within the next few years (**Figure 6, Appendix Figure A1**). Given this multifaceted landscape, it is crucial that medical education and training adopt a holistic approach, rather than focusing solely on a single therapeutic domain. Physicians must be well-prepared to identify and address the unique challenges faced by patients with rare diseases. By integrating knowledge across various medical specialties, healthcare professionals can effectively navigate the complexities of rare diseases and provide optimal care to patients. This comprehensive approach would ensure that physicians are equipped to meet the diverse needs of patients affected by rare diseases.

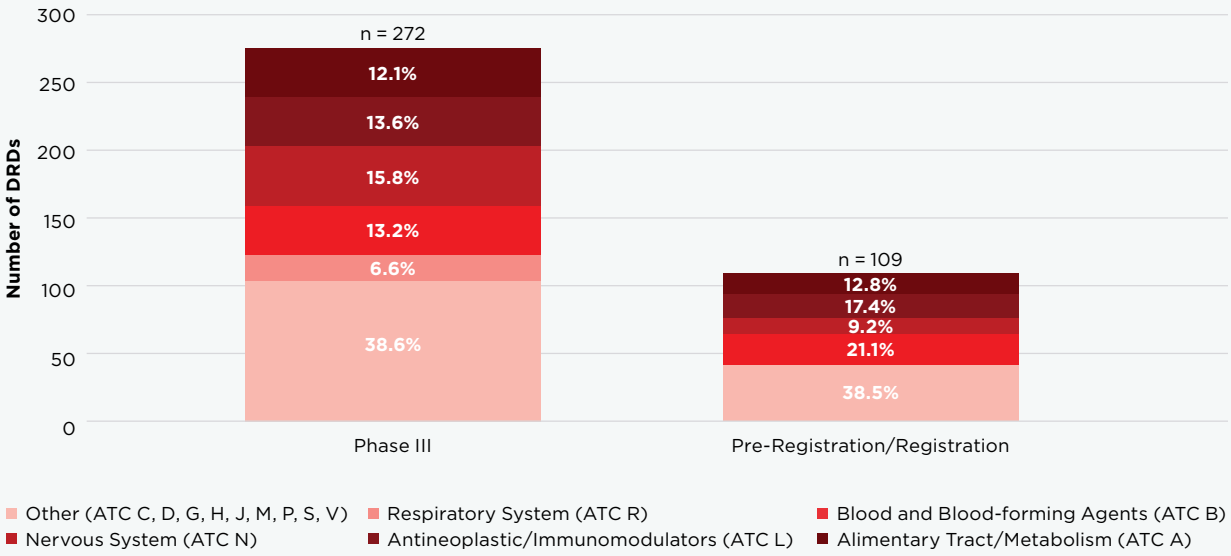


Figure 6: DRDs by ATC level 1 and phase, N = 1,147

"Other" includes Musculo-skeletal system, sensory organs, anti-infectives, dermatologicals, cardiovascular system, genito-urinary system and sex hormones, hormone preparations, antiparasitic products, and various.

Data Source: IQVIA Pipeline Intelligence. 2023.

Recommendation:

While education is essential for all rare diseases, particular attention should be given to first-in-class DRDs, which offer novel treatment opportunities. Education for physicians and other healthcare providers will be key to ensure these treatments reach patients.

Availability of Genetic Testing for the Diagnosis of Rare Diseases

Genetic testing plays a pivotal role in diagnosing rare diseases with precision and informing clinical decision-making, leading to timely and effective treatment for patients. Approximately one quarter of DRDs in phase III, pre-registration, or registration have indications for genetic conditions, necessitating genetic testing as a prerequisite for receiving therapy (**Figure 7**). The genetic condition category was assessed for each indication and secondary research was used to determine whether the indication was for a genetic disease. Testing and diagnosis are critical for patients with progressive rare diseases, to enable treatment as early as possible. Early diagnosis can minimize extraneous healthcare expenditures such as reducing the number of different physicians (specialities) patients typically visit over a period of several years before receiving an accurate diagnosis.[19,20]

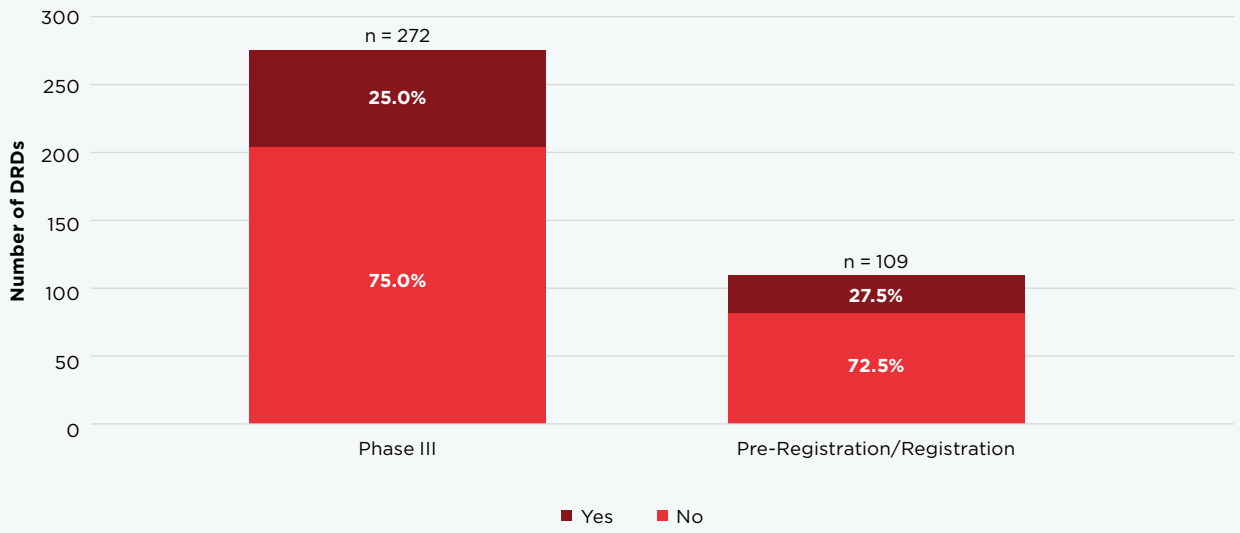


Figure 7: DRDs in phase III, pre-registration or registration, stratified by need for genetic testing and phase, N = 381
Need for genetic testing was determined based on the assumption that patients would require a genetic test confirming diagnosis prior to receiving their DRD.
Data Source: IQVIA Pipeline Intelligence. 2023.

Genetic Screening Programs

Efforts are underway to establish consistent access to genetic screening across Canada.[21] A recent 2023 report from Immunity Canada and the Network of Rare Blood Disorder Organizations outlines recommendations for comprehensive screening, which includes increasing funding for genetic testing, continual review of additional genetic conditions that can be added to screening panels, and developing standard operating procedures for conducting specialized tests.[21] In Canada, one method of administering genetic testing is through newborn screening programs, which operate independently in each province and territory. These newborn screening programs are crucial as numerous genetic conditions manifest in childhood, and over half of DRDs in the pipeline can be used to treat pediatric conditions (**Figure 8)**. However, this decentralized approach results in inequities and variability in the diseases screened across the country.[3,21] Given the anticipated launch of a substantial number of DRDs in Canada specifically targeting genetic diseases, establishing consistent and equitable access to genetic testing is imperative to connecting patients with the treatments that they need. In an effort to achieve consistent access to newborn screening across Canada, CDA-AMC has established a multidisciplinary

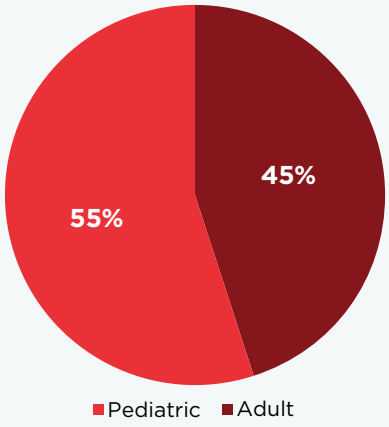


Figure 8: DRDs in phase III, pre-registration or registration, by those used for pediatric conditions, N = 381
Data Source: IQVIA Pipeline Intelligence. 2023.

Newborn Screening Advisory Panel to develop guidelines related to identifying new conditions to screen for, defining screening criteria, ensuring equity, and addressing ethical considerations.[22] Newborn screening is more extensive and equitable compared to the genetic screening available for adults across Canada. Valuable insights from newborn screening programs may be used to inform the development of adult screening programs, such as the establishment of a national panel to develop screening guidelines. Importantly, a portion of the funding from CDA-AMC's rare disease strategy will be allocated towards screening and the diagnosis of rare diseases.[23]

Next-Generation Sequencing

Next-generation sequencing (NGS) is a powerful genetic testing approach that enables the rapid and efficient analysis of either panels of multiple genes, all protein-coding regions of genes (exomes), or even entire genomes.[24] Despite its potential, the adoption of NGS-based testing, particularly whole-genome or whole-exome sequencing, has been limited in Canada due to the substantial costs associated with this type of testing.[24] Recently, several provinces have initiated dedicated HTA processes specifically for NGS testing. Notably, the Ontario Personalized Health Network and the Quebec Network for Personalized Health Care are actively developing distinct HTA frameworks for NGS interventions. Currently, the use of NGS to guide and inform patient care is confined to research settings. Only a select few NGS panels have achieved public reimbursement. The current funding availability for NGS panels varies across jurisdictions in Canada, with approved clinical contexts ranging from disease screening, hereditary cancer testing, to predicting the risk of breast cancer recurrence.[24]

One-quarter of DRDs in phase III or later are used to treat genetic conditions.

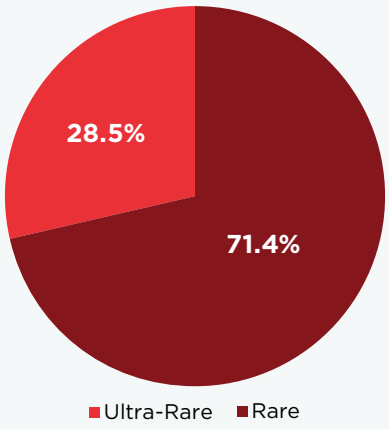
Recommendation:

Focus on an equitable pan-Canadian approach to investment in, and implementation of, genetic testing (including newborn screening and testing during childhood and beyond) across Canada.

Access to Care

Access to healthcare providers and treatment facilities is essential for patients with rare and potentially life-threatening diseases. Individuals living with rare conditions often navigate a complex pathway to diagnosis and treatment, visiting a number of specialists before receiving an accurate diagnosis.[20] The process of obtaining an accurate diagnosis for a rare disease takes an average of five to seven years.[20] For patients who have progressive rare diseases, this delay can significantly impact their quality of life and result in clinical deterioration.[25] Therefore, timely access to healthcare providers and prompt diagnosis and treatment is critical.

Barriers to Care



Status	N (%)
Rare	820 (71.4%)
Ultra-Rare	327 (28.5%)

Figure 9: DRDs by rare versus ultra-rare status, N = 1,147

Ultra-rare status was determined based on a prevalence of less than 1 in 50,000 patients with the disease.

Data Source: IQVIA Pipeline Intelligence. 2023.

Family physicians play a vital role in the healthcare system and serve as the initial gateway to specialist care, which is often required for patients with rare diseases. However, Canada currently faces a shortage of family physicians.[4,26] Approximately six million, or 15% of all Canadians do not have a family physician, and estimates indicate that this number will increase to 10 million within three to four years.[4,26,27] Moreover, Canada is also experiencing a shortage in specialist physicians, who play a crucial role in diagnosing and treating patients with rare diseases.[4,5]

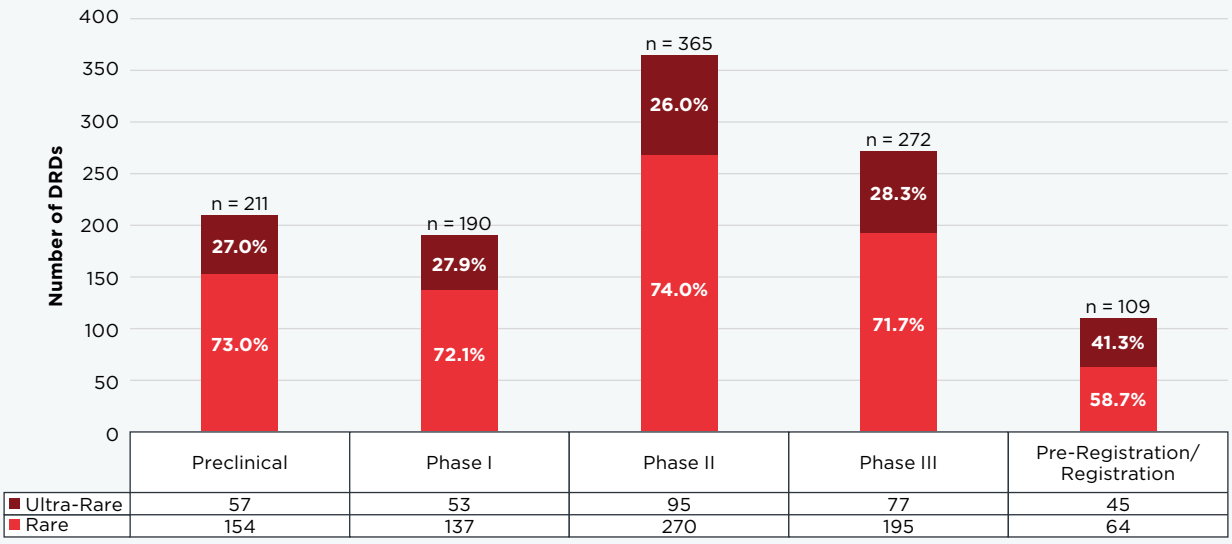
Ensuring access to healthcare providers and specialized facilities is paramount for patients with rare diseases. Beyond access to physicians, these individuals often require targeted treatment in facilities equipped to address their unique needs. However, several challenges persist, including geographic disparities in the distribution of care, in particular for unique subpopulations of patients with rare diseases, such as those with ultra-rare diseases (although there is no consistent definition for ultra-rare diseases), a threshold of a disease affecting fewer than 1 in 50,000 individuals has been suggested and used for the purposes of this report (**Figures 9-10**).[28]

More than 25% of DRDs in the pipeline are used to treat an ultra-rare disease.

Patients in Rural Regions

Access to healthcare facilities and physicians pose specific challenges for patients residing in rural areas, smaller provinces, and those affected by ultra-rare diseases. Infusion centres are predominately concentrated in large population centres in Ontario, Quebec, and British Columbia, with limited representation in Prince Edward Island and Yukon, and no representation in the Northwest Territories or Nunavut.[29] Consequently, patients living in provinces or territories without adequate healthcare facilities to treat or diagnose rare diseases may be required to travel to larger population centres to receive essential care. For instance, Nunavut has a single general hospital and one family practice clinic, both situated in Iqaluit.[30] Specialist services are primarily accessible in Ottawa, Winnipeg, Yellowknife, and Edmonton, resulting in significant expenditures: $109 million on medical travel and $69.5 million on physician services to service a population of less than 50,000 residents, outside the territory in 2020/2021 alone.[30] However, even within larger provinces like Ontario, patients living in rural areas are also required to travel substantial distances to access care.[31] These geographic barriers may be partially overcome with virtual care, which has greater utilization in rural regions of Ontario relative to the major population centres. In fact, virtual care in Ontario has allowed patients in rural

and northern Ontario to access specialist care up to 1,212 kilometers away.[31] However, infrastructure to support access to virtual care is needed – access to the internet may be a challenge in rural regions and thus movement towards increasing virtual care should consider ensuring technology is not a barrier to patients.[31]



	Preclinical	Phase I	Phase II	Phase III	Pre-Registration/ Registration
Ultra-Rare	57	53	95	77	45
Rare	154	137	270	195	64

Figure 10: DRDs by rare versus ultra-rare status and phase, N = 1,147
Ultra-rare status was determined based on a prevalence of less than 1 in 50,000 patients with the disease.
Data Source: IQVIA Pipeline Intelligence. 2023.

Similarly, subpopulations of patients with rare diseases, including those with ultra-rare diseases, may encounter significant barriers in accessing care due to the unique nature of their illnesses. Investment and policy development aimed at reducing barriers for those living in rural or underpopulated regions is imperative to facilitate medication and healthcare access for all Canadians affected by rare diseases as these treatments progress through the pipeline and become available.

Recommendation:

Investment and policy development aimed at reducing barriers for those living in rural or underpopulated regions is imperative to facilitate medication and healthcare access for all Canadians affected by rare diseases.

Infrastructure Requirements

Due to their unique nature, DRDs often have unique characteristics that require special administration, storage requirements, and handling protocols. Approximately one-third of DRDs in the pipeline are administered via intravenous infusion (IV) or specialized injection, which includes injections into the eye, brain, spine, or ear (**Figure 10**). Consequently, dedicated centres with the necessary equipment and trained healthcare providers are essential for the safe administration of these DRDs. Within the Canadian healthcare system, infusion centres play a critical role in delivering specialized care to patients requiring DRDs that are delivered through IV. With a focus on patient safety, clinical expertise, and multidisciplinary collaboration, private- and publicly funded infusion centres contribute significantly to optimizing treatment outcomes. There are currently 423 private infusion centres in Canada, benefiting roughly 130,000 patients annually.[29,32]

Approximately one-third of DRDs in the pipeline are administered via intravenous infusion (IV) or specialized injection.

Specialized Injections

Furthermore, approximately 7% of the DRDs in the pipeline are administered through specialized injections targeting areas such as the eye, brain, spine, or ears. These DRDs typically require specialized facilities for their administration (**Figure 11**). For instance, injections into the spine or brain, require access to an operating room or specialized treatment space to ensure patient safety and positive treatment outcomes.[6] Additionally, pre-injection preparations are also typically required and can include magnetic resonance imaging (MRI) for thorough anatomical assessment.[6] However, patients currently face delays in accessing the diagnostic technology needed prior to receiving an injection, with patients in Canada waiting an estimated 12.9 weeks for an MRI scan.[33]

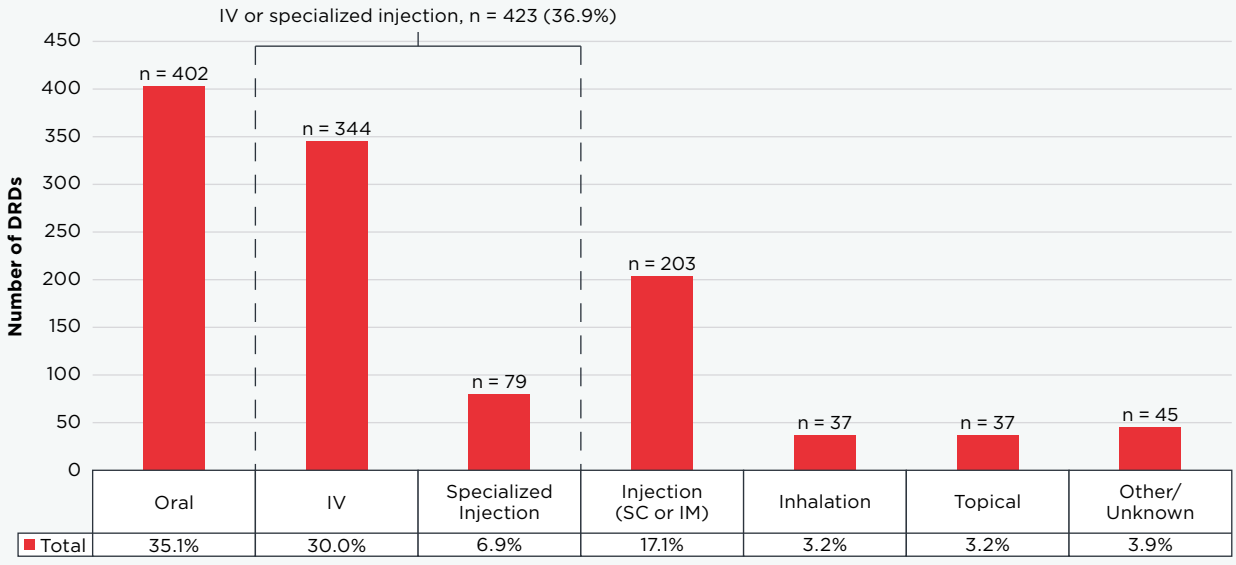


Figure 11: DRDs by route of administration, N = 1,147
Data Source: IQVIA Pipeline Intelligence. 2023.

Storage Requirements

Within the DRD pipeline, over half (51%) of DRDs are biologics, blood products, and next-generation biotherapeutics (NGBs), which include gene, cell, nucleotide-based, and RNA-based therapies (**Figure 12**).[34] Biologics, including monoclonal antibodies and other protein-based therapies, often demand precise storage conditions due to their sensitivity to temperature fluctuations. Exposure to temperatures outside of the recommended range can render these medications inert or decrease their effectiveness. Typically, biologics require refrigeration from 2°C to 8°C or freezing from -20°C to -80°C, while some may also require protection from light or humidity. Similarly, blood products must be refrigerated or frozen, yet they also have limited shelf lives. NGBs encompass a diverse array of advanced therapies and share similar storage requirements, which often involve ultra-low temperatures (e.g., -80°C), or liquid nitrogen freezing to maintain stability. Furthering the complexities of these requirements, some personalized medicine products, such as chimeric antigen receptor (CAR)-T cell therapy, involve a patient's blood or genetic material being drawn and sent for manufacturing, require specialized handling and storage, and have a limited shelf life after being processed.[35] As Canada anticipates an influx of biologic, NGB, and blood product DRDs, the demand for cold chain storage and transport is expected to increase, and will require investment to prevent medication spoilage and waste.[36] At present, Canadian pharmacies handle over 15,000 specialty medications requiring cold chain packaging and transport on a daily basis, incurring estimated yearly costs ranging from $400,000 to $2 million for cold chain preparation alone.[32] It is estimated that the expenditures associated with the wastage of specialty medications globally would cost $12 billion US dollars each year.[32] Proper storage conditions are critical to maintaining the efficacy and safety of these advanced biotherapeutics.

> Canadian pharmacies handle over 15,000 specialty medications requiring cold chain packaging and transport on a daily basis.[31]

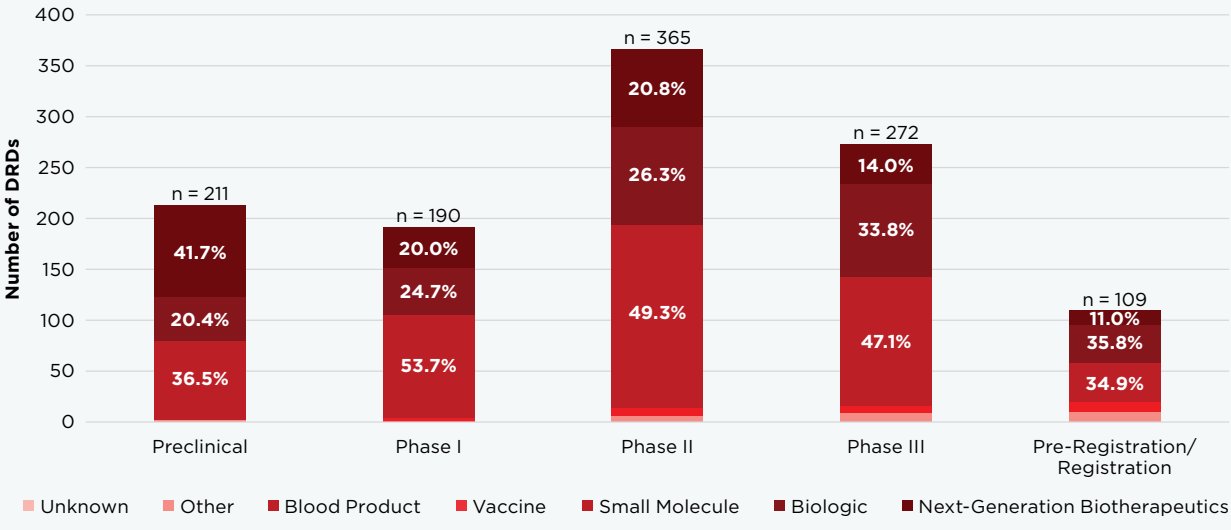


Figure 12: DRDs by therapy type, N = 1,147
Data Source: IQVIA Pipeline Intelligence. 2023.

Recommendation:

As Canada prepares for an influx of biologic, NGB and blood product DRDs, the demand for cold chain storage and transport is poised to rise significantly. This critical infrastructure requires investment, policy work, and the development of protocols to prevent medication spoilage and waste.

Collaboration and Innovative Funding Models

In Canada's healthcare system, government collaboration is crucial for enhancing patient care and outcomes, especially for patients facing the unique challenges associated with rare diseases. Novel multifaceted approaches will require innovative funding models and collaboration among provinces and ministries to ensure that patients with rare diseases from across Canada receive the care that they need.

Inter-provincial Collaboration

Inter-provincial coordination remains a challenge in Canada's decentralized healthcare system, especially when patients require care that crosses provincial boundaries. However, successful examples of cooperation across the country exist, particularly in cancer care through the Canadian Partnership Against Cancer (CPAC). This partnership has led to significant improvements in patient care, including enhanced access to treatments and diagnostic services.[37,38] Insights from inter-provincial collaboration in cancer care can further inform strategies for managing rare diseases.

Partnership between the provinces facilitated the rapid roll-out of colorectal cancer screening programs across 10 provinces.

Over the past decade, CPAC has played a pivotal role in enhancing cancer care. Their efforts have led to significant advancements in cancer screening, treatment, and data collection.[37,38] This interprovincial partnership facilitated the rapid rollout of colorectal cancer screening across 10 provinces within three years.[37] This collaboration ensures that more Canadians have access to early detection, ultimately improving early detection and care. Additionally, the CPAC emphasizes standardized data collection and reporting. By establishing protocols, provinces enhance outcome tracking and informed decision making across provincial boundaries. While these strategies have yielded remarkable results in cancer, similar principles have not been applied to rare diseases and should be prioritized. For example, the Canadian Organization for Rare Disorders (CORD) serves as a national advocacy network, representing the rare disease community in the development of Canada's National Strategy for Drugs for Rare Diseases. CORD also promotes newborn screening and genetic testing, while working to enhance access to treatments.[3] From a data perspective, CDA-AMC is actively involved in establishing a pan-Canadian Rare Disease-Based Registry.[10,11]

Inter-provincial Collaboration

Inter-provincial coordination remains a challenge, especially when patients require care that crosses provincial boundaries.

Inter-ministry Collaboration

Collaboration between ministries within provinces is key to bringing therapies with novel mechanisms of action and administration requirements to patients.

Innovative Funding Models

Models include amortization over time, outcome based agreements, and modifying the evidence standards that are typically required in the health technology assessment process.

Inter-ministry Collaboration

Traditionally, healthcare services have operated within distinct silos, such as provincial ministries. However, inter-ministry collaboration can address health needs more effectively. Valuable lessons emerge from successful models, such as gene and cell therapies, which required different facets of provincial governments to align on creating new pathways for patients to gain access, underscoring the importance of cross-ministry partnerships.[39]

Innovative Funding Models

To support increased collaboration, innovative funding models are essential due to the unique nature of rare diseases and escalating costs of DRDs. These models include:

- Amortization of Costs

  Amortizing costs over several years rather than a lump-sum payment may benefit both payors and patients. This way, payors can manage their budgets more effectively, and patients gain access to life-changing treatments.[40] Such models align with the long-term benefits of certain drugs, especially those that provide sustained outcomes over extended periods of time.

- Outcome-based Agreements

  In outcome-based agreements (OBAs) payors collaborate with manufacturers to define real-world outcomes, such as reduced hospitalizations. Payment for treatment is then contingent on the success of these outcomes.[41] Such agreements have been successfully used to bring a handful of DRDs to market in Canada.[41] OBAs encourage value-based care and ensure that payors invest in effective treatments.[41]

- Modification of Evidentiary Standards for HTA

  Traditional HTA relies on clinical trial evidence. However, for many DRDs, such data may be limited, making meeting HTA evidentiary standards set for rare diseases challenging. In such cases, payors need to adopt a more flexible framework where they could consider RWE, patient registries, and pragmatic trials to assess effectiveness.[42] To date, principles have been developed for innovative medicines through the pan-Canadian Pharmaceutical Alliance (pCPA) Temporary Access Process (pTAP) that informs the negotiation for medications that have gone through CDA-AMC's time-limited recommendation pathway.[43]

Although initial steps have been taken to ensure access to medications, additional collaboration with experts and developing adaptive pathways can further facilitate informed decisions. Canada's healthcare system requires agility within the government to improve care for patients with rare diseases. This involves innovative funding models, inter-provincial collaboration, and learning from successful strategies in cancer care. CPAC has enhanced cancer care through collective efforts, which can inform approaches for rare diseases. Innovative funding models for rare diseases, such as amortization, OBAs, and flexible payor frameworks, are crucial for managing costs and improving patient access to treatments.

Recommendation:

Collaboration will be key to ensuring equitable access to diagnostics, care and treatments for patients with rare diseases across Canada. Innovative funding models, including amortization over time, OBAs and modifying the HTA requirements, will be important in ensuring all patients can access treatment.

Summary of Findings and Conclusions

Over 1,100 DRDs are currently in the pipeline, with almost 200 DRDs expected to launch in Canada within the next decade. This influx calls for strategic investments across multiple domains to address potential challenges associated with introducing these drugs to the Canadian market and ensuring patients derive maximum benefit. While the emergence of new DRDs is promising for patients, Canada's healthcare system must be well-prepared to handle these medications effectively. Based on the analyses conducted in this report, patient participation is crucial to ensuring that appropriate care reaches patients. Collaborating with patient groups throughout the planning process is vital to meeting the needs of patients with rare diseases.

Recommendations for Health System Readiness of DRDs

The Need for Medical Education

While education is essential for all rare diseases, particular attention should be given to first-in-class DRDs, which offer novel treatment opportunities. Education for physicians and other healthcare providers will be key to ensure these treatments reach patients.

The Role of Genetic Testing

Focus on an equitable pan-Canadian approach to investment in, and implementation of, genetic testing (including newborn screening and testing during childhood and beyond) across Canada.

Delayed Diagnosis and Access Challenges

Investment and policy development that reduces barriers for those living in rural or underpopulated regions is imperative to facilitate healthcare access for all Canadians affected by rare diseases.

Address Infrastructure Challenges

As Canada prepares for an influx of DRDs, the demand for cold chain storage and transport may rise. This critical infrastructure requires investment, policy work and the development of protocols to prevent medication waste.

Adopt Innovative Funding Models and Increase Collaboration

Collaboration will be key to ensuring access to treatments for patients with rare diseases. Innovative funding models, including amortization over time, OBAs and modifying HTA requirements, will be important in ensuring patients can access treatment.

Patient Engagement and Partnership

Patient participation is crucial to ensuring that appropriate care reaches patients. Collaborating with patient groups throughout the healthcare planning process is vital to meeting the needs of patients with rare diseases.

While this report delves into specific considerations related to health system readiness additional factors warrant discussion. Notably, orphan drug regulatory pathways, HTA modernization, and the utilization and standardization of RWE and registries playing pivotal roles. Specialized orphan drug pathways are designed to accommodate the unique challenges posed by rare diseases, ensuring timely access to treatments. As we evaluate new technologies, adapting HTA processes becomes imperative. Some innovations may not neatly align with existing budget frameworks, necessitating the modernization of assessment methodologies. Moreover, leveraging RWE and utilizing disease-specific registries can significantly enhance understanding of rare diseases beyond the confines of clinical trials. These data sources provide valuable insights into patient experiences and outcomes.

This report aims to contribute fresh perspectives to the rare disease ecosystem, offering insights that complement existing knowledge and other ongoing initiatives (e.g., RWE, data registries, OBAs, etc.). Proactive planning and resource allocation are essential to navigate the complexities of rare diseases and provide exceptional care to affected patients.

Disclaimers

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This Report represents Takeda's recommendations based on the analysis of data from the IQVIA™ Pipeline Intelligence database as of the date of this Report. Takeda cannot guarantee that such data will remain accurate in the future.

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Appendix 1

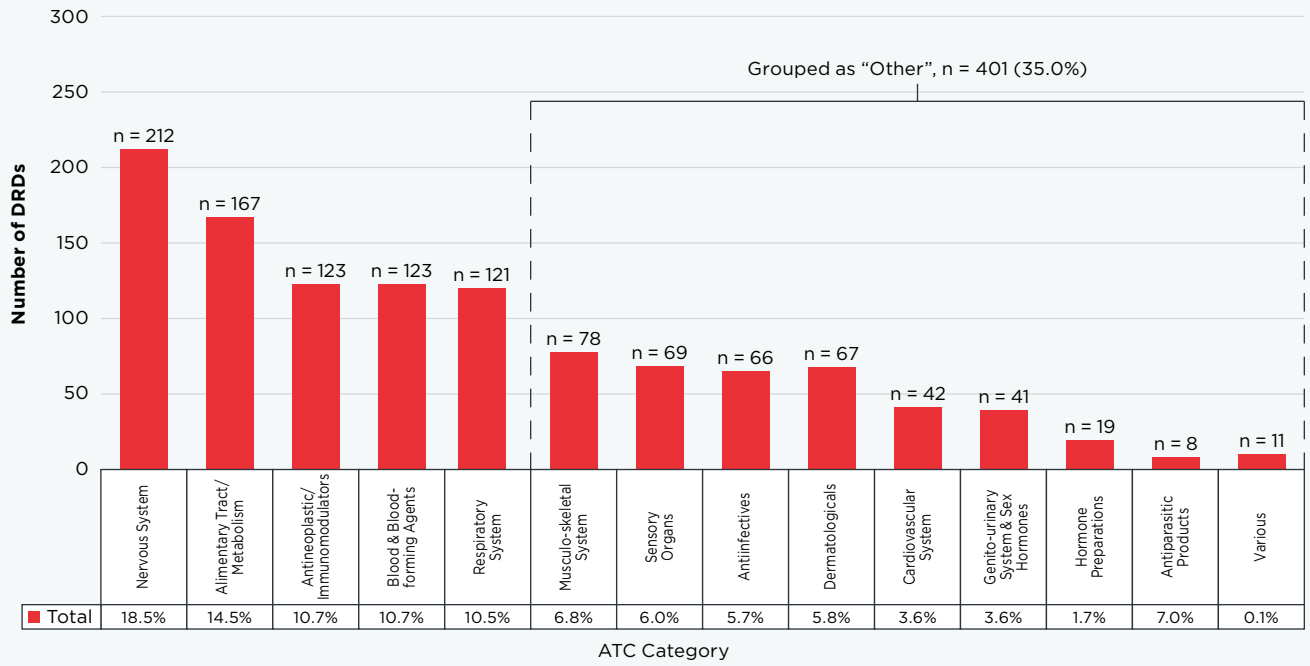

Figure A1: DRDs by ATC classification, N = 1,147
Data Source: IQVIA Pipeline Intelligence. 2023.

Appendix 2

Table of Abbreviations

ATC	Anatomical Therapeutic Chemical
CDA-AMC	Canada's Drug Agency-L'Agence des médicaments du Canada
CAR	Chimeric Antigen Receptor
CORD	Canadian Organization of Rare Disorders
CPAC	Canadian Partnership Against Cancer
DRD	Drug for Rare Disease
HTA	Health Technology Assessment
IV	Intravenous
MRI	Magnetic resonance imaging
NGB	Next-generation Biotherapeutic
NGS	Next-Generation Sequencing
OBA	Outcome-based Agreement
pCPA	Pan-Canadian Pharmaceutical Alliance
RWE	Real-World Evidence
pTAP	Temporary Access Process