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May 31, 2023

National Advisory Neurological Disorders and Stroke Council (NANDSC)
c/o NIH National Institute of Neurological Disorders and Stroke
P.O. Box 5801
Bethesda, MD 20824

Re: SMA is not Cured; New Research Needed to Address Unmet Needs of People with SMA

Dear NANDSC Members,

Cure SMA, which represents individuals with spinal muscular atrophy (SMA), applauds NANDSC and the National Institutes of Neurological Disorders and Stroke (NINDS) for its past support and commitment to SMA research and the everyday living needs of children and adults with the degenerative neuromuscular disease. As our annual SMA community survey and focus group discussions spotlight, significant unmet need still exists among people impacted by SMA. **We respectfully ask that that this distinguished panel recommit to meeting the needs of the SMA community as it considers promising research proposals in SMA and related areas.**

As you know, SMA was once the leading genetic cause of infant death. Historically, babies born with SMA Type 1, the most common and severe form of the disease, died before reaching their second birthday. Severe muscle weakness associated with SMA resulted in underdeveloped lungs and led to respiratory failure. Cure SMA was founded in 1984 by families of children with SMA with the very goal of changing the trajectory of the disease for children and adults with SMA. Since our founding, Cure SMA has invested more than \$15 million in basic research, including 133 basic research grants in the past two decades alone. Cure SMA provided seed money for academic research proposals that as they advanced through the research stages were successful in securing National Institutes of Health (NINDS) funds before eventually leading to the SMA treatments that are approved and available today. NANDSC should be proud of its role in helping to foster the innovation that has led to today's discoveries in treating SMA.

But the work is not done. We know this, because the SMA community has been clear that they continue to face significant challenges related to their SMA. Each year, Cure SMA surveys adults with SMA and families of children with SMA on their treatment status, improvements, and unmet needs.¹ Results from the annual survey show that the state of SMA has improved. More individuals are achieving motor function atypical for their SMA type, infants are getting diagnosed and accessing treatment within days of their birth, and mortality rates for people with SMA are decreasing. However, our community survey highlights that significant unmet need persists, particularly for children and adults with SMA who lost considerable motor function and muscles before accessing a SMA treatment. This group represents the largest segment of the SMA population. Adults with SMA and families of children with SMA are unified in supporting new research and treatments to address unmet needs. Individuals with SMA and their families viewed gaining muscle strength (90%), achieving new motor function (73%), improving daily functioning (68%), reducing fatigue (53%), and improving swallowing (36%) and communication (21%) as their top priorities for future research and treatments.

Adult, teen, and family representatives of the SMA community also highlighted their unmet needs directly with the FDA in an August 2022 listening session.ⁱⁱ *“Even though my muscles are stronger than in the past, I get tired really easily,”* said a **16-year-old girl with SMA** who presented before FDA officials. *“For me a treatment that targets muscle gain would greatly improve my independence and would ensure that I can continue doing the things that I love like power soccer.”* An **adult with SMA** who works as a research coordinator at a lab described how small tasks, such as lifting a half gallon of milk in and out of the refrigerator or reaching lab equipment from a shelf could lead to huge successes. These small tasks, she said, *“don’t take a ton more muscle, but they are all muscle I still don’t have. If science can create a safe effective treatment that helps me maintain, I fully believe and expect it will be able to create a combination treatment to allow me to gain some strength.”* And a **parent of a 2-year-old child with SMA** who received treatment before the onset of SMA symptoms also highlighted the need for additional research and treatment: *“The development of add-on, non-SMN targeted therapies so that there are additional options to treat future needs as they arise would provide our family a great deal of peace of mind about what the future holds for our son and family.”*

Cure SMA is responding to the SMA community feedback about unmet needs through our robust research program. Following a brief pause in research awards (due to the COVID-19 pandemic), Cure SMA has now committed another \$1.25 million for new research, including five basic research grants that were funded at the beginning of 2023.ⁱⁱⁱ These new basic research grants are focused on restoring strength and function in children and adults with SMA. A research project recently funded by Cure SMA has produced significant findings that were published in *Neuron*. The research, by Dr. Umrao Monani from Columbia University, demonstrated that disrupted SNARE complexes in SMA neuromuscular junctions link loss of SMN protein to subsequent motor neuron disease. This provides insight into the long-standing mechanistic question in SMA of how levels of SMN protein, present in SMA, result in motor neuron degeneration and death, a key finding for advancing our understanding of SMA and provides a novel pathway for therapeutic exploration.

Despite Cure SMA’s research commitment, we cannot alone meet the research proposals and possibilities required to address the SMA community’s everyday needs and challenges. Less than 25 percent of the high quality SMA research proposals that were submitted to Cure SMA during its most recent grant request for proposals were awarded due to lack of funds. The National Institutes of Health, including NINDS, must continue to be a partner in SMA research. NINDS and the NIH have a successful record of investing in promising SMA research that have led to approved treatments.^{iv} While Cure SMA appreciates the pledges that SMA remains a research priority, we have also heard that some in the research review community may view SMA as being cured (given existence of three FDA-approved treatments) and that additional SMA-related research is not necessary. We challenge anyone who may have that notion to meet directly with or shadow a person with SMA for one week or even a day to understand their continued everyday living challenges. Given NANDSC provides a secondary review for all NINDS grant and cooperative agreement applications^v, this panel of experts has a responsibility to ensure that the research needs of the SMA community be fairly considered based on the merits of the proposal.

The SMA community is thankful for the support from the research community and other key stakeholders in helping to spur the development of current SMA treatments. But

significant needs remain, even during this time of robust discovery. A young boy named Charlie was born with SMA Type 1 in August 2018. While a SMA treatment was available for nearly two years before his birth, the family’s diagnostic journey would mean that Charlie developed SMA symptoms and lost considerable motor function before accessing a treatment. When the family received the SMA diagnosis, Charlie was not lifting his head during tummy time and had limited muscle strength. *“He had already lost significant muscle strength,”* Charlie’s mom said. At age 3 months, Charlie received an SMA treatment and the family immediately began to notice improvements, especially in slowing further weakness. Today, Charlie is four years old. He excels at home and preschool and enjoys stacking building blocks high above his power wheelchair. *“Every day, we see in Charlie both the amazing impact of SMA treatments and the need for additional SMA research to help restore muscle strength and address scoliosis, both areas that greatly impact Charlie in his daily life.”*

Tomorrow’s treatment successes will come from today’s decisions and research investments. We respectfully urge this distinguished panel to consider the needs of Charlie and all children and adults with SMA, especially those who lost muscles and motor function before accessing a treatment. The learnings from SMA research can be translated to help address the unmet needs of other neuromuscular communities. Thank you for considering the views of Cure SMA and the children and adults living with SMA that we represent across the United States. For more information related to our request, your staff may contact Maynard Friesz, Vice President for Policy and Advocacy at Cure SMA, at maynard.friesz@curesma.org or 202-871-8004.

Sincerely,



Kenneth Hobby
President



Mary Schroth, M.D.
Chief Medical Director



Jacqueline Glascock, PhD
Vice President, Research



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Vice President, Policy

ⁱ Cure SMA Community Update Survey, 2023, <https://www.curesma.org/community-update-survey/>

ⁱⁱ SMA Community Representatives Share Unmet Needs with FDA, August 2022, <https://www.curesma.org/cure-sma-holds-patient-led-listening-session-with-fda/>

ⁱⁱⁱ Cure SMA Awards Basic Research Grants, February 2023, <https://www.curesma.org/blatnik-grant-announcement-2023/>

^{iv} “I have SMA, SMA doesn’t have me,” *Orphanet Journal of Rare Diseases*, <https://ojrd.biomedcentral.com/articles/10.1186/s13023-021-01701-y>

^v National Advisory Neurological Disorders and Stroke Council, 2023, <https://www.ninds.nih.gov/about-ninds/who-we-are/national-advisory-neurological-disorders-and-stroke-council>