February 24, 2025

Senator Pamela Beidle
Chair, Finance Committee
3 East Miller Senate Office Building
11 Bladen Street
Annapolis, MD 21401

The Honorable Chair Beidle, Vice Chair Hayes, and Members of the Finance Committee

RE: SB 757 – Genetic Testing Protection Act

Position: SUPPORT

My name is Kuldip Dave, Ph.D., and I am Senior Vice President for Research at the ALS Association. I am writing today in support of SB 757: Genetic Testing – Prohibition on Disability, Life, and Long-Term Care Insurance (Genetic Testing Protection Act), but most importantly, in support of the more than 200 families with ALS we currently serve in the state of Maryland as well as the tens of thousands more affected by the disease across the country.

Probably one of the greatest scientific achievements of our time has been mapping the human genome, a project led in Maryland. Now, the state and this Committee have the opportunity to lead the way in advancing medicine yet again through the Genetic Testing Protection Act, which if passed, will provide the safeguards needed to realize the full potential of the genetic discoveries made over the last two decades.

Genetic Basis of ALS and New Opportunities for Treatment

In 2019, researchers from Harvard University and the University of Queensland in Australia estimated that 40% of diseases have a genetic component.[1] This includes ALS. Amyotrophic lateral sclerosis, or ALS, is a devastating neurodegenerative disease that affects nerve cells in the brain and spinal cord. Over the course of the disease, people progressively lose the ability to move, to speak, and eventually, to breathe. Few treatment options exist, so the disease is always fatal, usually within five years of diagnosis.

We estimate that roughly 10–15% of ALS is driven by gene mutations that are either passed down in families or occur randomly during development. So far, researchers have identified more than 40 genes linked to ALS. One of these genes is *SOD1*. Mutations in the *SOD1* gene are the second-most common cause of familial, or inherited forms, of ALS. The most prevalent *SOD1* gene mutations in North America are associated with younger age of onset and shorter survival.

[1] Lakhani, C.M. et al. Repurposing large health insurance claims data to estimate genetic and environmental contributions in 560 phenotypes, *Nature Genetics* (2019).

In 2023, families devastated by *SOD1*-ALS were given new hope when the Food and Drug Administration approved the first genetically targeted ALS treatment. Tofersen, now known as Qalsody®, was developed to specifically target the RNA produced from mutated *SOD1* genes to stop the production of toxic SOD1 proteins that cause ALS.

In the phase 3 VALOR trial, Qalsody was shown to reduce levels of mutated SOD1 proteins in cerebral spinal fluid by 35% as early as eight weeks after participants began receiving the therapy.[2] By 12–16 weeks, Qalsody reduced bloodstream levels of neurofilament light chain (NfL), a biomarker of neuron damage and neurodegeneration, by 50%.

More recent peer-reviewed real-world data have confirmed that treatment with Qalsody decreases NfL levels and has disease-modifying activity.[3,4] Evidence is also emerging that treatment with Qalsody not only has the potential to stabilize the disease but also to restore lost function—something many in the neurodegenerative field never considered possible.

A study published last month in *The Annals of Clinical and Translational Neurology* reported on seven people with *SOD1*-ALS treated with Qalsody at Washington University in St. Louis from November 2021 to February 2024.[5] All participants showed either stabilization or slight improvement in function, as measured by the ALS Functional Rating Scale-Revised (ALSFRS-R).

The researchers estimated that the participants progressed an estimated 52% slower than expected following treatment with Qalsody. In addition, muscle strength improved for five of the study participants. Participants also gained, on average, a little more than five points on the functional independence measure motor score, a "notable improvement in functional independence," according to the researchers.

This study builds on growing evidence from Europe, where long-term studies in Italy[6] and Germany[7] have also shown stabilization and improvement among people with *SOD1*-ALS treated with Qalsody.

Until now, the prevailing hypothesis in the neurodegenerative field has been that disease-modifying therapies would either slow down or stop further progression. Qalsody, however, has shown that improvement in function (recovery) is possible. The fact that these data were

---

[2] Miller, T.M. et al., Trial of Antisense Oligonucleotide Tofersen for SOD1 ALS, *N Engl J Med* (2022).
[3] Meyer, T. et al., Neurofilament light-chain response during therapy with antisense oligonucleotide tofersen in SOD1-related ALS: Treatment experience in clinical practice, *Muscle Nerve* (2023).
[4] Wiesenfarth, M. et al. Effects of tofersen treatment in patients with SOD1-ALS in a "real-world" setting – a 12-month multicenter cohort study from the German early access program, *EClinicalMedicine* (2024).
[5] Smith, S.A. et al., Tofersen treatment leads to sustained stabilization of disease in SOD1 ALS in a "real-world" setting, *Ann Clin Transl Neurol* (2025).
[6] Sabatelli, M. et al., Long-term treatment of SOD1 ALS with tofersen: a multicentre experience in 17 patients, *J Neurol* (2024).
[7] Meyer, T. et al. Clinical and patient-reported outcomes and neurofilament response during tofersen treatment in SOD1-related ALS—A multicenter observational study over 18 months, *Muscle Nerve* (2024).

collected during standard of care treatment in real-world settings should further validate that the functional recovery is not just a characteristic of a tightly controlled double-blind trial but is real and significant.

Increasing Importance of Genetic Testing for ALS

Qalsody is the only ALS treatment, to date, to demonstrate results like these. However, because of its targeted nature, only people with a *SOD1* mutation can benefit, necessitating more routine integration of genetic testing into ALS clinical management. According to evidence-based consensus guidelines published in 2023 in the *Annals of Clinical and Translational Neurology*, everyone living with ALS should be offered genetic counseling and testing.[8]

The role of genetic testing and counseling will only become more vital moving forward as at least 10 other therapies targeting ALS-linked genes are being tested in clinical trials, and almost a dozen more are being developed preclinically.

Genetic testing results not only have implications for people living with ALS but also for their family members. Having a first-degree relative test positive for an ALS-linked mutation significantly increases a family member's risk of developing the disease. It also potentially paves the way for prevention.

In a study being conducted at Johns Hopkins, Dr. Nicholas Maragakis and colleagues are trying to see if Qalsody can delay the onset of ALS—or perhaps even prevent the disease from developing all together—in people with a *SOD1* mutation who have no ALS symptoms. Not everyone with a *SOD1* mutation will develop ALS in their lifetime, but what if we could stop the disease before it starts in those individuals who would eventually be affected—like using cholesterol levels in blood and treatment with cholesterol-reducing drugs to prevent heart disease? Imagine the economic, societal, and personal costs that would be saved.

Threat of Genetic Discrimination Holds Back Progress—And Harms Marylanders

Despite the tremendous benefits Qalsody and other genetically targeted drugs in development could provide to individuals and the entire ALS community, few people with ALS and their family members know their genetic status. Fear of their genetic information being used against them is one reason why they don't get tested.

In the fall of 2024, we surveyed more than 775 people with ALS and their proxies about genetic testing and counseling through our ALS Focus™ Survey Program. Twenty-two percent (22%) of participants had not received genetic testing for ALS, and another 5% didn't know if they had been tested. Within this group, two out of three said they were unlikely to get tested in the future. When asked why, 20% said they felt they would lose their long-term care, disability, or life insurance if the results were positive. Over a quarter (27%) thought their families would lose

[8] Roggenbuck, J. et al. Evidence-based consensus guidelines for ALS genetic testing and counseling, *Ann Clin Transl Neurol* (2023).

those same benefits if the results were positive. And another 12% preferred not to even answer these questions, which also raises concerns about fear of discrimination.

Thus, the threat of genetic discrimination creates a serious dilemma for Marylanders—risk their physical health because they don't know their genetic status or risk their financial health because they do.

The Genetic Testing Protection Act will help allay this fear by putting protections in place for accessing life and disability insurance by people who have undergone genetic testing, requested genetic testing, or received genetic test results. Such protections will not only benefit those living in this state, but through the amazing science being done in Maryland, bring life-changing new genetic therapies to everyone who needs them faster.

For all these reasons, I respectfully request your support for the Genetic Testing Protection Act. Thank you to Senator Washington for introducing this legislation and to the members of the Finance Committee for your time and consideration.

Sincerely,

Kuldip Dave, Ph.D.
Senior Vice President, Research
The ALS Association
Kuldip.Dave@als.org