Submission: National Strategy for High-Cost Drugs for Rare Diseases Consultations, March 26, 2021

Introduction and Executive Summary

Cystic Fibrosis Canada believes that Canada needs a strategy to fund highly effective therapies for rare diseases. We believe that the federal government's commitment to developing a strategy for high-cost medicines for rare diseases should lead a drugs for rare diseases access system that:

- Continually engages patients, patient groups, clinicians and researchers as meaningful decision-makers and key drivers in developing and implementing a strategy for highly effective medicines for rare diseases.

- Focuses on value and not cost. The working name, "National Strategy for High-Cost Drugs for Rare Diseases", speaks solely to the cost of medicines and not the value they bring to the Canadians with rare disease who need them, not to mention the benefits that providing access has on society.

- Is governed by a single framework that formalizes collaboration between public and private payers. This framework should outline a separate path for access to highly effective therapies for rare diseases and precision medicines. This path should start at the point of entry into Canada and should provide fast, fair, and comprehensive coverage to Canadians with rare diseases, regardless of where they live.

- Builds the evidence base. The strategy must define our rare disease research priorities and outline coordinated research on rare diseases, including the impact that new therapies have on rare disease populations, how we measure impact vis-a-vis real world evidence, and how we work with cross-jurisdictional and international research bodies.

- Leverages existing research, development, and infrastructure to develop effective and expedient processes that improve access and/or measure impact. For example, Cystic Fibrosis Canada manages the Canadian Cystic Fibrosis Registry. Now fifty years old and considered to be one of the most robust rare disease registries in the world, registry data is used by clinicians and researchers to improve care of patients, respond to emerging health care issues, develop quality improvement initiatives, and track and predict clinical outcomes over time.

  Replicating the Canadian CF Registry across other rare diseases would expedite implementation of a drugs for rare disease strategy. It would also allow our governments to make better informed regulatory, review and reimbursement choices.

About Cystic Fibrosis

Cystic fibrosis (CF) is the most common fatal genetic disease affecting children and young adults in Canada. There is no cure. Cystic fibrosis causes various effects on the body, but mainly affects the digestive system and lungs. The degree of cystic fibrosis severity differs from person to person even with the same mutations.

The most significant clinical impact is in the lungs, where thick sticky secretions lead to persistent infections and cycles of inflammation that are ineffective in clearing infections. This leads in turn to

progressive scarring of the airways and a progressive and sometimes rapid decline in lung function. Pulmonary / infection / cardiovascular complications cause eighty percent of cystic fibrosis fatalities.[1] Patients may suffer frequent pulmonary exacerbations (PEx) requiring weeks of hospitalization and I.V. antibiotics. PEx cause rapid decline of lung function and more rapid disease progression and are associated with a greater risk of death (Stanford, G. E., Dave, K. & Simmonds, N. J., 2021)[2].

Other consequences of having cystic fibrosis include malnutrition and very low BMI and cystic fibrosis-related comorbidities like cystic fibrosis-related diabetes (CFRD) and cystic fibrosis-related liver disease. Cystic fibrosis is a complex disease caused by mutations in the gene for the Cystic Fibrosis Trans membrane Conductance Regulator (CFTR). There are over 2,090 known mutations. Cystic fibrosis has a tremendous impact on the people who live with it, their loved ones, and on society. Every week in Canada, two people are diagnosed with cystic fibrosis, one of them through newborn screening. Every week in Canada, one person with cystic fibrosis will die.

Thanks to significant progress in treatment and care, the majority of children with cystic fibrosis will reach adulthood. The estimated median age of survival for Canadians born with cystic fibrosis in 2019 is 54.3 years of age.[3] Half of the Canadians who died from cystic fibrosis in 2018 were under 33 years. As the disease advances ever more time and effort are needed to manage the progressive and debilitating symptoms. Children with cystic fibrosis may need to quit school or go part-time, adults with cystic fibrosis may need to leave the work force or undertake part-time work, as may caregivers of children and adults with cystic fibrosis.

In recent years, precision medicines have been developed that treat the basic defect of cystic fibrosis. These medicines target the CF gene product, CFTR. In contrast to symptom management drugs that treat the downstream consequences of the defective protein one symptom at a time, CFTR modulators work by partially correcting the flawed protein throughout the body, leading to improved clinical outcomes for patients with cystic fibrosis.

Trikafta is the newest life-changing CFTR modulator. This third-generation modulator can treat up to 90% of Canadians with cystic fibrosis. It represents the single biggest advancement in treating cystic fibrosis in the history of the disease and has been proven to significantly improve health outcomes. The Washington Post named it number one of nineteen good things that happened in 2019.[4]

All modulators are tailored for specific CFTR mutations. Only the first-generation modulator, Kalydeco, is broadly available in Canada. Although it was first approved in 2012 not all Canadians who need it can get it through our public payers because it has been caught up in almost seven years of negotiations at the pCPA. Kalydeco treats about 4 percent of Canadians living with cystic fibrosis.

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[1] Canadian Cystic Fibrosis Registry 2019 Data Report, https://www.cysticfibrosis.ca/registry/2019AnnualDataReport.pdf

[2] Stanford, G. E., Dave, K. & Simmonds, N. J. Pulmonary Exacerbations in Adults With Cystic Fibrosis: A Grown-up Issue in a Changing Cystic Fibrosis Landscape. *Chest* **159,** 93–102 (2021).

[3] Canadian Cystic Fibrosis Registry 2019 Data Report, https://www.cysticfibrosis.ca/registry/2019AnnualDataReport.pdf

[4] https://www.washingtonpost.com/opinions/19-good-things-that-happened-in-2019/2019/12/17/719f50d6-2025-11ea-86f3-3b5019d451db_story.html August 21, 2020

Orkambi and Symdeko are both second generation modulators and could benefit as many as 50% of Canadians with cystic fibrosis, but neither is available through public payers in Canada, excepting Quebec which provides access only to those who meet the strict eligibility requirements of the 'patient d'exception' program. Orkambi is available to children and youth in Ontario, Alberta and Saskatchewan, but the eligibility criteria are so restrictive that few can access it.

Clinical benefits gained from Kalydeco are more modest than those from Trikafta. Although the patient populations served are distinct, early studies show that patients with a F508del mutation who are on Kalydeco are likely to benefit from Trikafta. On average, clinical benefits gained from Orkambi or Symdeko are substantially more modest than those from Trikafta and more patients reported intolerable side effects with Orkambi in particular, however individual responses were highly variable and some patients report having benefited greatly from one, or another of the earlier modulators. Any Canadian who is on, or eligible for, Orkambi or Symdeko is likely to benefit substantially from Trikafta.

Canadian research released in August 2020 demonstrates that if Trikafta was brought to Canada in 2021 it could result in extraordinary health benefits by 2030, including 15% fewer deaths, 60% fewer people living with severe lung disease and an increased estimated median age of survival for a child born with cystic fibrosis of 9.2 years.[5]

Trikafta was fast-tracked for access by the U.S Federal Drug Agency (FDA) and the European Medicines Agency (EMA). Trikafta has received regulatory approval in 33 countries, 27 within the EMA centralized regulatory approval in addition to receiving approval in the United States, United Kingdom, Norway, Iceland and Liechtenstein. Trikafta has received public reimbursement in the United States, United Kingdom, Ireland, Austria, Denmark, Germany, and Slovenia.

A year and a half after the FDA approval, Canadians with CF are still waiting for Trikafta and patients who could have benefited from it have died in the interim. This is why we need a strategy for access to highly effective medicines for rare disease now. CF can't wait.

> *Growing up, I spent a lot of my life trying to show everyone that I was tough and that I could handle CF because I didn't want their worry or their pity. I have to live my life knowing that it's most likely going to be shorter than my parents' lives. Shorter than my younger brother's life. No one should have to live like that. Now that I'm an adult living with CF, the realities of the disease are catching up to me. My health is worse than it's ever been before. Not having enough breath to do the things I want to do on a daily basis is incredibly frustrating. I want to have enough breath to run up the stairs. To hike down to the dock and go fishing with my dad. To clean the house. CF is slowly stealing my life from me. I have dreams. I want to get married and not break my husband's heart when CF stops mine.[6] – Adult with CF*

5 https://www.cysticfibrosis.ca/news/new-research-shows-15-reduction-in-cystic-fibrosis-deaths-by-2030-if-trikafta-is-made-available-now?p=2 March 25, 2021

6 Cystic Fibrosis Canada. CADTH submission on Orkambi. March, 2018.

About Cystic Fibrosis Canada

Cystic Fibrosis Canada has dramatically changed the cystic fibrosis story. We have advanced research and care that has more than doubled life expectancy. Since being founded by parents in 1960, Cystic Fibrosis Canada has grown into a leading organization with a central role engaging people living with cystic fibrosis, parents and caregivers, volunteers, researchers and healthcare professionals, government and donors. We work together to change lives through treatments, research, information and support.

Despite our remarkable progress together, we are not yet done. Not when half of the people with cystic fibrosis who died over the past three years were younger than 34. Not when a child born with cystic fibrosis still has only a 50% chance of living to 54. We will keep pushing, keep going further until all people with cystic fibrosis can and do experience everything life has to offer — and enjoy everything life has to offer.

Cystic Fibrosis Canada funds basic, discovery science and clinical research, and has helped establish core facilities across the country. We provide financial support to the forty-two multi-disciplinary cystic fibrosis clinics that see nearly all Canadians living with cystic fibrosis and maintain close relationships with the clinical and research communities. We have invested over $261M in research and clinical care support.

The close relationships with the research and clinical communities allows us to better understand the disease. We are the most respected and trusted source for information on cystic fibrosis in Canada and provide an information and resource service to the community that includes publishing a comprehensive resource compendium for the community. In addition, we maintain close relationships with our sister organizations around the world, which allow for the rapid sharing of information and adoption of best practices.

In 2018, we launched the Cystic Fibrosis Canada Accelerating Clinical Trials (CF CanACT) network now with ten sites that serve 13 of the 42 cystic fibrosis clinics reaching over 60% of Canadians with cystic fibrosis. CF CanACT also works closely with our international partners to conduct protocol reviews, share Data Safety Monitoring Boards, and help speed clinical trial progress.

Cystic Fibrosis Canada also manages the Canadian Cystic Fibrosis Registry (the Registry). The Registry contains the clinical information on nearly all Canadians with cystic fibrosis, living or deceased, with data going back to the 1970's. The Registry publishes an annual data report that describes the current status of the cystic fibrosis population in Canada and national trends over time. The data in the Registry is also used by investigators in Canada and around the world to better understand the disease and the impact of therapeutic efforts as well as proposed improvements to care.

We work closely with our patient community to advocate to improve their health and well-being. In 2020, Cystic Fibrosis Canada's National Advocacy Network consisted of 250 well-trained advocates and a basket of tools to help them in their efforts. We've been able to help the cystic fibrosis community by amplifying their voices through coordinated efforts that have addressed both national and regional priorities.

Cystic Fibrosis Canada's contributions have led to significant improvements care and quality of life for people living with cystic fibrosis. As a result, Canada has one of the highest median ages of survival in the world.

Issue 1: Improving patient access consistently across Canada

From Health Canada discussion paper: Patients with rare diseases live in every part of the country, but access to high-cost drugs to treat them varies greatly depending on where they live and how their drugs are paid for. Options for improving access and improving national consistency for people with rare diseases include:

- ***A single framework for decision making on high-cost drugs —*** *Getting federal, provincial and territorial governments to agree on a single principled approach for deciding 1) which high-cost drugs for rare diseases to cover and 2) which patients should be covered under what conditions would create greater consistency across the country as well as predictability for patients.*

- ***A transparent co-ordinating body*** *— Creating a co-ordinating body to improve communication and collaboration among key players (including private and public drug plans) would create consistency in decisions on what drugs to pay for, ensure agreed-on conditions for consistent access to drugs were followed and clearly communicate rationale and decisions, as well as information on process and timelines.*

- ***Patient and clinician engagement*** *— Improving engagement with patients, patient groups, and clinicians to increase awareness of policies and programs related to accessing high-cost drugs for rare diseases.*

- ***Co-ordinated support for research on rare diseases in Canada*** *— While each rare disease is different, there are common challenges and factors affecting research and discovery of treatments. Nationally co-ordinated research support could increase knowledge of rare diseases affecting Canadians and lead to new discoveries, thus bringing these treatments to Canadian patients.*

Issue 1: Questions

1a. *How can access to high-cost drugs for rare diseases be made consistent in order to improve patient access to these treatments?*

- Focus on value, not cost. The working name of this strategy speaks solely to the cost of medicines and not the value they bring to the Canadians with rare disease who need them, not to mention the benefits that providing access has on society.

  Price must always be considered in the context of the value of these medicines, and any name that is applied to this strategy should include mention of the highly effective nature of these medicines. The strategy should help improve access to “highly effective” therapies for rare diseases.

- Another goal of the proposed strategy is to promote more cooperation among federal, provincial and territorial governments, along the lines of the pan-Canadian Pharmaceutical Alliance’s (pCPA) work. While Cystic Fibrosis Canada supports the spirit of collaboration, our experience has shown that good faith only goes so far when it comes to access to drugs for rare disease. We need fewer review bodies, more streamlined processes, and a sense of urgency. Too much time and too much process costs lives.

The pCPA has no public timelines for its negotiations, nor are its negotiations transparent. Adding a transparent coordinating body on top of a body that is not transparent won't fix what is broken. Before adding any new bodies to the system, we need to consider how current bodies are meeting, or not, the rapid access needs of Canadians with rare diseases. Currently, the bodies that regulate, review and reimburse drugs for rare diseases **do not** meet these needs.

There has been some progress in shortening Health Canada review timelines for game-changing drugs to 180 days or less through Priority Review. As well, the new Aligned Review process allows CADTH, INESSS and the PMPRB to do their reviews while Health Canada undertakes its review, which expedites regulatory, pricing and Health Technology Assessment processes.

Those are steps in the right direction, but the overall process is still too long and uncertain for Canadians with rare diseases like CF. The unimplemented changes of the PMPRB guidelines have created a chilling effect on manufacturers' willingness to bring innovative medicines to Canada. Since the introduction of PMPRB price controls in 2017, there has been a dramatic decline of 40% in the number of new globally available treatments sold in Canada in 2019 compared to the previous year, according to a 2020 Life Sciences Ontario report.

- We need a single framework that encourages and values transparency, accountability, and expediency, one that actually gets medicines into the hands of the Canadians who live with rare diseases who need them now. This framework should:

    - Outline the roles and relationships between public payers, private payers, manufacturers, patient groups, and patients in rare disease drug regulation, review, and reimbursement decision-making processes.

    - Establish long-term, sustainable funding model that involves all payers – federal, provincial, and private plans need to collaborate for capacity.

    - Provide an expedited, separate pathway for highly effective therapies for rare diseases, one that starts at Health Canada and carries through to provincial reimbursement.

    - Define priorities and outline coordinated research on rare diseases, including the impact that new therapies have on rare disease populations and how we measure impact vis-a-vis real world evidence.

    - Lever existing research, development, and infrastructure to develop effective and expedient processes that improve access and/or measure impact.

- We need a separate path for highly effective therapies for rare diseases. Game-changing medicines for rare diseases and precision medicines are unique in that they serve small, targeted populations. Treating these drugs like drugs for larger populations has created inequities in the system, as Canada's evidence requirements and evidence realities for accessing drugs for diseases are very different.

- Cystic Fibrosis Canada strongly supports improving engagement of patients, patient groups and clinicians throughout the drug discovery, development and drug access decision-making processes. The scope of what is being proposed in the choice presented here limits improving engagement to "increasing awareness of policies and programs related to accessing high-cost drugs for rare diseases".

- What is being proposed is not meaningful and impactful engagement of patients, patient groups and clinicians. The goal of engagement should be to create a better system of access for those who need it, not to increase awareness of a system that does not serve them well.

- Cystic Fibrosis Canada supports coordinated research on rare diseases in Canada, provided it is supported by a robust international research collaboration strategy. While focused research in Canada may build capacity for "made-in-Canada" solutions, it will take years to build said capacity and Canadians with rare diseases need access now.

1b. Which of the proposed options, or combination of options, would be the most effective for improving access and improving consistency? (Select all that apply)

- ✓ A single framework for decision making on high-cost drugs
- ✓ A transparent co-ordinating body
- ✓ Patient and clinician engagement
- ✓ Co-ordinated support for research on rare diseases in Canada

Issue 2: Incorporating Best Evidence

From Health Canada discussion paper: How to ensure decisions on covering high-cost drugs for rare diseases are informed by the best evidence available. Evidence on how well high-cost drugs for rare diseases work is often limited, which makes it harder to decide which drugs should be covered.

Options for addressing the challenge of covering drugs with limited evidence include:

- *Innovative approval and coverage models — Approval of and funding for drugs for rare diseases could be tied to how well they work, meaning payment would depend on patients having specified outcomes, which manufacturers would track through long-term studies and regular reporting on the effectiveness and safety of their drug. This would require an agreement on what level of benefit would be sufficient as well as clear, objective indicators for measuring benefit (which could be difficult to develop). If data showed poor performance in the longer term, payments would be reduced or discontinued.*

- *A national expert panel — The panel would have the authority to 1) study data and evidence to make informed recommendations on who should be treated with high-cost drugs for rare diseases and 2) monitor how the drugs are being used, how well they are working and making recommendations on continued funding.*

- *A national data system — This system would capture more comprehensive and consistent information about the prevalence of rare diseases in Canada, how treatments for rare diseases are used by Canadians and how they are working.*

- *Independent national and international networks — These networks would build on existing partnerships to facilitate knowledge and data sharing on real-world experience of patients in a way that is independent and free from conflict of interest.*

Issue 2: Questions

2a. How can decisions on covering high-cost drugs for rare diseases be made when the evidence is limited?

- Cystic Fibrosis Canada supports using best evidence to inform drug access decisions. Innovative approval and coverage models for drugs for rare diseases, including those that pay for performance, require robust real-world data to inform the decision-making around drug access. Data is the driver of innovative decision-making in countries like Germany, which has a simplified submission process for drugs for rare diseases.

- Canada needs a robust data strategy. Rapid access by Canadians to innovative drugs is necessary if Canada is going to collect reliable real-world evidence, Canada would otherwise be dependent on data arriving from other jurisdictions (who would necessarily have earlier access than Canada). Innovative access models must prioritize building this capacity and keep the time required in mind but improving access to drugs for rare diseases should not be delayed. Most of the concerns raised by pay for performance approaches can be managed with robust and reliable data.

- Cystic Fibrosis Canada is concerned that creating a national expert panel to study data and monitor the impact of drugs will add another layer to an already onerous system and may not, in and of itself, bring more disease-specific rare disease expertise to the table, which should be a goal of any drugs for rare diseases evaluations. Some countries have an open, rotating seat for specialists as part of their drug evaluation processes.

- Cystic Fibrosis Canada strongly supports the creation of a national data strategy. There are already systems and platforms in place that can be leveraged to expedite implementation of a data strategy. Building on existing infrastructure and working with researchers, clinicians and health charities can save both time and money.

  Cystic Fibrosis Canada created the Canadian CF Registry in the early 1970s with the goal of monitoring important clinical trends in the Canadian CF population. The Registry is comprehensive with data from almost all Canadians with CF who attend one of 42 specialized clinics, about 99% of Canadians with CF. It is considered to be one of the most robust CF registries in the world.

  The Registry has played an invaluable role in helping to improve the duration and quality life of people with cystic fibrosis. It captures longitudinal clinical outcomes and episodes of treatment data. Data collected is used to improve our knowledge of disease patterns and care of patients with cystic fibrosis, respond to emerging health care issues, and to develop quality improvement initiatives and track clinical outcomes over time. It allows the conduct of sophisticated studies, such as simulating the long-term impact of Trikafta on the health of Canada's CF community, and to measure clinical effectiveness of new treatments.

The Registry can be used for long-term efficacy and safety studies as is being done in other jurisdictions around the world. The Registry is part of a global consortium of CF Registries who work closely with each other to harmonize data definitions and collaborate on research of interest. Most recently, in response to the global COVID-19 pandemic Cystic Fibrosis Canada collaborated with 19 other country-specific cystic fibrosis registries to examine the impact of the pandemic on the CF population globally.

It also offers tangible benefits through its patient portal, which equips and empowers patients with data on their own clinical outcomes so that they use this information in managing their health and in discussions with their health care providers.

Replicating the Canadian CF Registry across other rare diseases would expedite implementation of a drugs for rare disease strategy. It would also allow our governments to make more informed regulatory, review and reimbursement choices. It would then be up to governments across Canada to use the RWE that such a national Registry would provide in drug review and reimbursement processes, which few do currently.

Cystic Fibrosis Canada has also partnered with SickKids and SickKids Foundation on an experimental precision medicines program. The Program for Individualized Cystic Fibrosis Therapy (CFIT) is developing tools and technologies that will help predict who will respond to CFTR modulators.

- Cystic Fibrosis Canada strongly supports building and leveraging independent national and international networks. We manage the Cystic Fibrosis Canada Accelerating Clinical Trials (CF CanACT), which allows researchers to connect with Canadians with CF who are interested in participating in clinical trials.

  World-class clinical trials are an integral part of the process that brings new therapeutics and better care to Canadians by providing the data necessary for initial review and approval of drugs. Clinical trial networks like CF CanACT facilitate the development of new treatments by increasing capacity and enhancing participation of Canadians in clinical trials leading to better and more reliable data on which to base decisions.

2b. Which of the proposed options, or combination of options, would be most effective for strengthening the evidence base? (Select all that apply)

- ✓ Innovative approval and coverage models
- × A national expert panel
- ✓ A national data system
- ✓ Independent national and international networks

Issue 3: Spending and System Sustainability

From the Health Canada discussion paper: How to ensure spending on high-cost drugs for rare diseases does not put pressure on the sustainability of the Canadian health care system. Most drugs for rare diseases are very expensive and can pose a challenge to the long-term sustainability of government- and employer-sponsored drug plans. Options for controlling the impact of high-cost drugs on health-system budgets include:

- *Sharing of costs and pooling of risks — Working together with other payers to help everyone negotiate better agreements with pharmaceutical manufacturers (and possibly help bring drugs to market that would otherwise not be commercially viable).*

- *Investments up front to reduce the risk in early development — Rather than relying solely on price to compensate drug manufactures for research and development, the cost of developing new drugs for rare diseases could be shared among research funders and companies to reduce risk and lower expenses. This could include up-front investment by governments and health charities for research, development and production of rare-disease treatments. Negotiated agreements with manufacturers could limit prices later on.*

- *Pay for performance — Exploration of innovative funding models that are tied to how well a drug works, including defunding drugs that offer only marginal or unproven benefits.*

- *Supports for "made-in-Canada" innovation — Development of domestic innovative or generic capacity to sustain all elements of drug discovery, research and development, through to manufacturing, trials, approval and sale. This would help keep costs lower than if researchers sell their discovery to a multinational company to be brought to market*

- *International collaboration — Working together with other countries to share non-confidential information to inform negotiations and leverage better pricing.*

Issue 3: Questions

3a. How can we ensure spending on high-cost drugs for rare diseases does not put pressure on the sustainability of the Canadian health care system?

- Cystic Fibrosis Canada supports sharing of costs and pooling of risks to negotiation better agreements with pharmaceutical manufacturers, which may also help bring drugs to market that would otherwise not be commercially viable, provided these efforts focus on the value of medicines and not just price.

  We support the policy goal of lowering drug prices in Canada. We expect pharmaceutical manufacturers to bring their products to market at a reasonable price. But we also expect the government to ensure that the regulatory environment in Canada does not unnecessarily limit our ability to access new life-saving therapies.

  We also want to see any cost savings reinvested in improving access to drugs for rare diseases and precision medicines. For example, our federal government has left 20% in savings on the table by not implementing the Patented Medicines Price Review Board (PMPRB) changes to the basket of comparator countries on July 1, 2020. That is money that could be put toward implementing an access strategy for drugs for rare diseases now.

- Cystic Fibrosis Canada agrees that investments up front can reduce the risk in early drug development by not relying solely on manufacturers for research and development, but we feel that while this approach might be suited for a research and innovation portfolio it goes beyond

the scope of an access to drugs for rare diseases strategy and is unlikely to lead to significantly lower drug prices.

- For example, using what was an extraordinarily innovative approach for the time, the U.S. based Cystic Fibrosis Foundation (CFF) funded nearly all of the early development of the currently available disease modulators, in the biggest rare diseases market in the world. Based on the CFF's return on investment, the price of these medicines might have been reduced by only 15%. In addition efforts in the earliest stages of development to limit downstream pricing are likely to preferentially impede the development of drugs for rare conditions.

- Cystic Fibrosis Canada does not support a pay for performance model, as presented in the discussion paper. We appreciate that the effectiveness of medicines is important to reimbursement decisions, but we struggle with how performance will be defined and measured and believe such a system may actually impede access. As indicated earlier, the focus needs to be on value including especially value as determined by patients, and not merely the healthcare system. Current valuation systems do not adequately account for patient value.

  For example, CADTH has determined that a sustained improvement of 5% in ppFEV1 (a measure of lung function) is the primary marker of clinical effectiveness of CF modulators for HTA purposes. But ppFEV1 is just one measure of clinical effectiveness and is by itself inadequate to capture the whole value of highly effective modulator therapies to Canadians with CF[7].

  Performance measures would need to consider other important outcomes like improved BMI, cough reduction, decreased use of current therapies and drugs, and others that are very important to the overall health of a person with CF.

  The inadequate use of evidence under a poorly implemented pay for performance model would deny access for Canadians with CF who are receiving significant benefits from modulators but whose benefits are not considered fully in drug review and reimbursement processes.

  A pay for performance model requires both patient input into the measurement of value as well as a robust and reliable real world evidence data collection system neither of which we have.

- Cystic Fibrosis Canada believes that developing supports for "made-in-Canada" innovation is beyond the scope of a drugs for rare diseases strategy. The Government of Canada should already be supporting made-in-Canada innovation by investments in a research and innovation portfolio. Tying this to an access strategy for drugs for rare diseases will not improve access.

- As evidenced by our practices, both through the Registry as well as CF CanACT, Cystic Fibrosis Canada is both a strong supporter and a leader in international collaborations. Especially for rare diseases where Canadian data alone may be insufficient, international partnerships are key to leveraging research to understand the disease, improve care, and build the evidence base necessary for rare disease populations.

[7] Cystic Fibrosis Canada. CADTH submission on Orkambi. March 2018.

3a. Which of the proposed options, or combination of options, would be most effective for getting rare-disease treatments to patients? (Select all that apply)

- ✓ 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

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

Cystic Fibrosis Canada welcomes a discussion with Health Canada and our public payers about cloning our Registry to expedite implementation of an access strategy for drugs for rare diseases and precision medicines.

From a disease-specific perspective, our registry and clinical trials network should be used by public payers to provide real world evidence that informs drug review and reimbursement decisions.

Our clinical trials network – CF CanACT - should also be leveraged by our public payers as a mechanism to bring new CF medicines to Canada and to develop Canadian real world evidence to inform decision-making.

Finally, the benefits that an experimental precision medicines program like CFIT could bring to assessing the impact that these medicines have on individuals should be considered by our public payers.

For more information contact:

Dr. John Wallenburg
Chief Scientific Officer
Cystic Fibrosis Canada
e: jwallenburg@cysticfibrosis.ca
p: 1-800-378-2233 ext. 234