Testimony of Khrystal K. Davis, JD
Rare Disease Parent, Caregiver, & Patient Advocate
Founding President, Texas Rare Alliance

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Legislative Proposals to Support Patients with Rare Diseases

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Chairwoman McMorris Rodgers, Chairman Guthrie, Ranking Member Pallone, Ranking Member Eshoo, and distinguished members of the Health Subcommittee of the House Committee on Energy and Commerce. I thank you for the opportunity to testify before you today. I am a widow—who recently lost my husband of 14 years to glioblastoma, a rare brain cancer—I am a rare disease parent, and I am a patient advocate. Today, I represent the 1 in 10 Americans affected by more than 10,000 rare diseases. I am the founding President of Texas Rare Alliance, a non-profit education and advocacy organization working to improve access and health outcomes for nearly 3 million Texans living with a rare disease—a staggering and devastating statistic. More Americans currently live with a rare disease than have HIV, heart disease, and stroke combined. Only 5 percent of rare conditions have an FDA-approved treatment. It is crucial we foster research and development of additional rare disease treatments and that rare disease patients can access disease-modifying treatments upon approval.

As a patient advocate, I am committed to helping the rare disease community and its patients—it's what I do day in and day out. My mission and life's work are guided by a personal tenet to

leave the rare disease community in a better place than I found it. I frequently collaborate with other rare disease community stakeholders to help foster an environment that increases the research and development of disease-modifying treatments for our patient communities. This also includes helping secure predictive and reliable pathways for patients to access rare disease treatments. I, along with other patient advocates, need your help in advancing reasonable and meaningful policies that will foster drug development, FDA approval, and access to treatments that help improve and prolong patient lives.

I. Hunter's Diagnostic Odyssey

On July 31, 2011, our newborn son, Hunter, was taken to the NICU at birth and intubated for respiratory failure. The doctors believed his lungs were underdeveloped, but his carbon dioxide levels continued to rise, and he faced organ failure. The doctors believed something else was wrong but didn't know what it was.

Fortunately, Hunter was successfully extubated and came home after 11 days in the NICU. We thought everything would be okay, but we were mistaken.

Hunter lost nearly all movement at two weeks of age. We didn't know what was happening. *At one point, my husband asked me if I had shaken Hunter.* I could never hurt our baby, but he was hurting. The coming days and weeks led to more heartache and questions but no answers.

On September 30, 2011, our world changed forever. Doctors diagnosed our eight-week-old baby with Spinal Muscular Atrophy (SMA). SMA presents like ALS in babies, robbing their ability to move, swallow, and ultimately breathe, making it the number one genetic cause of death for babies.

Doctors told us there was no treatment and no hope. They instructed us to take Hunter home and enjoy what time we had left with him, which they expected to be about three months.

II. Hunter's Pathway to Treatment

We could not afford to follow the doctors' advice who diagnosed Hunter. The stakes were just too high. We had to try to save our sweet baby.

Desperation drove our relentless pursuit of a treatment.

A researcher answered our plea and agreed to help. He provided us with the chemistry of a compound. We manufactured that compound in the US and took it to Mexico for an N-of-1 trial.

And so Hunter's reverse Dallas Buyer's Club adventure began.

He received his first lifesaving treatment just eight weeks after his diagnosis-the day before Thanksgiving- making him the first SMA patient to receive a lifesaving treatment.

Hunter continued his treatments.

That left me unable to reconcile how quickly we secured a lifesaving treatment for Hunter with how long it takes to bring treatments to desperate patients with other life-threatening rare conditions. I knew by experience we could do much better, and I began advocating to improve access to diagnosis and treatments.

My goal is to help secure presymptomatic diagnosis and treatments for all rare disease patients.

A. Hunter's Experience Compared to Other US SMA Patients

While Hunter continued his treatments in Mexico, SMA patients in the US went without access to a disease-modifying treatment, with the exception of patients receiving the active treatment in the placebo-controlled clinical trials.

B. My Mission to Advocate for Access for All SMA Patients

In March of 2016, I was asked to attend an FDA meeting as a core member of the Families for Acceleration of SMA Treatments (FAST) on May 4, 2016. At the May 4, 2016, meeting with the 23 FDA executives, employees, FAST core members, and SMA parents, we advocated for early access to the first SMA treatment on the grounds that real-world evidence established the primary endpoint had been met. Accordingly, we asked the FDA to:

- Stop the Nusinersen placebo trials,

- Provide a means of early access to the Nusinersen for the weakest patients,
- Approve Nusinersen early, and
- Approve the Nusinersen for ***all*** SMA patients.

The FDA heard our pleas and responded quickly:

- The FDA requested "an interim analysis as a way to evaluate the study results as early as possible…",[1]
- On August 1, 2016, Biogen and Ionis announced the Endear interim analysis met positive results,[2]
- Given the positive interim analysis, Endear and Embrace trial participants could transition to the active treatment.[3]
- Biogen listed an EAP for Nusinerson on clinicaltrials.gov on August 12, 2016,[4]
- Biogen completed its NDA for Nusinersen on September 26, 2016.[5]
- The FDA approved Spinraza (nusinersen), the first treatment for SMA, on December 23, 2016, for pediatric and adult SMA patients,[6] making it the fastest FDA approval ever.

Like many other SMA infants and children, Hunter participated in the Spinraza Expanded Access Program. He received his first Spinraza treatment on November 21, 2016, just two days shy of the fifth anniversary of his first treatment in Mexico.

III. Curtis's Rare Diagnosis and Battle

Hunter's SMA diagnosis would not be the only devastating rare diagnosis our family would face. On June 6, 2022, my husband, Curtis Davis, was diagnosed with glioblastoma, a rare brain cancer so deadly that it lacks remission, only a period of time for patients (following tumor resection, chemotherapy, and radiation) where they await the dreaded news of recurrence. We understood that Curtis's glioblastoma diagnosis was a death sentence. Yet, we still held out hope that we could secure another medical miracle, as we had with Hunter over a decade before. *Sadly, this time, science and luck would not be on our side.* A large part of this stems from the fact that glioblastoma falls squarely within the ninety-five percent of rare conditions lacking a disease-modifying treatment.

In the year that followed his diagnosis, Curtis fought fiercely and courageously. He researched new trials and treatments. He kept his mind busy working as much as he could. He kept fit by walking three to six miles daily while receiving his chemotherapy and radiation, frequently passing and greeting his doctors on the sky bridge at MD Anderson Cancer Center in Houston, Texas. He had the spirit and determination to beat the disease. Had it been anything other than one of the most virulent cancers, he may well have.

Despite having the poorest biomarkers, his tumor invading his motor strip, and being on high-dose steroids, Curtis was in the twenty-five percent of glioblastoma patients who survived more than one year. This is because Curtis had access to innovative treatments that slowed the progression of his glioblastoma for some time. These innovative treatments allowed us to spend more time and make more cherished memories with Curtis. I am grateful to all parties who played a role in the research and development and in securing access to the treatments for Curtis.

Curtis died peacefully in our home on June 14, 2023, at the age of 54. I was by his side when he died, and I watched him take his final breath. Curtis's life ended far too soon, and he had numerous other adventures, trips, and business endeavors planned, and he welcomed all the unforeseen adventures he might encounter. What Curtis looked forward to most was knowing and loving his future grandchildren.

Curtis was my husband and partner in adventure and an amazing father to our five children. He was an exceptional partner in all aspects of our relationship, which included his partnership in being a caregiver for Hunter. With the loss of Curtis, I am now the sole parent left to care for and meet Hunter’s needs. The prospect of my becoming Hunter’s sole caregiver hit Curtis and me particularly hard and weighed heavily on us during the time we spent together following his diagnosis.

Although glioblastoma is a rare cancer, it has claimed well-respected and loved persons by those here in our nation’s capital, including Senator Ted Kennedy, Beau Biden, and Senator John McCain.

IV. The Unmet Need for Rare Disease Treatments

A. The Rare Disease Landscape in the United States

The facts are not great. 1 in 10 Americans, over 32 million, has a rare disease.[7] Half of rare disease patients are children (16 million American children).[8] Thirty-five percent of the deaths in the first year of life are caused by rare diseases.[9] Thirty percent of children with a rare disease will not survive to their fifth birthday.[10] There are seven thousand rare diseases.[11]

Ninety-five percent of all rare diseases do not have an FDA-approved disease-modifying treatment.[12] It will take thousands of years to realize treatments for all rare diseases if FDA-approved therapies continue at the current rate.[13]

I am intimately aware of what it means to lack an approved rare disease treatment for the rare disease community. It is devastating. We need more conditions like SMA to cross over from the ninety-five percent of rare diseases that lack an approved SMA treatment to the five percent with an FDA-approved disease-modifying treatment. To achieve this, we must encourage continued research and development of breakthrough therapeutics.

V. Understanding the True Economic Burden of Rare Diseases

The National Economic Burden of Rare Disease Study in the US published by the EveryLife Foundation for Rare Disease covered 379 rare diseases affecting 15.5 million people in the U.S. for 2019. The study estimated the overall rare disease economic burden to exceed $966 billion.[14] This included "$418 billion in direct medical cost and $548 billion in indirect and non-medical costs absorbed directly by families living with rare diseases."[15]

Accordingly, in-direct and non-medical costs (costs absorbed directly by families) in 2019 accounted for nearly 60% of the overall cost.[16] **Prescription medications and outpatient prescription administration were only about 10% of the overall economic burden and less than what was spent on inpatient care.[17] We can't expect to address affordability if we are focusing on a small percentage of the problem.**

VI. Protecting the Pathway to Rare Disease Research

Congress recognized the unmet need for rare disease treatments by passing the Orphan Drug Act (ODA) in 1983.[18] The ODA incentivizes the development of treatments for rare diseases, many of which are life-threatening, and most lack an approved treatment.[19] Congress

reaffirmed its commitment to the rare disease community in 2016 by passing the 21st Century Cures Act,[20] a bipartisan effort President Obama signed into law. The Act included many provisions to improve the discovery, development, and delivery of orphan therapies for rare disease patients, together with substantial NIH funding.[21]

VII. The Initial Funding for Rare Disease Research and Development Largely Comes from Patient Communities

Rare disease patient communities and organizations spend considerable time and effort fundraising to provide initial funding for research and development for rare conditions lacking disease-modifying treatments. This early funding is often a critical first step to securing additional funding from the NIH, Venture Capital, and the pharmaceutical and biopharmaceutical industry. These efforts are paying off. Cystic Fibrosis, MPS I, Pompe Disease, Duchenne Muscular Dystrophy, SMA, and Sickle Cell Disease are examples of rare conditions with innovative disease-modifying treatments where the patient communities and organizations provided early funding to advance research and development to help move the treatments from bench to bedside.

It is common for individuals to leave their careers to start an organization or join the efforts of existing organizations to raise funding to advance research and help secure a treatment following a rare disease diagnosis lacking a disease-modifying treatment. Luke Rosen, a respected and formidable rare disease patient advocate known for his relentless passion, walked away from his

career as a successful actor when his daughter, Susannah, was diagnosed with KIF1A. Luke formed KIF1A.org and realized the organization needed $250,000 to begin advancing research.[22]

Casey McPherson of Austin, TX had to leave his career as a successful musician following his daughter's diagnosis with a rare disease.

> "After my daughter Rose was diagnosed with a rare disease, I was left to raise millions of dollars and develop a genetic treatment, on my own, like many other parents. I had to quit my career. She, like many other children, requires round the clock care. America is no longer my land of opportunity, but a prison of regulations for my child. Rose lost her ability to talk, struggles with walking and her future is uncertain. Science isn't the problem, our regulations have turned the healthcare industry away from rare disease, making it near impossible for us to diagnose, develop, and commercialize treatments for thousands of these rare diseases, affecting millions of suffering and dying children, like my Rose."[23]

Amber Freed left her career as a successful equity analyst when her son Maxwell was diagnosed with SLC61A. Amber formed SLC61A Connect to help secure a disease-modifying treatment for Maxwell and other SLC61A patients. She understands that we have reached a point in time where precision diagnoses are possible and the treatments are within grasp but not reach. "Treatments are led by brave parents who in solidarity agreed that no option is not an option for their children."[24] Amber shared with me on her fundraising efforts since forming SLC61A,

> "I have philanthropically raised $5,000,000 and it has been used to incubate good ideas with the hope of de-risking programs enough they can be handed off to

pharma or receive NIH funding. Every cog in the wheel is an essential component to drug development – none of us can do it alone."[25]

VIII. Repurposing Rare Disease Therapeutics – Pitting Patients Against Shareholders

Scientific advancement in genomics, biomarkers, and high throughput screening (HTS) helps identify treatment pathways for potential rare disease treatments, including repurposing existing rare disease treatments. It's much easier to leverage existing rare disease treatments for additional rare indications than to develop new rare disease treatments. When existing rare disease treatments are efficacious for another rare condition, it saves time and money affording the opportunity to improve and save the lives of rare disease patients sooner. We are ever mindful that time is not on our side in the rare disease community, and we need the ability to utilize every opportunity to secure treatments for rare disease patients as quickly as we can.

The IRA significantly threatens repurposing existing rare disease treatments to additional rare conditions by making orphan drugs designated for more than one indication eligible for price negotiation. This means that in situations where existing rare disease treatments could be extended to treat other rare conditions, pharmaceutical and biopharmaceutical companies must consider the potential impact of price negotiation on revenue for its orphan drug before including an additional indication for a subsequent rare condition.

This scenario exemplifies how the IRA's failure to exempt exclusively orphan drugs from price negotiations could negatively impact access to existing rare disease treatments that could save

and improve the lives of rare disease patients. The ORPHAN Cures Act would eliminate the exposure of orphan drugs to price negotiation under the IRA—so long as they only treat rare conditions—creating a path for the rare disease community to more nimbly access existing rare disease treatments.

IX. The IRA Threatens Funding for Rare Disease Research and Development

A major concern related to the Inflation Reduction Act (IRA) is that funding from VC's, to continue the early research, is disappearing, along with investment by pharmaceutical and biopharmaceutical companies. This is particularly alarming and disheartening in the rare disease space where early funding comes from the patient community. Rare disease therapeutics already face funding challenges different from those developed for common conditions due to the small patient populations that impact the return on investment tied to follow-on funding. An IRA provision makes orphan drugs subject to price negotiation when a second indication is added. Additional threats that make investors scrutinize funding rare disease research and development will have a deleterious impact on rare conditions working to secure a disease-modifying treatment.

Congress passed the Orphan Drug Act (ODA) in 1983 to incentivize the research and development of rare disease treatments. The IRA’s provision that makes orphan drugs eligible for price negotiation weakens and undermines the ODA’s impact in driving research and development of rare disease treatments.

I encourage the committee to recognize and respect the lives of rare disease patients and the relentless efforts of rare disease patient communities in funding rare disease research by protecting orphan drugs regardless of the number of rare disease conditions they treat, as the bipartisan Optimizing Research Progress Hope and New Cures (ORPHAN Cures Act) provides.

X. The Commitment to Rare Disease Research Is Paying Off

2018 represented a historic year for the rare disease community. For the first time, rare disease approvals exceeded general approvals from the Center for Drug Evaluation and Research (CDER) at the FDA.[26] "In 2018, 34 of CDER's 59 novel drugs (58%) were approved to treat rare or "orphan" diseases that affect 200,000 or fewer Americans."[27] Increased approvals of rare disease treatments is a welcome sign for the rare disease community. However, to avoid barriers to research and development to ensure continued work needed to secure FDA-approved therapies for rare diseases with unmet needs.

XI. Rare Disease Research Benefits Us All

Research for rare diseases greased the wheels for a COVID-19 vaccine. Prior to the COVID-19 pandemic, most had not heard of mRNA technologies. This is not true for researchers in the rare disease community. There are more than 145 ongoing mRNA clinical trials for rare diseases, including Cystic Fibrosis.[28] This represents more than 25% of all mRNA clinical trials.[29]

Rare disease researchers pivoted to work on developing treatments and vaccines for COVID-19. One of these researchers is Dr. David Fajgenbaum, a clinician and researcher who also happens to be a rare disease patient with Castleman Disease.[30]

Today, mRNA COVID vaccines protect most vaccinated patients in the US. As of April 28th, 234.6 million vaccines have been administered in the US. 226.5 million of those vaccines- 96.5%- have been the Pfizer & Moderna mRNA vaccines.[31] **We need research into breakthrough technologies like mRNA technology to continue and protect all of us.**

Matthew Might, Ph.D. is the Director of the Hugh Kaul Precision Medicine Institute. His son, Bertrand, is one of countless children who have lost their lives to devastating rare diseases. Dr. Might is a researcher and subject matter expert in precision diagnostics and precision therapeutics, and his work continues to enrich the rare disease community.

I would like to share one of Dr. Might's publications that has become a very important source in my rare disease advocacy efforts, "Why rare disease needs precision medicine—and precision medicine needs rare disease."[32]

A significant benefit to society is that understanding precision diagnostics for rare diseases accelerates the understanding of the human genome.[33] In turn, this can help identify the root

cause of common diseases.[34] Once the root genetic cause of common diseases in individual patients is determined, researchers and clinicians can pharmacologically influence the genes—that means we would be better situated to treat and potentially cure common diseases in individual patients.[35]

Continued research and development in the rare disease community is essential to benefiting patients in the rare disease community as well as those with common chronic illnesses like Alzheimer's, diabetes, and cardiovascular disease.

XII. IRA Challenge: Innovation

There are multiple studies related to the impact of the IRA on the development of rare disease treatments. We all want drugs to be affordable and we want insurers to work with us to make them affordable. We do not want to see manufacturers abandon research and development on new treatments for rare diseases.

Recent studies confirm concerns about the impact of the IRA on innovation on drug development, the impact is signifcant (these studies pertain to drug development generally, and the statistics are not orphan drug specific). One model calculated that had the IRA been in place beginning in 2014, the reductions in revenue on the impacted drugs would have been up to 40%. They concluded between 24 and 49 therapies currently available today would most likely not have come to market and therefore would be unavailable for patients and their providers. The

report concluded a conservative estimate that as many as 139 drugs over the next 10 years are at risk of not being developed at all.[36] Another model from the University of Chicago estimated the reduction in research and development would translate to 79 fewer small molecule drugs or 188 indications, and 116.0 million life years lost over the next 20 years.[37]

As a rare disease patient who is familiar with drug development for our community, I understand the increased hurdles to securing funding and advancing development for our small patient populations. The far-reaching negative impact will decrease innovation in our rare disease community that so desperately needs reasonable policies that spark innovation rather than suppress it.

XIII. IRA Challenge: Utilization Management

I worry about the impact of the IRA on utilization management practices that insurers use to deny care, as they did for Hunter's friend Ben. In his case, despite achieving a successful outcome on treatment as part of a clinical trial, his insurer denied his coverage after the clinical trial due to his underlying disability as he had advanced to needing a ventilator. His advanced stage of disability was the justification for his coverage being different from others who were not at the stage of needing a ventilator, despite that the treatment was medically necessary for him.

It is not far from this scenario to see how insurers might game the drug negotiation process to find ways to restrict access through utilization management. Insurers could use government price

controls to exact large additional discounts and rebates from manufacturers of competing products that are not subject to price controls. If unable to offer such large discounts, payers may increase their use of utilization management or increase cost-sharing for those products, without consideration of which product is best for the patient. Insurers could impose prior authorization, fail first or step therapy. They could place medicines that do not offer large discounts on higher tiers that require higher patient cost-sharing. Payors could even exclude more medicines from formularies.[38]

In the end, it will be the rare disease patient that loses. They may be unable to achieve coverage for the drug their doctor prescribes, or they have to pay more out-of-pocket to get it.

XIV. Orphan Cures Act and MINI Act:

I am grateful to see that bipartisan legislation is being considered today to address the need for new and novel products to treat rare diseases. The legislation known as the ORPHAN Cures Act would expand and clarify the exclusion for orphan drugs under the Drug Price Negotiation Program ensuring rare disease drugs continue to be developed. The Maintaining Investments in New Innovation Act, known as the MINI Act, similarly addresses drug products with genetically targeted technology by providing a longer timeframe on the market before being subject to the new program.

I have had longstanding concerns about the impact of the government setting prices on rare disease drugs. While the IRA provides a negotiation exemption for orphan drugs that treat only

one rare disease, this exemption is far too narrow to provide a meaningful incentive for continued innovation for rare diseases. The rare disease community remains very concerned about protecting medicines that could be used for more than one rare indication. The program referred to as the Medicare Drug Price Negotiation Program is disincentivizing investments in orphan drugs and areas of high unmet patient need as drugs with broader indications will provide a superior return on investment. If this program is to continue, I hope we can, at a minimum, leave rare and novel treatments out of it.

XV. Patient Access Act: Helping Rare Disease Patients with Travel to Access Rare Disease Treatments

I am pleased that the committee is working towards introduction of the Patient Access Act that would exclude from anti-kickback and other sanctions certain travel and lodging arrangements between manufacturers of drugs and individuals being administered such drugs. I know families whose insurers would not cover their treatment for SMA after our clinical trial concluded. These families needed patient assistance programs to give them continued access to the drug that gave their children an optimal quality of life. We were among the lucky ones to have the treatment covered and have the means to get our child to the treatment site. But not all families live near a preferred site of service, especially in rural Texas, so having housing and transportation costs covered as part of the treatment is essential for them to be able to actually access that treatment.

I think policymakers may not understand that these life-saving treatments for rare diseases are not necessarily available in every community. It is not uncommon for some rare disease

treatments to only be available at a few sites spread out across the United States. This can make accessing rare disease treatment unattainable for families who lack the resources required to travel. For parents who learn a new treatment is available that could save their child, to then realize that they cannot afford the cost of travel, it is devastating. This bill rights that wrong.

XVI. QALY Ban Thank You

I want to thank you Chairwoman McMorris Rodgers for personally advocating for the House to pass H.R. 485, the Protecting Health Care for All Patients Act, as well as the other committee members who worked to advance the legislation out of the committee and successfully voted out of the House. The legislation is a "must do" for people with rare diseases, disabilities, chronic illnesses, elderly patients, and really for all patients. The use of quality-adjusted life years and similar measures devalues their lives in assessing whether patients are worthy of treatment. They should be barred from use in all health care programs, not just Medicare. Metrics utilized to access and determine the reimbursement for healthcare should not devalue already vulnerable patients. I am grateful the bill passed without weakening current law protections, simply extending those nondiscrimination protections to beneficiaries in programs like Medicaid.

On a personal note, Curtis was familiar with my advocacy efforts opposing the utilization of QALYs in the years preceding his glioblastoma diagnosis. One of the first things he wanted to know following his diagnosis was what his QALY was. The question was a punch in my gut, and I answered him honestly. I told him I didn't know his QALY, but it wouldn't be good.

XVII. Conclusion

I personally felt the devastation of being told there was no hope and that my newborn would die in 3 months from an imminently-terminal rare disease. I've cried tears for babies and children who lost their battle with SMA and other rare diseases and watched families say goodbye. We found our way to a treatment for Hunter and helped other SMA patients access a treatment earlier.

I was devastated once again when my husband, Curtis, was diagnosed with glioblastoma, effectively a death sentence. Upon his death I became a single parent, which is hard for any parent, and it's exponentially harder for single parents to children like Hunter living with rare conditions.

I am not alone in experiencing devastation and loss in the rare disease community, and yet I wish I were.

My mission is to help secure presymptomatic diagnosis and treatment for all rare disease treatments. I cannot and do not improve access for the rare disease community alone. I am grateful for the community of patient advocates I am privileged to advocate alongside. We understand the importance of collaborating with all stakeholders in the rare disease community, including policymakers like yourselves. We need your help in securing reasonable and meaningful policies that address healthcare spending while preserving access to treatments for the rare disease and greater patient communities. Advancing policies that accelerate the

development of rare disease treatments is essential to bringing new treatments that save and improve the lives of rare disease patients.

Thank you for your consideration.

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