CADTH

Patient Input Template for CADTH Reimbursement Reviews

Name of Drug: **Tofersen**
Indication: **Treatment of adults with amyotrophic lateral sclerosis (ALS) associated with a mutation in the superoxide dismutase 1 (SOD1) gene**
Name of Patient Group: **ALS Society of Canada**

1. About Your Patient Group

Founded in 1977, the ALS Society of Canada (ALS Canada) is working to change what it means to live with ALS. Grounded in and informed by the Canadian ALS community, we respond to the urgent unmet need for life-changing treatments by investing in high-quality research that will fuel scientific discovery and by engaging industry, supporting increased clinical capacity, and advocating for equitable, affordable, and timely access to proven therapies. Responding to the tremendous need for current and credible ALS knowledge, awareness, and education, we empower Canadians affected by ALS to navigate the current realities of ALS, be informed consumers of ALS information, and advocate effectively for change. In Ontario, we provide direct community services to help people navigate ALS. Our work is powered by generous donors who share our vision of a world free of ALS.

2. Information Gathering

The following submission reflects data that ALS Canada gathered through an online survey and focus group interviews. All the data was contributed anonymously.

ALS Canada developed and administered a 20-minute online survey disseminated in English and French. Survey respondents were recruited by ALS Canada through promotion via email, social media, and ALS Canada's website, with the following populations invited to take part: people living with ALS ("patients") and their caregivers and family members ("caregivers/family members"). The responses were collected from January 15 and February 14, 2025.

598 patients and caregivers responded to the English and French online surveys. Almost all respondents were from Canada (primarily Ontario and Quebec), with less than 1% participating from the U.S. and France. More than 75% of respondents are, or were, caregivers/family members of someone diagnosed with ALS. The remainder are currently living with ALS. Among the respondents living with the disease, approximately 65% indicated they had been diagnosed with ALS between six months and two years ago, with the rest having received their diagnosis more than 3 years ago. More than half of respondents were 55 years of age or older. At the time of the survey, of the 175 respondents who are living people living with ALS, only 12 had direct experience with tofersen.

In February 2025, ALS Canada supplemented the information gathered through the survey by conducting semi-structured virtual focus group interviews with 3 patients and 1 caregiver, all of whom had direct experience with tofersen.

Their demographics are summarized in the chart below, and specific treatment experience can be found in Section 6:

Name	Patient/Caregiver	Gender	Age	Type of ALS	Diagnosis Date	Location
PT	Patient	Female	43	SOD1	February 2016	Saskatchewan (Canada)
TB	Patient	Male	50	SOD1	April 2018	Alberta (Canada)
TA	Patient	Male	28	SOD1	July 2020	Saskatchewan (Canada)
KS	Bereaved Caregiver	Female	41	SOD1 A5V	June 2019	Alberta (Canada)

3. Disease Experience

Amyotrophic lateral sclerosis (ALS) is a terminal disease that gradually paralyzes people because the brain is no longer able to communicate with the muscles of the body that we are typically able to move at will. As the connection with muscles of the body breaks down, someone living with ALS will lose the ability to walk, talk, eat, swallow, and eventually breathe. Of those who receive an ALS diagnosis, 80% will die within two to five years of diagnosis. There are currently about 4,000 people living with ALS in Canada. Every year, approximately 1,000 Canadians die of ALS and a similar number are diagnosed.

For the 90 to 95% of people living with ALS without an obvious family history, traditionally referred to as “sporadic”, it is estimated that between 11 to 16% of cases are caused by known ALS variants. To date, many genes have been identified that when altered, can contribute to ALS. The four most common genetic causes of ALS are due to variants in four genes: C9orf72, SOD1, FUS, and TARDBP. Approximately 5 to 10% of people living with ALS will have a family history of the disease. A family history means multiple family members were affected by the disease due to a hereditary variant in a gene related to ALS.

87% of the survey respondents indicated no family history of ALS.

A diagnosis of ALS and the realities of living with the disease have a profound and pervasive effect on the lives of not only those who are struck by this devastating disease but also anyone who loves and cares for them. The following is a summary of the key themes that emerged from the respondents of this survey – people living with ALS, caregivers and family of those who are living or have lived with the disease – on its impact on their lives.

Symptoms

With respect to a wide range of symptoms patients experience due to ALS, among the most severe are difficulty with mobility (i.e. walking, standing), decreased muscle tone, difficulty communicating verbally, muscle stiffness and fatigue. These symptoms were also among the most important to control for people living with ALS, in addition to difficulties breathing, choking episodes, pain and muscle cramping or twitching.

Impact on Quality of Life

When asked how living with ALS has negatively affected their quality of life, **patients** indicated that their social life, family life, ability to pursue hobbies and emotional well-being had suffered the most. When asked the same questions, **caregivers/family members** indicated that their family life, intimate relationships, and emotional well-being suffered the most.

Below are a few examples of answers from **patients** and **caregivers/family members** when asked to describe in their own words how ALS has impacted their quality of life.

"ALS has stopped life as I knew it."

"I lost the ability to enjoy nature and life fully."

"The future as planned and foreseen has been lost, retirement plans have been lost, friends have been lost. The ability to share certain memories has been lost."

"Struggles with my faith and spiritual well-being."

"I live half the week at my mom's place and hardly see my husband anymore. I struggle with back and joint problems due to caregiving-related injuries."

"I have not hugged anyone in months."

"I miss the little things like being able to fully enjoy a glass of wine."

"I feel I am living in an ALS world which is very narrow and focused instead of the real outside world where I existed before."

"Several years after my partner's death, I am still recovering physically and mentally from the complete exhaustion."

"Je ne peux plus manger avec des personnes pour boire un peu et jaser entre amis(es) et membres de la famille. Je suis presque forcé d'etre isolé."

The majority of **patients** indicated that they started needing assistance with eating, drinking, transitioning from lying to sitting, walking, speaking and bathing within a year after their diagnosis, with more than 60% of the respondents receiving 5 to 20 hours of assistance per week from caregivers/family members to perform activities of daily living. Approximately 60% of **caregiver/family members** respondents indicated needing assistance with these aspects of daily living "completely changed" their daily life.

Assistive devices are a critical aspect of the care of people living with ALS as well. Of the **caregivers/family members** surveyed, approximately 60% noted the need for specialized bathroom equipment, followed by hospital bed/mattress, walker, non-invasive ventilation support, standard/power wheelchairs and communications devices.

"My life is now basically restricted to 4 rooms in our house."

"For the past 6 months, most of the time, I stay at home and don't do anything."

"Living with ALS has made me totally vulnerable and dependent of my family. I need their support all the time."

"I still have to work full time (on site), so my day starts at 5 am to get him [person living with ALS] up, toileted, and partly dressed and into his wheelchair. Put lunch and drinks in an accessible place. Get medications ready for the majority of the day. Get myself ready. Head to work at about 6 am until about 3 pm (unless he has to call me home to use the bathroom or for other urgent needs). Get home, do physio, do housework, cook meals and prep lunches for the next day. Showering occurs twice a week and takes about an hour. Overall, I feel like I never stop and don't have much time to myself."

"I don't want to be a burden, so I push myself, but many days I find keeping up a facade of functioning well is exhausting."

"I went from being the sole income earner of a family of four, to being 100% dependent in less than a year."

"I went from being capable and independent to being almost completely dependent on others and unable to do simple things, like prepare a sandwich, for yourself."

"I had no life outside of caring for my husband. It consumed me. I couldn't leave the house. Friends disappeared."

"Life—walking alongside the one suffering and losing all their motor abilities, and mostly their capacity to breathe—is nothing short of a nightmare."

"Caregiving took 100% of my time and effort. I operated on adrenaline and was exhausted by the end of each day."

"Need for a scooter or wheelchair limits ability to travel even locally."

Disease Experience for Familial ALS

Given that this submission is specifically for a drug that targets a genetic form of ALS, it is important to provide context on the experiences of people with familial ALS. Their journey is shaped by both the presence of ALS in their family and the knowledge that they may one day face the same diagnosis. For people with familial ALS, the disease experience is often deeply personal. Many have witnessed firsthand how ALS has impacted their parents, siblings, or other relatives, creating an ongoing emotional and psychological burden.

"I have assisted in care for members of my family with ALS since I was able to walk. That's how I learned how to walk, pushing wheelchairs for people that needed it. I learned how to read by reading the paper to them because they couldn't hold the paper properly. It shaped who I am."

"We grow up with the knowledge that this is the way we are going to die. You just wait till you get it, and we deal with it the best we can."

"I had members of family who started showing symptoms when they are in their late 20s, early 30s that ended up dead before their 45th birthday."

Unlike sporadic ALS, where the diagnosis often comes as a shock, people with familial ALS or a genetic predisposition may spend years anticipating the possibility of developing symptoms. This often leads to heightened anxiety and vigilance, impacting all areas of their lives. When a diagnosis is confirmed, it is often met with a profound sense of inevitability yet also an acute awareness of how quickly the disease can progress based on their family history.

"For most people, hurting your knee, hurting your shoulder when you're 30 years old is not a concern. But for me, the first thing that runs through my mind is, what if it's ALS? What if it's coming for me? It's constant anxiety, and you just can't stop."	*"I saw my dad's side of family completely get decimated by ALS, so I knew what I was in for when I got my diagnosis. I knew what it would take for me. No ignorance. Just the weight of knowing exactly what was going to happen."* *"I felt like I was always waiting for the other shoe to drop. Everything felt like a warning sign that I couldn't just brush off."*

Many grapple with the reality that their children, siblings, or extended family members may also be at risk. This adds another layer of complexity to decision-making, particularly regarding genetic testing, reproductive choices, and the emotional weight of potentially passing on the mutation.

"The part that people seem to forget is how the children proceed with our lives. Do we test or not test? Is it worth it to find out and try solving it now, or do we wait for our fate? Imagine staring down the barrel of a gun and playing Russian roulette - only this time, there's two chambers and not ten. These are our odds of having a death sentence that can arrive at any point."	*"As a mother, there's a lot of guilt that I felt that here I am passing this disease on to my kids. They don't deserve to see me go down like this, and they don't deserve to get this disease, either."* *"When you have a genetic form of ALS every conversation about the future comes with extra weight. Do I tell them upfront? Do I wait? What if I want kids – do I risk passing it on?"*

4. Experiences With Currently Available Treatments

Currently there are two available treatments for people living with ALS in Canada.

Rilutek (riluzole)

72% of **patient** respondents indicated that they are taking/have taken Rilutek (riluzole). 52% of **caregivers/family members** respondents indicated that they support/supported a person living with ALS who used/had used Rilutek.

When asked about the benefits they may observe or have observed from Rilutek and the importance of these benefits, both **patients** and **caregiver/family members** identified slowing disease progression, maintaining ability and increased survival as being very important to them. However, while these outcomes are considered important, several **patients** and **caregivers/family members** indicated they could not definitively say they had observed these benefits.

Caregiver/family members were also asked about the benefits they have personally experienced as a result of the person they care/cared for taking Rilutek. Most respondents indicated that they did not experience any significant personal benefit from the treatment. Among those who did, the most commonly reported benefit was having more time with their loved ones due to delayed disease progression.

Most **patients** and **caregivers/family members** reported not experiencing or observing any significant side effects while taking Rilutek, but among those who did, the most significant to manage were tiredness, weakness, drowsiness and nausea. Rilutek is administered orally, which was not an issue for most patients. However, some patients with swallowing difficulties (a common symptom of ALS) reported challenges with administration.

Most of the **patients** and **caregivers/family members** indicated they had not faced difficulty accessing Rilutek. However, some patients indicated difficulty due to a lack of private coverage, strict public funding criteria, out-of-pocket costs and supply shortages.

Radicava (edaravone)

43% of patient respondents indicated that they are taking/have taken Radicava (edaravone). 20% of **caregiver/family members** respondents indicated that they support/supported a person living with ALS who used/had used Radicava.

When asked about the benefits they may observe or have observed from Radicava and the importance of these benefits, both **patients** and **caregiver/family members** identified slowing disease progression, maintaining ability and increased survival as being very important to them. However, several respondents indicated they could not definitively say they had observed these benefits.

Caregivers/family members were also asked about the benefits they have personally experienced as a result of the person they care/cared for taking Radicava, and the majority of respondents indicated that they did not experience any significant personal benefit from the treatment. Among those who did, the most commonly reported benefits were having more time with their loved ones due to delayed disease progression and increased independence for the person they care for, allowing for some reduction in caregiving demands.

Patients and **caregivers/family members** reported not experiencing or observing any significant side effects while on Radicava. Radicava can be administered both intravenously and orally, with IV infusions being phased out in favour of the oral formulation. The oral formulation was well tolerated by most patients, though some respondents with swallowing difficulties reported challenges in taking the medication. The shift to oral administration has been generally viewed as a positive change, reducing the travel to infusion clinics and not having to schedule daily activities around their infusion schedule.

Most **patients** and **caregivers/family members** indicated they have not had difficulty accessing Radicava.

Other Treatments

Patient and **caregivers/family member** respondents reported using a variety of additional treatments other than Rilutek, Radicava and tofersen.

Many had previously taken Albrioza, which was previously available in Canada but is no longer accessible following the company's decision to withdraw the therapy after the PHOENIX trial results.

Some respondents mentioned symptom management medication, including Baclofen, mexiletine, gabapentin and pregabalin. Supplements and alternative treatments such as Vitamin B12, probiotics, Omega-3, ashwagandha and magnesium were also mentioned.

Others reported participating in clinical trials for investigational ALS treatments including studies for ibudilast and other experimental treatments.

5. Improved Outcomes

Patients and caregiver/family members respondents expressed strong preferences for treatment improvements that go beyond what is currently achieved with currently approved therapies – Rilutek and Radicava. When asked what they would like to see in a new treatment for ALS that is not currently achieved, most patients and caregivers/family members identified the following as improvements they would like to see in future treatments:

- Symptom reversal
- Maintaining function and independence
- Slowing disease progression
- Increased survival

Patient and caregiver/family member respondents expressed a strong desire for treatments that extend survival while maintaining quality of life – with a preference for therapies that not only slow ALS but also restore loss of function whenever possible. Most importantly, respondents emphasized the desire for more time with their loved ones in a way that allows them to continue actively participating in life.

Below are a few examples of answers from **patients** when asked to describe how their quality of life/daily life might be different if those desired improvements were achieved with a new treatment:

"I would feel more like my old self and do all the thing I used to do. I would feel whole again."

"You don't know what you've got til it's gone. I badly would like to walk normally again, work around the

"If there was symptom reversal, I would be able to be an active person again and enjoy being outdoors and having a better social life and home life."

garden, eat without fear of choking, sleep without a mask and on and on the list goes."	*"Je pourrais continuer de profiter de la vie avec l'amour de ma vie."*
"My kids would see me as "dad" not the guy in the wheelchair who can't even hug or talk to them."	*"I would regain my independence, be able to look after myself, be less of a burden, be able to look forward with hope."*

Below are a few examples of answers from **caregivers/family members** when asked to describe how their quality of life/daily life might be or might have been different if those desired improvements were achieved with a new treatment:

"Reversal of symptoms is the dream. I would give anything, other than my children, to still have my husband with me. It's too hard to even think about it, knowing that it can't be."	*"It would lift a huge emotional and physical burden from caregivers. I get choked up thinking about all the positive impacts these improvements could provide."*
"I would have had more time, and more quality time, with my mom. She spent so much time managing her symptoms, that she needed assistance with much in her life. She would have loved to have more time with her family -- particularly her grandson, in her last year."	*"We both would feel more in control of our lives. Instead of us taking control of the illness, it took control over our lives and eventually took my husband away."*
"I would give anything to have had even one of those improvements be a possibility."	*"Ce serait le jour et la nuit. Un traitement qui inverserait les symptômes permettrait de guérir les patients finalement, de sauver les familles d'une grande détresse et de libérer les aidants."*

When considering trade-offs in choosing a therapy, **patient** and **caregivers/family member** respondents are willing to accept some side effects if the treatment offers clear benefits in maintaining function, slowing progression, or improving survival. However, respondents noted that treatment's accessibility and affordability remain key considerations.

6. Experience With Drug Under Review

The drug under review is specifically indicated for people living with ALS who have a pathogenic variant (also known as a mutation) in the superoxide dismutase 1 (SOD1) gene. SOD1 variant accounts for approximately 20% of familial ALS cases and about 2% of all ALS cases overall.

12 survey respondents indicated having accessed tofersen. All participants accessed the therapy through the clinical trial. To better understand the impact of this therapy, 4 individuals with direct experience were interviewed. Their specific treatment experience is summarized in the chart below, and their demographic can be found in Section 2:

Name	Patient/Caregiver	Diagnosis Date	Drug Access Method	Period on Tofersen
PT	Patient	February 2016	Clinical Trial	2016 – Present
TB	Patient	April 2018	Clinical Trial	2019 - Present
TA	Patient	July 2020	Clinical Trial	2020 - Present
KS	Bereaved Caregiver	June 2019	Clinical Trial	2019 – 2023

Patient and **caregiver/family members** reported some side effects, though most were manageable. The most cited side effect was migraine, which some experienced in varying frequency. 2 individuals reported more severe side effects, including idiopathic intracranial hypertension and papilledema. However, these were monitored and managed effectively with prescription medication. When asked about the trade-offs between side effects and potential benefits of tofersen, respondents overwhelmingly expressed that the benefits far outweighed the challenges. 2 **patients** who experienced migraines and papilledema spoke directly about these challenges:

"The side effects are 100% worth the benefit. Everything is pretty minor. Even if I lost my eyesight because of papilledema, I can still be alive. I'd rather be alive."

"There is no side effect serious enough that would make me decide not to be on tofersen because then the decision is that I'm going to be stuck in a wheelchair, I'm going to progress, and I'm not going to be here at all. So, I don't think a migraine for a couple of days is a big deal."

Through interviews and survey responses, 3 treatment outcomes from tofersen emerged as the most meaningful to patients and caregivers. The following outcomes not only shaped their experiences with the therapy but also reflected the values they see as most important in any ALS therapy:

1) Delaying Progression
2) Having more time with loved ones
3) Improving quality of life

Many described their disease progression as slowing or halting, allowing them to preserve function far longer than expected. Others emphasized how stability meant more time with their families while still being able to communicate, engage and remain independent. This also contributed to increased quality of life and improvements in certain functions, such as breathing and mobility. These values are deeply intertwined.

Delayed progression means more time, more time means more opportunities to be present with loved ones, and maintaining function preserves independence and quality of life.

Below are the experiences of patients and caregivers that illustrate the meaningful impact of tofersen in these key areas:

1) Delaying Progression

When **PT** got diagnosed with ALS at the age of 34, she was told to go home and get her affairs in order. Having seen 26 members of her family die from ALS, she did not expect to be alive in 2025. She was experiencing muscle wasting, issues with mobility in her ankles and significant cramping that would last 8 hours straight. She started accessing tofersen 8 months after her diagnosis and remained on it ever since. She experienced significant changes in her symptoms, where her speech improved, she started feeling stronger, had less muscle cramping and fasciculations. She could stand on her toes and hold her heels up in the air. In 2023, **PT** developed pneumonia – a condition that is typically detrimental for people living with ALS due to its impact on respiratory function. She expected to see a decline in her breathing abilities. However, when she underwent a breathing test to assess any decline, the results showed that her respiratory function had not declined at all. She says, *"It has been like a miracle for me and my whole family to see finally how well I am doing, improving and maintaining."*

Prior to accessing tofersen in 2019, **TB** participated in multiple clinical trials and did not experience any significant benefit, and his progression continued. At the time of his diagnosis, symptoms were initially confined to his right leg, but the disease progressed quickly to his leg before he started accessing tofersen. However, since accessing tofersen in 2019, **TB** saw his progression stabilize completely and has not experienced any further progression of ALS. He says, *"I think it is like night and day what tofersen is doing to me rather than when I was on trial for Pimozide or when I was prescribed Radicava or Albrioza."*

TA accessed tofersen just days after his ALS diagnosis in 2020 at the age of 23. At that time, his symptoms were relatively mild, including cramping and fasciculations. He also struggled with foot-related issues and needed a back brace for support. Through his participation in the clinical trial, he not only avoided progression but saw improvements. His lung function has increased over time, and he no longer uses a back brace or experiences foot-related issues.

KS shared the experience of her husband, who accessed tofersen shortly after his ALS diagnosis in 2019. At the time of his diagnosis, he had already experienced some progression, primarily in his dominant right hand, with noticeable atrophy in his hand and forearm. Her husband had the SOD1 A4V/A5V variant, which is a very aggressive form of familial ALS. Given his prognosis, they expected a rapid decline, but his experience with the treatment was dramatically different. Once he started tofersen, his disease progression slowed significantly in his arm and hand and stopped everywhere else. His neurologist had initially prepared them for the likelihood that he would lose shoulder function and struggle to lift his arm. However, for 4.5 years, none of these expected losses occurred. His shoulder function remained intact, and outside of the original weakness in his right hand and forearm, he showed no further progression for the first nine months of the treatment. Unfortunately, as time went on, new symptoms did begin to emerge, and he developed a droop in his smile and some difficulty with swallowing. Yet, his strength remained. Though he ultimately

passed away, he lived far beyond what was expected for his form of familial ALS, where his 2 uncles and dad all died within 9 months of diagnosis. **KS** says, "*He wasn't so progressed to the point where ALS dominated every moment of our existence in a sense. For my kids, he was Dad. Dad couldn't smile or eventually couldn't make jokes. But he was there, and he was very, very present".*

2) More Time with Loved Ones

KS says, "*The greatest gift tofersen gave my family was time. My husband was diagnosed with ALS when our daughter was just 4 years old. Tofersen allowed him to live 4.5 more years, which made all the difference for our daughter. Instead of only knowing her father through pictures and videos, she was able to have real, concrete memories of him, memories of time spent together, of moments they shared, and of who he was as a person. It wasn't the magic bullet that we all hoped it would be, but short of that, it gave us more time to make memories".*

When **TB** received his ALS diagnosis, he was told to go home and prepare to die. His biggest concern was his children – how much time he would have left with them and whether he would get to see them grow up. But instead of watching this time run out, tofersen allowed him to spend more years with his family, making new memories and being present in his children's lives, who are now 20 and 17. He has been able to witness their milestones, something that once seemed impossible.

3) Improving Quality of Life

Being diagnosed with ALS at just 23 years old was devastating for **TA**. But despite that, he still gets to do everything he loves – things most people his age take for granted, like playing volleyball, boating and driving. He continues to work 16-hour days on a farm. TB says, *"If I didn't have access to tofersen, I wouldn't be alive right now for all I know, or maybe in a wheelchair. I would have ended up on disability, not be able to make a living or still be living on my own. I'm still able to pay taxes and be a functioning member of society and that means a lot to me."*

PT and **TB** spoke about how they are still able to do things they love, giving them a sense of normalcy and fulfillment. Whether it's golfing, running, hiking, playing hockey or simply spending time with their kids, they can still do the things that bring them joy. They also both talked about the importance of being able to continue to work and contribute to society, maintaining their independence and sense of purpose.

For **PT**, this ability to remain present in her children's lives carries even more profound meaning. Having grown up with a parent who had ALS, she knows firsthand what it is like to take on the role of a caregiver at a young age. She reflects on that experience with gratitude, recognizing that she is still here, still able to be present for her children in a way that ensures they can have a childhood.

KS and her family were able to make memories together, not consumed by all the things they were losing. Her husband remained engaged and active throughout this diagnosis, and he was still able to play hockey with their kids, run around outside with them and continue working full-time. KS says *"Short of being the magic bullet, tofersen is keeping people alive and giving them a better quality of life. And isn't that the purpose of any medication?"*

Public Reimbursement

All **patient** and **caregiver/family members** respondents who have direct experience with tofersen agreed that the drug should be publicly funded and accessible in Canada. Given the rapid progression of ALS, timely access to treatment is critical. Many people with familial ALS have watched their family members navigate the disease with no treatment options and they first understand how devastating the lack of available treatments can be. The idea that a treatment now exists yet may remain out of reach due to cost or reimbursement criteria is deeply concerning.

"The obvious and undisputable right thing to do is to give people access to this medication through, coverage by the government because it not only saved my husband's life for all those years, but it also made him a lot less expensive to the healthcare system." **– KS**

"Tofersen getting publicly funded is a matter of life or death for me and you can't put a price on life." **- TB**

"If the drug was not reimbursed, I would never ever be able to get another treatment because of how cost prohibitive it is and that means I'm going to get die a lot quicker." **- TA**

"Public reimbursement means we can keep contributing to the society and not just be a burden to the system." **- PT**

7. Companion Diagnostic Test

Genetic testing confirming a pathogenic variant in the SOD1 gene is required for this therapy. Among survey respondents, 56% of **patients** reported that they had accessed genetic testing for the most common ALS-related genes, including SOD1.

Overall, **patients** and **caregivers/family members** shared that the process of getting genetic testing was seamless. Both those interviewed and survey respondents noted that the process was efficient with results provided in a timely manner. Testing was covered for most participants, meaning cost was not a barrier to access. Only 2 participants reported having to pay for genetic testing, which was done out of the country.

While the logistical aspects (cost of testing, accessing the facility, etc.) of genetic testing were generally smooth, the emotional and psychological impact of receiving a test result was significant. Many participants described the stress and anxiety that came with waiting for results. For participants who have children, the results carried even greater weight. Some spoke about the emotional difficulty of knowing they may have passed the variant to their children, while others grappled with the uncertainty of whether their other relatives would eventually face the same diagnosis. Another layer of complexity arose in families where not all members had undergone genetic testing. Some participants described the challenge of being the only one in their family who tested, leaving them with difficult conversations about whether their siblings, children or other family members should also pursue testing.

At the same time, many participants also shared that while waiting for results was difficult, having a definitive answer brought a sense of clarity and control. For some, it validated what they already suspected, while for others, it meant they could start making informed decisions about their future, including discussing treatment options ahead of time. Instead of living in uncertainty, a confirmed diagnosis allowed them to plan.

"When my dad was diagnosed with SOD1 ALS, there was nothing. No treatment, no options, just the knowledge that we had to watch it happen. Now I can get genetic testing and knowing there is an option like tofersen. I can plan, take action and figure out what's next"	*"For me, getting genetic testing is not about just confirming but it's also about having a path forward. I can make informed decisions and actually do something about it and access a treatment that didn't exist for my grandpa, uncles and cousins."*

Overall, while access to genetic testing itself was straightforward, coping with the results and their implications was much more complex, with many expressing the need for ongoing emotional support, clear information and resources to help navigate these difficult realities for themselves and their families.

We acknowledge that discrepancies exist in access to genetic testing across Canada. ALS Canada and the Canadian ALS Research Network (CALS), network of clinicians across Canada specializing in ALS research and clinical care, are committed to working together to improve access to genetic testing for ALS, ensuring every person with a SOD1 variant receives the necessary care and treatment. As part of these efforts, ALS Canada launched a pilot project to introduce Canada's first national genetic counsellor dedicated to supporting people affected by ALS. This initiative aims to expand access to genetic counselling services through virtual care, helping individuals understand their genetic risk, navigate testing and explore potential treatment options.

8. Anything Else?

When asked if there was anything else respondents wanted to share about their experience with ALS or tofersen that they feel would be important for CDA reviewers to know, **patients** and **caregiver/family members** said:

- *"My life is basically in your hands with this decision. This is my reality. The choice you make will determine whether I have a chance to keep living and spending time with the people I love."*
- *"My dad lost his mother, and 2/3 siblings from this disease. He never got the testing because he didn't have any ability to change the outcome. Drugs were out there but didn't have the necessary improvements on the disease to make him get the testing. To read the stories of tofersen approval elsewhere has given us an amount of hope that is unquantifiable. The potential for there to be something, should that dreadful day ever arrive, is quite literally life changing. We've already lost so much so young, please give us the chance our parents never had in being able to fight this fight."*

- *"I have the polymorphism/mutation of SOD1 but am currently symptom free. My son has the mutation but is currently symptom free. Availability of treatment is very important as this disease has had a great impact not just for the loved one, I cared for but for our entire family."*
- *"Patients and families just want some hope and more quality time together. This disease rips everything away from you, other than your relationships with those you love and who love you and those relationships. There is no luxury of time as a person with ALS. Potential treatments need to be provided as quickly as possible."*
- *"The financial implications of ALS are terrible and if this medication can keep people functioning it is well worth the cost. I have seen people on Tofersen thrive! It is amazing!"*
- *"Premier médicament ayant un effet notoire pour la SLA. Devrait être accessible rapidement étant donné la vitesse à laquelle progresse la SLA. Peut faire une réelle différence pour les gens qui ont la forme génétique SOD1."*
- *"Living with this disease, knowing there is no cure, is an incredibly hopeless and isolating experience. For my mom, it was a slow and heartbreaking withering away, and it's something I wouldn't wish on anyone."*
- *"As my wife died from ALS and had the SOD-1 mutation, I am beyond thrilled that this drug may help my children and grandchildren if they inherit this disease."*
- *"It has been shown that Tofersen greatly slow the progression of people with the SOD1 mutation. There should be no question or reason why this drug should not be available in Canada."*
- *"L'accès au Tofersen a changé ma perception de la maladie et m'a redonné espoir. Avec l'annonce du diagnostic, je préparais ma mort. Maintenant, je fais des projets et j'ose croire que je verrai ma fille grandir. C'était ce qui était le plus douloureux pour moi. Je vis cependant avec la crainte que ma fille hérite de la maladie. Je vis également avec la crainte de ne plus avoir accès au Tofersen. Parce que sans le Tofersen, je meurs. Avec le Tofersen, j'ai l'espoir de vivre plus longtemps et avec une meilleure qualité de vie."*
- *"Tofersen is a hard-fought miracle for families like mine and it's doing exactly what everybody in best case scenarios hoped it would do. It's time for this disease to stop just decimating families the way it has ours."*

Additionally, a **caregiver/family member** respondent, who indicated that they were the primary study coordinator for the therapy's clinical development program, from 2015 until July 2022, from Phase 1, through to completion of VALOR, and oversight of the ongoing open-label extension at one of the Canadian trial sites, shared the following:

- *"Through my involvement on the tofersen clinical trial programs, I have first-hand experience in observing the undeniable, clinically meaningful benefit people living with SOD1-ALS have experienced when treated with tofersen. Tofersen is the first time (and to this day still the only time) in*

my almost 15-year career working in ALS, where my patients were not dying of ALS, but rather living with ALS. Clinically, my first-hand experience mirrors what the extended combined VALOR + OLE data is telling us: that tofersen has a better effect when initiated early, and there can be both stabilization and improvements across ALSFRS-R, breathing capacity, and quantitative measures of muscle strength. But what does this mean practically, in the real world? Study participants I cared for have gone back to work full-time, coming off of disability; they now ride bikes with their children; walkers are getting dusty in closets, no longer needed; parents are walking their children down the aisle at their wedding. These are all examples of living life, because of tofersen, that patients have shared with me, or that I have seen first-hand. Tofersen is the first truly transformational, disease modifying treatment for ALS, one which undeniably should be offered to, and covered for, every individual with SOD1-ALS."