January 9, 2025

Independent Citizens' Oversight Committee (ICOC)
California Institute for Regenerative Medicine (CIRM)
c/o: Claudette Mandac
cmandac@cirm.ca.gov

Dear Members of the CIRM Governing Board and ICOC,

On behalf of Cure Sanfilippo Foundation and the Sanfilippo syndrome community, we write to express our urgent plea for your support and funding to advance the development of stem cell gene therapy for Sanfilippo syndrome type B, **"Hematopoietic Stem Cell Gene Therapy for MPSIIIB (Sanfilippo B) Syndrome (TRAN1-16907)."** This life-altering disease has left countless families with no treatment options, and we implore you to help bring hope by supporting the research team in translating this extremely promising therapeutic approach.

Sanfilippo syndrome, often referred to as childhood Alzheimer's, is a rare genetic condition caused by the inability to break down heparan sulfate, a complex sugar molecule. This results in the progressive buildup of toxic substances in the cells, leading to devastating neurological decline and other harmful multisystem impacts.

Children with Sanfilippo syndrome face a heartbreaking progression: initial developmental delays, followed by loss of speech, cognitive abilities, and motor functions, culminating in premature death—often during their teenage years. Children go from talking to screaming to silence; from eating their birthday cake with joy to being fed through a gastrostomy tube; from running wildly on the playground to being unable to even roll over in bed. Each successive loss brings a new wave of grief and hardship. As both a parent of a child with Sanfilippo and a pediatrician, I can testify to this reality.

Sanfilippo type B, caused by mutations in the NAGLU gene, shares these devastating hallmarks of the syndrome. The need is so great that families are typically enrolled rapidly from wide-ranging geographies. Cure Sanfilippo Foundation has a broad reach among clinicians, advocacy partners, and the public at-large which would be leveraged to support enrollment of a future clinical study of this lentiviral HSCT therapy. To date, there are no approved treatments or cures for any form of Sanfilippo syndrome.

Despite these grim realities, there is profound hope in the potential of stem cell gene therapy. Groundbreaking work in related fields has already demonstrated the transformative promise of this approach. For example, an analogous treatment being developed by Orchard Therapeutics, using similar lentiviral hematopoietic stem cell transplantation (HSCT) technology for Sanfilippo type A, has shown encouraging early results through improved neurocognitive outcomes and disease stabilization. This therapy was also developed by TRAN1-16907 investigator, Dr. Brian Bigger. The lentiviral HSCT approach has also been successfully applied in treating metachromatic leukodystrophy (MLD), a now FDA approved treatment, underscoring the feasibility and life-changing potential of this technology. Dr. Masiuk, Dr. Kohn, and Dr. Bigger have an impressive track record in developing regenerative therapies and implementing clinical trials, giving us full confidence that they will efficiently and effectively move this treatment to a first-in-human trial for Sanfilippo B.

For the Sanfilippo community, the prospect of stem cell gene therapy offers a glimmer of hope amidst immense suffering. This therapy has the potential to slow disease progression or halt it entirely, giving children the opportunity to live fuller, healthier lives. Even more promising is the durable nature of a metabolic cure provided by lentiviral HSCT therapy. Families affected by Sanfilippo syndrome live every day with the heart-wrenching knowledge that time is against them. Supporting this critical work could mean the difference between life and loss for these children.

Following this letter, you will find testimonies from families whose lives have been irrevocably altered by the diagnosis of Sanfilippo syndrome. Their stories illustrate the urgency of the work described in Dr. Masiuk's proposal and the hope that a durable treatment would bring to their lives. These families—and countless others—are depending on organizations like CIRM to champion innovative treatments that could change the course of this disease.

We urge the board to consider the great unmet need in Sanfilippo type B in the context of CIRM's prioritization of advancing the field of neurodegeneration. Your funding support will not only accelerate critical research but also offer tangible hope and intervention to the many families in desperate need.

Thank you for your leadership and commitment to advancing regenerative medicine. We are grateful for your consideration and stand ready to collaborate with the study team to support this vital work.

Sincerely,

Cara O'Neill, MD, FAAP
Chief Science Officer & Co-Founder
Cure Sanfilippo Foundation
cara@curesanfilippofoundation.org

Subject: Letter of Support for **TRAN1-16907** Nov 2024
Hematopoietic Stem Cell Gene Therapy for MPSIIIB (Sanfilippo B) Syndrome

Dear Members of the Application Review Subcommittee,

We are writing to strongly encourage the California Institute for Regenerative Medicine to provide research grant funding for the **Hematopoietic Stem Cell Gene Therapy (HSCGT) for MPSIIIB (Sanfilippo B) Syndrome** under the leadership of principal investigator **Katelyn Masiuk** M.D., Ph.D.

We are a family of four in San Jose, California and have a personal interest in this research. Our vibrant son Matthew, age 3, is a happy, thoughtful child with a big heart for others. He saves treats for mommy, loves running around and being silly with his big brother and cousins, and prays for his grandparents nightly. He had a bright future ahead of him until he received the devastating diagnosis of Sanfilippo Syndrome Type B. In just a few years, this disease will eliminate his personality as well as all physical abilities and neurological skills, ending his life before adulthood.

We've seen that raising a child with Sanfilippo Syndrome is a heavy burden, requiring 24/7 caregiving responsibilities, frequent medical appointments (100+ for us in 2024), and healthcare expenses. The disease affects families from diverse ethnic backgrounds — Black, White, Hispanic, Asian, Arab — and across all socioeconomic classes. Lower-income families bear a disproportionate burden balancing limited time and financial constraints, and would receive an outsized benefit with the advent of this treatment.

Dr Masiuk's research proposal offers a timely lifeline for Matthew and others like him. It follows in the footsteps of a similar treatment for the related variant Sanfilippo Type A, which shows early positive results. Dr. Masiuk is joined by the world-renowned Dr. Don Kohn who is a pioneer in the development of lentiviral gene therapy, and Dr. Brian Bigger who has led the development of ex vivo lentiviral therapies for other forms of mucopolysaccharidosis, including the program in MPSIIIA. These early advances inspire confidence that Sanfilippo Type B (MPSIIIB) can be cured in the near future.

Time is of the essence for children with Sanfilippo Syndrome. We urge you to consider the profound impact this grant will have on families across our beautiful state of California and around the world.

Thank you for your dedication in advancing regenerative medicine breakthroughs. We trust that your committee will recognize the potential and provide the necessary funding to bring hope to families like ours.

Sincerely,
Daniel & Minnie Lau, parents of Matthew

1/10/2025

Subject: Letter of Support for **TRAN1-16907: Hematopoietic Stem Cell Gene Therapy for MPSIIIB (Sanfilippo B) Syndrome**

Dear California Institute of Regenerative Medicine,

My name is Morgan Rachal, mother of Lydia Rachal who was diagnosis last year in April 2024 with MPSIIIB at 18 months old. I am writing to ask you to approve the needed funds for TRAN1-16907, Hematopoietic Stem Cell Gene Therapy for MPSIIIB. Luckily, we were able to get her diagnosed early in her life with this terminal disease because of social media awareness. Because of that, we hope to get treatment before the brain damage begins. This is a parent's worst nightmare, to be told that their child is going to suffer and die without treatment. Lydia had a perfect birth and has met all her milestones. Still to this day, Lydia is still on track and learning more every single day as a typical normal child would be. She has so much potential. Her early steps therapy team told us she would not even qualify if she didn't have the diagnosis because of how on track she was with her abilities. It crushed my husband and I's souls to think that one day we will have to watch her lose all these abilities and deteriorate right in front of our eyes because of this disease. As a mother and nurse who feels helpless during this diagnosis, the only thing I know to do is fight for my daughter for treatments. It is the only chance she has at life. Lydia getting into treatment would be the biggest blessing for our family. Time is not on our side as this disease will eventually cause brain damage and Lydia will lose everything she has learned. It is our fervent hope Lydia will get to experience the fullness of childhood before time runs out. We hope the funding committee will prioritize the urgency and importance of this project and take the necessary steps to support it. Thank you for your consideration.

Sincerely,

Morgan Rachal

morganwrachal@gmail.com | 318-471-

12/3/2024

Subject: Letter of Support for **TRAN1-16907: Hematopoietic Stem Cell Gene Therapy for MPSIIIB (Sanfilippo B) Syndrome**

Dear California Institute of Regenerative Medicine,

I am Muna Hattar-Mendoza, from Covina, California. I am writing to support funding for TRAN1-16907 led by principal investigator Katelyn Masiuk, MD, PhD. I am interested in this research because my daughter Rose has MPSIIIB (Sanfilippo Syndrome Type B).

When Rose was 2, she was not only walking but running everywhere she went. She was not only talking but making jokes and singing songs. Now, Rose still walks, but for short distances. This Halloween was the first year we took Rose trick or treating in her adaptive stroller/ wheelchair instead of walking. Now, Rose uses a talker (adaptive communication device). She still gets her point acrost but if she's trying to make jokes we miss it. She still sings, but there are not lyrics to her songs anymore. Worst of all, we know there is more suffering to come. Still worst of all, we know there is currenlty no treatment available. Everytime, I meet a family whose child is newly diagnosed my heart sinks because I remember they are facing the suffering and death of their child without the hope that comes with treatment.

You can read more about our life with Rose in the San Diego Union Tribune: https://www.sandiegouniontribune.com/2023/05/16/parents-dream-of-a-cure-for-sanfilippo-syndrome-a-childhood-dementia-that-comes-with-a-death-sentence/?fbclid=IwZXh0bgNhZW0CMTEAAR3TQ8UKLrzkgBbCsNEYSBjWNcE0G1e6zjSWDzIJNBy2iyzNbVYEyxfcse4_aem_R75ssuaLpvUFB0A0xhYAjw

But I remain grateful. I am grateful for the scientist willing to spend thier lives doing research in this area. I am grateful for the Cure Sanfilippo Foundation's comitment to advocating for treatment and one day a cure. I am grateful for Rose being in my life. She has taught me so much about what really matters. What really matters is love, not romantic, feel good kind of love. Rather, what matters is a willingness to care for those who cannot care for themselves, a willingness to do something good, maybe even for someone you do not know.

So today, I believe Rose is inviting you to do this good: to change the lives of children and families suffering everyday and to save families from the grief of losing a precious child. I am grateful for California Institute of Regenerative Medicine willingness to hear this invitation and I do implore you fund this life changes, family changing, community changing research.

Sincerely,

Muna Hattar Mendoza
(626)347-6322
munahattarmendoza@gmail.com

Rose and her sister

December 5, 2024

RE: Letter of Support for **TRAN1-16907: Hematopoietic Stem Cell Gene Therapy for MPSIIIB (Sanfilippo B) Syndrome**

Dear California Institute of Regenerative Medicine,

We are Roger and Susan Chapin, parents of Blair, who suffered from Sanfilippo Syndrome Type B. We are writing to urge your approval of the necessary funding for TRAN1-16907, Hematopoietic Stem Cell Gene Therapy for MPS IIIB (Sanfilippo B) Syndrome.

Blair was born seemingly perfect, with no indication of the devastating journey ahead. We had no family history or knowledge of this disease. Like any parents, we were unprepared to hear that our child had a terminal condition with no treatment or cure. The only advice we were given was to take her home and love her—which we did with all our hearts.

Despite our unwavering love and every resource we could muster, we could not shield Blair from the pain and suffering this disease inflicted. Over time, she lost her ability to speak, walk, eat, and find peace or comfort. Witnessing this decline was excruciating—not just for Blair but for our entire family.

Sanfilippo Syndrome Type B robs children of their lives and families of hope. As parents who have experienced the unimaginable toll of this disease, we implore you to fund this critical research. TRAN1-16907 offers a rare opportunity to transform a future filled with grief into one of hope for children and families impacted by this condition.

Thank you for considering this vital investment in research and the lives it can save.

Sincerely,
Roger and Susan Chapin (407-491-4499/susanchapin@icloud.com)

December 2, 2024

Subject: Letter of Support for **TRAN1-16907: Hematopoietic Stem Cell Gene Therapy for MPSIIIB (Sanfilippo B) Syndrome**

Dear California Institute of Regenerative Medicine,

My name is Jennifer Sarkar, and my husband, Samir Sarkar, and I are Los Angeles, California residents. We are the proud parents of our 12-year-old son, Carter, who was diagnosed with Sanfilippo Syndrome Type A in 2016. I am requesting you approve the much-needed funding for TRAN1-16907, Hematopoietic Stem Cell Gene Therapy for MPSIIIB (Sanfilippo B) Syndrome.

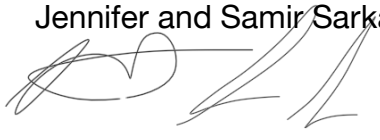
When we first received Carter's diagnosis, we were told there were no treatment options, no cure, and no path forward—to "go home and love your child while you can." Hearing those words shattered our world. Knowing that our sweet, vibrant boy would face the challenges of a neurodegenerative disease was devastating. Sanfilippo Syndrome is often referred to as "childhood Alzheimer's," a comparison that still doesn't fully capture the heartbreak of watching your child slowly lose their abilities. Over the years, we've seen Carter's struggles grow and a significant loss of skills and abilities. As parents, it is an unimaginable pain to feel helpless against the progression of this disease, especially now eight years into diagnosis, and there is still no cure or treatment option for Sanfilippo syndrome. Despite this, Carter continues to teach us what resilience looks like.

Funding this project is not just about providing hope to families like ours; it is about addressing an urgent need. Right now, children with Sanfilippo Syndrome have no viable treatment options. Families like ours live day by day, knowing time is slipping away. By funding TRAN1-16907, you are giving these children a chance to live, grow, and experience childhood in a way that is currently out of reach for our community. If this treatment becomes a reality, it could mean that no other child has to lose their childhood to this cruel disease, and no parent has to endure the agony of watching their child slip away.

It is our hope that children like Carter will get to experience an actual childhood before time runs out. Please consider the urgency and importance of TRAN1-16907. By funding this research, you have the opportunity to be part of a groundbreaking solution, transforming the future from one of grief to one of hope for families facing Sanfilippo Syndrome. Thank you for your time and thoughtful consideration.

Sincerely,

Jennifer and Samir Sarkar



Date: 12/6/2024
Subject: Letter of Support for TRAN1-16907: Hematopoietic Stem Cell Gene Therapy for MPSIIIB (Sanfilippo B) Syndrome

Dear California Institute of Regenerative Medicine,

We are Sean and Rebecca Jordan and our daughter, Liv, has Sanfilippo Syndrome Type B. We are writing to let you know that TRAN1-16907, Hematopoietic Stem Cell Gene Therapy for MPSIIIB (Sanfilippo B) Syndrome is something that could help our daughter and our family tremendously and we are asking you to approve the funds needed for this treatment.

Our daughter was diagnosed at age 2 ½ and is currently 10 years old. At age 3, she very quickly went from being able to understand us and communicate with us using words, to not understanding and being non-verbal. It was devastating to watch her lose skills, especially knowing that the science is here and funding is standing in the way.

This disease desperately needs a working treatment. A treatment that will alleviate symptoms and improve quality of life. A treatment that will give us more good years with her, together as a family, and her as a member of our community.

She still has many skills that need to be preserved. If we could keep her stable and healthy, and right where she is at now, she would have a good quality of life. She loves so many things including quality time with her favorite people, running, jumping on her trampoline, and being in nature to name a few. She thoroughly enjoys breakfast, lunch and dinner and all the snacks in between, and we want her to be able to eat by mouth for as long as possible. She brings a lot of joy to those around her and is a great example for others to enjoy the simple things in life.

We hope for many, many more years with our beautiful girl. We hope you understand the importance and urgency of this treatment for families like us. Thank you so much for your consideration.

Sincerely,
Sean and Rebecca Jordan

Please feel free to contact us:
sean_jordan23@hotmail.com
rebeccajordan28@gmail.com

12/5/2024

Subject: Letter of Support for TRAN1-16907: **Hematopoietic Stem Cell Gene Therapy for MPSIIIB (Sanfilippo B) Syndrome**

Dear California Institute of Regenerative Medicine,

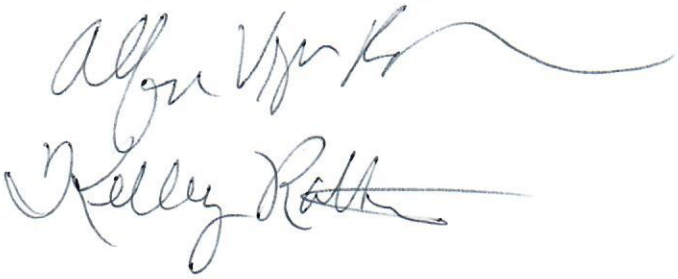
We are Dr. A. Vijay and Kelley Rathinam of Atlanta, Georgia and are parents of our beautiful daughter, Madelyn, who suffers from Sanfilippo type B. I am writing to ask you to approve the needed funds for TRAN1-16907, Hematopoietic Stem Cell Gene Therapy for MPS IIIB (Sanfilippo B) Syndrome.

As you are aware, Sanfilippo was discovered in the 1960s and it is unfortunate that 60+ years later there are still no treatments for this devasting disease. There have been lots of stops and starts in terms of research and investment in the space for many years and we are all hopeful with the scientific advancements over the last decade in the areas of gene therapy and enzyme replacement therapy, some treatment options will finally emerge. Over the years, countless children and families have suffered/perished without treatment and parents and caregivers have shepherded these children through the gut wrenching, sad and lonely journey of cognitive and physical decline. As parents, we are watching this devasting disease progress in Madelyn and don't want other parents or children to go through the same thing.

In summary, time of the essence for Madelyn and other children suffering with this terrible disease. It is our fervent hope that children like Madelyn get to experience the fullness of childhood before time runs out. We hope the funding committee will prioritize the urgency and importance of this project and take the necessary steps to support it. Thank you for your consideration.

Best regards,

Dr. A. Vijay and Kelley Rathinam



January 10, 2025

Subject: Letter of Support for **TRAN1-16907: Hematopoietic Stem Cell Gene Therapy for MPSIIIB (Sanfilippo B) Syndrome**

Dear California Institute of Regenerative Medicine,

Our names are Tim and Valerie Byers of Spring, Texas. Our 14-year-old son, Will, has MPSIIIB (Sanfilippo Syndrome, Type B) and we are writing to encourage the approval of funding for TRAN1-16907, Hematopoeitic Stem Cell Gene Therapy for MPSIIIB, led by principal investigator Katelyn Masiuk, MD, PhD.

Will was a vibrant, active 4-year-old when he was diagnosed with Sanfilippo Syndrome. We were completely devastated when his blood test results arrived; how could we be expected to go on knowing that we would have to watch our son suffer and eventually die due to this disease? In an instant, our parenting dreams were crushed. There would be no baseball teams or homecoming games or college searches. Our son's life, which we thought would be limitless, was now distinctly limited.

Even with the diagnosis, we couldn't understand how this disease would ravage our talkative, bright boy. But it did. His voice grew silent, his steps slowed, his balance faltered. At 14, he can no longer feed himself, relying on us to again spoon-feed him his meals. However, we take much comfort in the fact that we can still make him happy, as evidenced by his heartwarming smiles and giggles.

We love our son unconditionally, but if he could have received some treatment, any treatment, that could have cured, treated, or even slowed down the progression of Sanfilippo syndrome, we would have taken it. Will's life is valuable and any option to treat his condition is valuable. As parents who have watched the devastating effects of Sanfilippo firsthand, we want to support any research that could stop other parents or children from the same experiences. We urge you to consider funding this research. By doing so, you have the chance to change the future from one of grief to one of hope for all children with MPSIIIB. Thank you for your consideration of TRAN1-16907.

Sincerely,

Tim Byers Valerie Tharp Byers

Timothy Byers, PE & Valerie Tharp Byers, EdD

willpowermps@gmail.com