

Spotlight on the Canadian Specialty Pharmaceutical Market

Rare Diseases *and* Conditions in Canada

The Reality and the Hope

Innovative treatments and access strategies have the potential to make life a lot better for Canadians living with rare diseases and conditions. By working together, stakeholders can make it happen.

Strides and setbacks in accessing treatments for rare diseases and conditions

SMA patient Catherine Boivin on equalizing access to innovative therapies

CF Get Loud's campaign vocalizes triumphs and frustrations in the access landscape

By the *Numbers*

A rare disease is, by definition, uncommon. Taken collectively, however, rare diseases touch millions of Canadians – which means that timely and equitable access to the right treatments can have an enormous impact on Canadian lives.

RARE DISEASE REALITIES

7,000

The approximate number of rare diseases identified in the world to date.¹

80%

The proportion of rare diseases that have a genetic origin.¹

1:12

The estimated proportion of Canadians who live with a rare disease.¹

50%

Proportion of rare diseases that begin in early childhood and involve progressive, life-threatening deterioration.¹
In fact, rare diseases account for **30-40%** of neonatal deaths.²

5%

Approximate percentage of rare diseases with a currently available treatment.²

7

Number of curative therapies for rare diseases and conditions,³ of which 3 are currently available in Canada.⁴

THE RARE DRUG MARKET

40%

Percentage of pipeline drugs in pre-registration phase that target rare diseases.⁵

300

Approximate number of cell and gene therapies in development, collectively targeting more than 100 diseases.⁶

32%

Growth of the Canadian market for expensive drugs for rare diseases (EDRD) from 2012 to 2019 – more than 6 times the growth rate for all prescription drugs in Canada.⁷

9.4%

Share of total drug-spend in Canada devoted to expensive drugs for rare diseases (EDRD), including oncology and non-oncology medications.⁷

\$2.1M

Approximate cost of Zolgensma, a medication for spinal muscular atrophy, approved in Canada in 2020 and dubbed the “most expensive treatment in the world.”^{8,4}

\$200,000

minimum annual cost of 76% of all EDRD approved in Canada, as of 2019.⁹

ACCESS STATUS AND SETBACKS

50%

Approximate proportion of EU-approved drugs for orphan diseases (neglected rare diseases) that end up approved in Canada.¹⁰

18-24

Delay in months between Health Canada approval and public reimbursement of orphan-disease drugs.¹⁰

99%

Price discount that would be required if applying new Patented Medicine Prices Review Board (PMPRB) regulations to two new cystic fibrosis drugs.^{11,12}

26

Number of European Union member countries (out of 28) who have their own framework for reviewing rare disease drugs.¹³

\$500M

Funds earmarked in the Canadian government's 2019 federal budget to a program for rare diseases.¹⁴

0

Frameworks for rare diseases in Canada. This may change with the government's recently released consultation on “Building a National Strategy for High-Cost Drugs for Rare Diseases.”¹⁹

Rare Disease Update: Status, Strides, Setbacks

A COMMON LANGUAGE FOR RARE DISEASES AND CONDITIONS

The language around rare diseases can get confusing. Here's a primer:

Rare disease:¹ A rare disease is a life-threatening, severely debilitating, or serious and chronic condition affecting a fairly small proportion of people – generally fewer than 1 in 2,000. Examples of rare diseases include cystic fibrosis, muscular dystrophy, and hemophilia.

Rare condition:¹⁵ This term includes rare diseases as well as rare subtypes of common diseases. These subtypes represent special cases, such as specific genetic mutations, that may respond to precision treatment. Adenosquamous carcinoma, a rare subtype of lung cancer, would be considered a rare condition.

Ultra-rare disease:¹⁶ A disease that occurs in no more than 1 in 100,000 people.

Orphan drug:¹⁷ Defined as medications for rare diseases that are debilitating or life threatening, these drugs respond to a public health need but may be difficult to develop and launch under standard marketing conditions.¹⁸

Expensive drugs for rare diseases (EDRD):⁷ This term describes medicines with at least one FDA or EMA orphan designation and estimated treatment costs exceeding \$100K per year for non-oncology drugs and \$7,500 per 28 days for oncology drugs. Orkambi and Symdeko (both for cystic fibrosis) as well as Vimizim (for Morquio syndrome) fall into this category.

It's a strange time to be alive if you have a rare disease. On the one hand, medical scientists now understand the core dysfunctions underlying many of these diseases. As an outgrowth of this knowledge, life-changing therapies are tumbling into the market. But can you get your hands on these miracle therapies? It depends: on where you live, on whether your provincial or private payer approves your case, on the drug manufacturer's ability to bridge the access gap.

Maybe your doctor can state your case to payers. Or maybe not. If you have a lot of stamina, perhaps you can do your own lobbying – which, as patient advocates like Bryarly Parker of Alberta can attest, often require Herculean efforts to succeed. The mother of Max, a two-year-old boy with spinal muscular atrophy (SMA), Parker engaged her network of family, friends and fellow advocates to ask the province to fund the SMA medication Zolgensma for her son. A one-time drug that replaces the faulty gene at the root of the disorder, Zolgensma costs upwards of \$2 million. Parker's tribe came through with a flood of emails, including 1,000 on a single day, asking the government to step up for Max.² The government listened and Max got his medication. "Some paths led us down incredible roads, while other paths were extremely frustrating and led to many tears," she wrote on Instagram after the decision¹⁹ – sentiments echoed by patient advocates throughout the country.

It's a bit like a treasure hunt. You need to solve all the clues to get the grand prize: a life-changing medication. Miss one of the clues and you're out of the game. How did our country, whose national health system other nations point to as a model, get to this awkward place?



Missing: a national vision

Rare diseases and conditions are a breed apart. The small number of affected people makes it difficult to collect the type of clinical trial evidence traditionally required by regulators. The rarity of these diseases also slows down clinicians' understanding of their natural progression, making it challenging to establish optimal starting and stopping criteria for medications.²⁰ Monitoring treatment efficacy and collecting real-world data pose similar problems.

Under the orphan drug umbrella, drugs for ultra-rare diseases (DURDs) also deserve special status. A 2018 analysis of CADTH submissions concluded that DURDs can be viewed as a distinct category and that applying normal rare-disease assessment criteria to these medications may have tipped the balance toward more negative recommendations.¹⁶

Despite a clear need for special consideration, Canada does not have a distinct framework or strategy for these drugs. By way of contrast, 26 out of 28 member EU countries boast separate pathways for reviewing rare disease drugs.¹³ These frameworks may include commercial options such as outcomes-based agreements (OBAs) for high-cost drugs requiring additional evidence and budget impact schemes.⁴

Not surprisingly, the lack of a pan-Canadian framework makes it difficult for pharmaceutical manufacturers to launch rare disease drugs in Canada. As an example, it took over a year for Health Canada to approve the cystic fibrosis medication Trikafta for children aged 12 and over, while the

US authorized the drug for ages 6 and up within 3 months of submission. When a drug has the potential to change lives, as does Trikafta, such delays become ethically difficult to justify.⁹ Rather than wait – and potentially miss the window for useful intervention – regulators need mechanisms to approve medications with great promise but incomplete evidence.⁹

Fortunately, Health Canada's "Notice of Compliance (NOC) with conditions" policy allows for accelerated review of drugs for severe, debilitating diseases with no existing treatments.⁹ When early evidence suggests a benefit from a drug, Health Canada can fast-track its approval on condition of additional post-marketing monitoring and testing. This process has sped up NOC for some rare disease drugs.

Listing lags

Next hurdle: payer listing. Indeed, delays between NOC and listing average 559 days, or 670 days excluding Quebec – far longer than the figure for most other developed countries such as the US (120 days), UK (38 days) or Germany (a mere 13 days).²¹ As described by Homira Osman, VP of Research & Public Policy at Muscular Dystrophy Canada, the wait triggers a lot of anxiety among patients:² *When will it be reimbursed? Will it be case-by case? Will my case qualify?*

Even when most provinces agree that a rare disease drug treatment offers benefits that justify the costs, the drug almost never meets conventional cost-effectiveness criteria.²² Caught between these contradictions, provinces struggle to come up with fair reimbursement schemes.

In some cases “the bar set for reimbursement is just not attainable,” says Dr. Vijay Ramaswami, a pediatric oncologist at Sick Kids in Toronto, citing the medication Vitrakvi as an example. The first tumour-agnostic cancer medication approved by Health Canada, Vitrakvi received a negative listing recommendation by the pan-Canadian Oncology Drug Review (pCODR) committee in August 2019 – a reversal of an initial recommendation from pERC to reimburse the drug for four tumour types.²³ As a rationale for its decision, which to Dr. Ramaswami “makes no sense,” pCODR cited uncertainty about clinical benefit relative to available treatment options or best supportive care.²³ After generating additional evidence, Vitrakvi manufacturer Bayer resubmitted to CADTH and pCODR and received a positive draft “recommendation with conditions” in May 2021.²⁴ While good news for patients, this outcome took two years to achieve – a testament to the twists and turns in the process.

Some patients can get into clinical trials before a medication is listed – perhaps because they live close or can be transported to a trial site. Others are out of luck. While patients in the trials can proceed to the open-label extension, “we can’t get these incredible new technologies to [other patients] because of the long process to approval and reimbursement,” says Dr. Angela Genge, an amyotrophic lateral sclerosis (ALS) trialist and Director of the Clinical Research Unit of the Montreal Neurological Institute.² “It is unfair for patients.”

“The bar set for reimbursement of rare disease drugs is just not attainable.”

Dr. Vijay Ramaswami, Hospital for Sick Children, Toronto

Stop-gap solutions

Patients in the access queue have a few other options while waiting for a listing. Those fortunate enough to live in Quebec can obtain “medically necessary drug funding” via the *Patient d’exception* program. Upwards of 50,000 patients have used the service, which costs the province \$4 to 5 million per year.² The program boasts an impressive track record, reviewing 80% of patients in 25 days and approving about three-quarters of applications.²

Traditionally, provincial health ministers have had the latitude to make funding decisions on specific cases. While formalized CADTH and pCPA processes have made this tactic less prevalent over the years, case-by-case coverage still exists for some medications. Coverage for Spinraza for adult patients, for example, is granted on a case-by-case basis in Ontario, Saskatchewan, and Alberta.²⁵

Private insurance offers another common route to access. In 2020 alone, Canadian Life and Health Insurance Association (CLHIA) members paid out more than \$650 million for rare disease drugs to over 13,000 insured Canadians.²⁶ Compelled by ethical considerations, these plans may step in when medications previously covered by special access programs receive NOC. While helpful to patients, this ad-hoc arrangement highlights a significant gap in the current access pathway. A case in point is trientine, a generic medication for a rare and potentially fatal liver disorder called Wilson disease. Until recently, patients had to go through a special review process to obtain the medication, which costs up to US\$333,000 per year.²⁷ Following NOC in 2020, coverage of this high-cost drug has landed firmly in the private payer sphere.

Even for privately insured patients, high co-pays may impede access. Patients cannot be expected to afford, say, 20% of a medication that costs a half a million dollars per year. In such cases the manufacturer often ends up picking the tab. Manufacturer-funded bridging and compassionate use programs via patient support programs also plug up access gaps for many patients waiting for coverage to kick in or for those without any coverage at all. As of 2020, a patient association noted that the Vertex Pharmaceuticals compassionate care program for CF medications was supplying free product for life to 130 Canadian patients.²⁸

Manufacturers cannot be expected to supply free product indefinitely, of course. From a business standpoint, the viability and sustainability of compassionate programs depends on the expectation of a future public listing. What’s more, manufacturer support hardly ensures fair access. As noted by Eva Villalba of the Quebec Cancer Coalition, “not all patients are referred to patient support programs, which means that some patients get access and others don’t.”⁴

In brief: the current access landscape is far from smooth, with each disease and each drug following its own trajectory. Every patient has a different story to tell, not all of them with happy endings. Fortunately, stakeholders recognize the opportunity to do better and are working on more consistent, sustainable access solutions.

WORK IN PROGRESS

The will is there, but what is the way? It starts at the top: coordination at the federal level. In recognition of this need, the federal government recently published a discussion paper outlining three key motives for a national strategy for rare disease drugs: to improve patient access, to optimize decisions on drug coverage, and to ensure the expenditures don’t erode the sustainability of Canada’s healthcare system.⁹ The paper invites patients and patient groups, regulatory agencies, researchers, payers and industry to weigh in on the development of such a strategy, earmarked for a 2022-23 launch.

In line with this vision, CADTH is working on a policy change for rare disease drugs, proposing to use real-world evidence and managed entry agreements as part of the process.²⁰ Going still further, Quebec’s INESSS has proposed a national strategy for the entire rare disease care path, from screening to treatment.²⁰ These initiatives could kick off by mid-to-late 2021.

The national-strategy vision finds further support among patient groups, with the Canadian Organization for Rare Diseases (CORD) leading the charge. In a recent Health Insight article, CORD president & CEO Durhane Wong-Rieger describes the sophisticated and seamless treatment arc currently available to hemophilia patients and proposes the country play catch-up with other rare diseases.²⁹ To this end, CORD put forth its vision for a national strategy, broken down into 12 action steps, in a letter addressed directly to Prime Minister Trudeau and to Health Minister Patty Hadju.³⁰ The proposed steps include establishing a viable market for

early drug launches (through such measures as early access programs, patient registries, and patient support programs) and leveraging OBA-style agreements for approved medications with strong potential but uncertain evidence. Also pleading the case are the RQMO [Regroupement Québécois des Maladies Orphelines] and the Quebec Cancer Coalition.^{31,15}

Manufacturers have the same idea. The Canadian Forum for Rare Disease Innovators (RAREi), a national network of biopharmaceutical organizations that develop therapeutics for rare diseases, envisions a separate rare-disease pathway that offers managed access options, encourages dialogue, and draws inspiration from jurisdictions such as the US and Europe.²⁵

The evidence-access loop

For a national strategy to do any good, it must address the biggest problem facing rare disease drugs: incomplete evidence. The difficulty of gathering evidence for rare disease drugs puts them in a catch-22 position: just as new job seekers face the self-reinforcing spiral of inexperience, lack of evidence for rare disease medications drags down their progress through the drug life cycle – further limiting the ability to gather evidence.

Solving this conundrum requires a greater reliance on real-world evidence (RWE) and a way to obtain it. As noted by Dr. Craig Campbell, a physician/scientist and associate professor at the University of Western Ontario, “right now, access is [already] happening before reimbursement. Why not make that work for us by systematically collecting RWE?”²⁵ To this end, he suggests a post-marketing commitment – from the entire stakeholder community serving a disease – to generate data on what’s working and what isn’t. With rare diseases – and especially with those classified as ultra-rare – such evidence-gathering efforts need to draw on multiple sources, from prospective trials to system-level data. Existing registries, such as the robust Canadian Fabry Disease Initiative,³² serve as a natural launch pad for this approach.

Systematic RWE collection takes time, of course, and time is exactly what many rare-disease patients don’t have. When evidence is limited but patients can’t wait, innovative funding models such as outcomes-based agreements (OBAs) provide a mechanism to speed up access. As detailed in Health Canada’s proposed national strategy for high-cost drugs, such agreements depend on clear, objective measures of benefit.⁹ If the evidence ultimately reveals a more modest benefit than expected, OBAs allow for reduction or discontinuation of reimbursement.

Private payers appear ready to champion such arrangements. In a recent submission to the Government of Canada, CLHIA lent its support to innovative coverage models that tie funding of rare disease treatments to their effectiveness, noting the potential for these models to facilitate access to treatment and mitigate financial risks.²⁶

“Access is already happening before reimbursement. Why not make that work *better* by systematically collecting RWE?”

Dr. Craig Campbell, University of Western Ontario

A NATURAL FIT: OBAS FOR RARE DISEASES & CONDITIONS

OBAs seek to accomplish two things: improve patient access and mitigate financial risk. They work best for innovative, costly medications that promise to change lives – if they get to patients in time.

Rare diseases tick all the boxes for OBAs: low patient populations, high unmet need, innovative and high-priced treatments. The risk-management safeguards built into OBAs, from discounts and budget caps to pay-for-performance schemes based on predetermined outcomes, enable patients to benefit from new treatments as early as possible, when it matters most. In theory, an OBA could kick in right after NOC, giving patients immediate access while the evidence required for a fuller review process rolls in. If the medication works, everybody wins. If it doesn't, the payer and patient have a fair exit strategy.

Of course, OBAs only work if stakeholders agree on the outcomes to measure, with patients a key source of input. And not all rare disease drugs require an OBA: for some medications a simple market access agreement may do the job.

NO TIME TO LOSE

Stakeholders agree not only on the need for change, but on such priorities as a national plan and innovative market access agreements. But persistent ground-level inequities make it clear the needle needs to move faster.

No medication exemplifies the choppy playing field more poignantly than the SMA drug Zolgensma, which received a conditional listing just six weeks after NOC in one province. By the spring of this year, Alberta had received two applications for Zolgensma coverage, for a boy named Max and a girl named Reign.³³ On paper, neither application met CADTH'S recommended criteria for coverage. Max's request got the green light. Reign's did not.

In a March 2021 letter to Health Canada, Catherine Boivin, a SMA patient and advocate based in Montreal, pointed out another inconsistency in Zolgensma access: The province of Ontario, which now offers newborn screening for SMA, has the means to diagnose babies before they develop symptoms, when treatment can make the greatest difference. Elsewhere in Canada, patients can only access the medication after having suffered a significant deterioration. To rectify this imbalance, “a national framework must include strategies for early diagnosis.”³⁴

Less talk, more action

Must, should, need: such “planning” words don't suffice for Tania Stafinski, Director, Health Technology & Policy at the University of Alberta's School of Public Health and a key player in the School's PRISM [Promoting Rare-Disease Innovations Through Sustainable Mechanisms] initiative. Recalling the stalled efforts of the Expensive Drugs for Rare Disease (EDRD) working group, Stafinski maintains that rare diseases “require a different way of thinking. We all need to be OK with trying things, even if they may fail. What we can't do is continue to wait.”



“Access to rare disease therapies requires a *different way of thinking*. We need to be OK with trying things, even if they may fail.”

Tania Stafinski,
University of Alberta School of Public Health

A report from Montreal research group InVivo concurs that the waiting game has gone on too long. As outlined in the report, Health Canada announced its intention to develop a policy framework in 2012 – and almost 10 years later, Canadians with rare diseases are still waiting for this framework to materialize.¹³ Lack of political will also knocked the wind out of Alberta's limited rare disease policy, established in 2008 to cover just a handful of rare diseases.³⁵

A further hindrance to implementation: lack of trust between stakeholders. As with many hot-button issues, funding for expensive drugs tends to raise the emotional temperature and inhibit productive discussion. In a recent Standing Committee on Health meeting, a provincial cancer association characterized Cystic Fibrosis Canada (CF Canada) as being “too aligned to industry,”¹² and the February 2021 PMPRB communication plan called out patient groups for “spreading disinformation.”³⁶ CF Canada's Kelly Grover countered that “specifically targeting the credibility of this community [is] not reasonable or appropriate for a federal agency.”¹²

Less pricing, more patient

The resolute focus on costs and budgets, while understandable, is detracting from the more important issue at hand: levelling the playing field for Canadian patients who, through no fault of their own, struggle to attain the quality of life most others take for granted. Adrian Kupescic, Bayer Canada's Director of Public Affairs and Sustainability, has argued that “framing a policy discussion in such a way that suggests providing medicines will be burdensome to our system is just wrong. It almost assumes that coverage will come at the expense of other important programs. It is discriminatory.”³⁷

How then to balance costs with doing the right thing? Perhaps Boivin expresses it best: “When making decisions about covering costs while keeping access top of mind, policymakers must consult multiple stakeholders including patients and clinicians, with the understanding that patients and those who care for them have valuable insights toward making informed, cost-effective decisions.”³⁴

And where does all of this leave patients with rare diseases and conditions? While waiting for life-saving therapies, patients are getting louder. They have no other choice. They understand, perhaps better than any other stakeholder group, the urgency of finding equitable access solutions and the need for collaboration – not tomorrow, but today.

Champion of change

In conversation with SMA patient
and advocate Catherine Boivin

Spinal muscular atrophy (SMA) hardly defines Catherine Boivin's life. With a Master's degree in theatre design from Concordia University, the 41-year-old Montreal resident has worked as a designer for the stage and film and as a creative researcher for the Cirque du Soleil Entertainment Group. At the same time, Boivin has embraced the role of SMA patient advocate and is working with her fellow advocates to ensure all Canadians with SMA have an equal shot at life-changing therapies. In this candid exchange, Boivin shares her perspectives on SMA, access, and advocacy.

Can you tell us how you came to be an SMA advocate?

After my diagnosis of SMA at 18 months, my parents were told I would probably need to be institutionalized and not survive past early childhood. Well, here I am! In my young adulthood I devoted myself to my studies and career, without intending to become a spokesperson for my disease. But when [novel SMA medication] Spinraza came along and the PMPRB reforms in Canada came to my attention, I realized that people with SMA and other rare diseases were about to face some big challenges and felt called to use my research and communication skills to make a difference.

How was your experience getting access to Spinraza?

It's been an interesting ride. In January 2019 the drug finally got listed for adults in Quebec only, based on a managed approval process, though we're still fighting for fair access across the province. I myself had to wait almost a year after listing to get access, due to the complexity of my case and hospital-level delays. Since I began taking the medication I've taken it upon myself to document all the changes in my health, whether good or bad. My neurologist submits these records – which are in effect patient-reported outcomes measures – to the government along with the required annual evaluations, hoping they'll continue to support my treatment. But at present there's no guarantee or clear process.

How has the drug worked for you?

It's working. Before starting on the drug I had very low energy levels and felt I was in decline. It was getting harder and harder to put in a full workday. My right arm, which is my better arm, was getting weaker and I had chronic shoulder pain. Routine activities like brushing my teeth – and even eating – were becoming difficult. All this has improved with Spinraza. My shoulder pain has disappeared. While I can't say I feel 20 years younger, I no longer feel super-weak.

What was your reaction to the CADTH and INESSS recommendations for Spinraza?

[Note: In 2019, CADTH gave a positive recommendation to Spinraza for a narrow subset of pediatric patients.³⁸ After an initial negative recommendation, INESSS issued a "listing with conditions" recommendation in 2018.³⁹]

I found it hard to believe this was happening in Canada, while small countries in Europe were already enabling their patients to access the drug. One of the sticking points was a lack of long-term efficacy data to support cost-effectiveness, but this requirement doesn't make sense for rapidly progressing conditions with few or no other treatment options. I would love to see assessors work with manufacturers on a longitudinal strategy for data collection.

In many other countries, patients have been able to access Spinraza through OBAs or similar agreements. Should this approach be considered in Canada?

The short answer is yes, though I don't think it would work for every rare disease drug. It all depends on having measurable outcomes and agreeing on which ones to use. An OBA scheme would be workable for Spinraza as it's a drug you have to take for life and there are many ways to assess progress. There's a caveat, though: existing measures of progress were designed for young children and don't capture the spectrum of improvements in adults, especially non-ambulatory ones like me. For example, one of the measures involves testing a certain reflex – which disappears naturally after age 1. In non-ambulatory adults it would make more sense to measure something like improvement in writing speed and endurance.

How do you see the patient's role in designing or participating in OBA-type agreements?

Patients know best which outcomes make the greatest difference to their quality of life, so they must be part of the process. Industry should also be consulting with patient organizations to ensure their clinical trials include meaningful outcomes.

To play devil's advocate, might extra consideration for patient-centric measures lead to indiscriminate support for drugs with little clinical benefit?

We have to remember that no patient wants to stay on a drug that doesn't work. Spinraza is a complex therapy that requires lumbar punctures and regular visits to the hospital. I have heard of adults who decided to stop Spinraza because it didn't give them enough benefit or caused other problems. If a patient wants to continue, there's a good reason for it.

Is there anything that industry could be doing to support better access?

Industry is already supporting some great projects, like the newborn SMA screening initiative. It's a good example of the power of building partnerships and relationships, and such public-private collaborations help defray government costs. There's always room for more collaboration all around.

“Patients should be part of the OBA creation process because they know best which outcomes mean the most to them. We should also remember that no patient wants to stay on a drug that isn't helping.”

What keeps you going as a patient advocate?

When Spinraza first came out, my thoughts went to families with newly diagnosed children. I was encouraged to think the drug will allow them to have a very different life experience from my own. I envision a future where all people have fair and equal access to such life-changing treatments, from the day they are born. My advocacy work is about making this vision a reality.

SCREENED AT THE STARTING GATE - AN EXAMPLE OF POSITIVE CHANGE⁴⁰

Newborn screening gives children with SMA a chance to realize their developmental potential. Late last year, Ontario became the first province to add SMA screening to its newborn screening panel. Not content to rest on these laurels, Muscular Dystrophy Canada, an umbrella organization representing people impacted by SMA and other neuromuscular disorders, has embarked on a collaboration with Novartis Canada to deploy SMA screening across Canada. Novartis has committed up to \$2 million to the project. “It's an excellent example of what industry can do to help improve access to therapies,” says Boivin.

Advocating Out Loud

Meet two cystic fibrosis (CF) patient advocates who have been vocal about what needs to change in the CF treatment landscape.

Stephanie Stavros, founder and co-director of the patient advocacy group CF Get Loud, has been fighting CF since birth. She made news in 2020 when she became the first person in Canada to be approved for compassionate care for Trikafta, after tirelessly lobbying to government and to the manufacturer of the drug. Now approved by Health Canada for selected CF patients, Trikafta costs about \$420,000 per year.

Beth Vanstone, who shares the CF Get Loud director position with Stephanie, has been advocating for CF patients since her daughter Madi was born with the disease 19 years ago. After successfully lobbying for funding for Kalydeco, a \$350,000 per year medication targeted to people with Madi's type of CF gene mutation, she continues to speak for CF patients facing treatment access barriers.

In this no-holds-barred chat, Stephanie and Beth talk about their triumphs, frustrations, and the fault lines in the Canadian access landscape.

ON THE JOURNEY TO CF GET LOUD

Stephanie: I spent the first 34 years of my life hiding my CF because I didn't want it to limit me, but when I got to end-stage disease and found out my own country didn't have

my back, I decided to stop hiding. I've spent the last two years fighting for myself and the rest of the CF community. Launching CF Get Loud has been part of that process. The name of the group wasn't chosen by accident: our community has to literally fight for the breath to speak up.

Beth: I'll never forget when we entered Madi in a clinical trial of Kalydeco when she was 10 years old. Within two days I knew she was in the treatment group and within a month all her issues resolved. She told me, 'Mummy, I can breathe through my nose.' I joined CF Get Loud because I want other parents to experience moments like this.

ON ACCESS TO MEDICATIONS FOR ADVOCATES AND FUNDRAISERS

Beth: You submit your child to test after test, you take trips to the hospital to do extra tests for research, you work to raise money. You do this for years. If we're not going to get access to the drugs after all that, then why are we doing this? We have to help decision-makers understand that we're part of this process and they have to meet us partway.

Stephanie: I've had a similar experience. From the age of 8 months to 10 years, I participated in clinical research every 3 months. I spent 37 years asking how I can help, doing fundraisers, galas, zoo walks, you name it. To be

“Patient-reported outcome measures reflect quality of life, and what's more important than that?”

Stephanie Stavros

denied access to Trikafta after that felt like a kick in the gut. I'm obviously grateful to the manufacturer for coming through with compassionate care, but it breaks my heart to see other children and adults in hospital with deteriorating lung function.

ON THE PMPRB'S NEW PRICING REGULATIONS, COMING INTO EFFECT JANUARY 2022

Stephanie: Two of our CF medications, if subjected to these regulations, would require a 99% price reduction to come into Canada. No manufacturer can possibly offer that, so what ends up happening is that the regulations prevent or delay the introduction of drugs like Trikafta into the country.

Beth: Unrealistic price limits aside, the PMPRB rules have created an extra layer of bureaucracy in a country that's already hard for pharma manufacturers to do business with.

ON THE HTA ASSESSMENT PROCESS IN CANADA

Stephanie: The average time from Health Canada approval to listing is 600 days. People don't realize the layers of red tape involved. When patients new to the game learn of a drug submission and start celebrating, I secretly think, “if you only knew.”

ON OBA-TYPE AGREEMENTS FOR RARE DISEASE DRUGS

Stephanie: Innovative agreements like OBAs definitely play a role. When a drug shows great promise but there is uncertainty around efficacy or price, it makes sense to provide the drug first, track the data, and then review and adjust access criteria and price accordingly. It's a common-sense approach for people who need quick access.

Beth: If an OBA can get a baby with a neuromuscular disease on a drug more quickly, so they'll still be able to move their legs by age 2, let's do it! Right now the pharma companies are saving many lives through their compassionate care programs, but we need more equitable ways to share the risk and OBAs can do that. There is an opportunity to collect data on how patients are doing with these medications and use the data to drive access.

“If an OBA can get a baby on a drug quickly so they can still move their legs by age 2, let's do it!”

Beth Vanstone

ON THE ROLE OF PATIENT ADVOCATES IN SHAPING POLICY

Beth: I see our role as educating policymakers, who are often unaware of how this or that regulation affects patients. I've learned that you have to be both specific and persistent as an advocate. Know what you're asking for and why – and don't accept offers that make no sense. For example, at one point I was told Madi could access Kalydeco if she was in the hospital – but the whole point of the medication was to keep her out of the hospital.

Stephanie: You're touching on something very important, which is that the metrics and cut-offs used in our current system don't make sense for rare diseases. For example, the average gain of lung function on Trikafta is 14 percent. This may not seem like much to the average person or to regulators, but to someone like me it's the difference between a transplant, supplemental oxygen, and normal life.

ON THE IMPORTANCE OF PATIENT-REPORTED OUTCOME MEASURES (PROMS)

Stephanie: PROMs should be part of the conversation with assessors and payers because they reflect quality of life, and what's more important than that? With CF you're slowly drowning in your own lungs. If you can come up for air, all kinds of things improve in your life. PROMs capture that.

ON THE DRIVE TO KEEP FIGHTING FOR CF PATIENTS

Beth: We won the two-year battle with the provincial government and got funding for everyone with Madi's gene type, but it didn't feel right to stop there. Plus my in-box is flooded with questions from other parents: when, what, how... the least I can do is help make things fairer for this vulnerable community.

Stephanie: I feel like I've won the life lottery. I have a new shot at life, which is the biggest gift of all. I don't want to waste this opportunity, so I plan to stay loud!

On the reading list

[Bringing rare disease therapies into Canada](#)

[What if All Rare Diseases Were Treated like Hemophilia?](#)

[What to expect from Canada's drug pipeline in 2021](#)

[Rare Disease Day: Lack of strategy is hurting patients](#)

[What it feels like: Living with ALS](#)

[Ontario to cover cost of drug for rare neuromuscular disease on a 'case-by-case basis'](#)

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