

# **Newborn Screening for Spinal Muscular Atrophy**

Testimony of Cure SMA

Delivered by Spencer Perlman

Good afternoon. Dr. Bocchini and members of the advisory committee, thank you for the opportunity to testify today. My name is Spencer Perlman and I am a member of the Cure SMA Board of Directors. Cure SMA leads the way to a world without Spinal Muscular Atrophy, the number one genetic cause of death for infants. We fund and direct comprehensive research that drives breakthroughs in treatment and care, and we provide families the support they need for today.

I'm testifying this afternoon as a representative of the entire SMA community regarding the committee's nomination and evaluation process for candidate conditions on the uniform newborn screening panel.

In the ten years since I last stood before this committee, there have been significant advancements towards the development and approval of a treatment for SMA. Through these advancements that we have also gained a much greater understanding of the disease and the importance of early intervention. We are at an exciting precipice, hopefully on the brink of seeing an approved treatment for SMA. Thus, I am requesting that the advisory committee give renewed consideration to the forthcoming nomination and evaluation of SMA for universal newborn screening.

As you know, SMA is an autosomal genetic disorder and the leading genetic killer of children under the age of 2. It occurs in about 1 of every 10,000 births, with 1 in 50 people in the general population being carriers of the disease. Approximately 50 percent of affected children suffer from type 1 SMA, the most severe form. Historically, more than 95 percent of these children die in infancy or require extensive respiratory support by their second birthday.

Newborn screening is an issue that is of paramount importance within the SMA community. SMA families, as well as investigators and clinicians within the SMA community, recognize that newborn screening holds great promise for most effectively delivering a treatment or cure for this deadly disease.

In just over a decade, the SMA drug pipeline has grown dramatically. Of the 18 programs currently in the pipeline, six are in clinical trials, and several of those are in Phase 3 clinical trials, following on positively reported Phase 2 trial results. We expect at least one if not more of these drug development programs file a New Drug Application to the FDA in 2017. Therefore, it is of the utmost importance that SMA be added to the recommended uniform

screening panel (RUSP) as soon as possible to ensure patients and families become aware of the disease and need for treatment and are provided access to these treatments once approved at the earliest possible moment.

Both human natural history data and animal model data suggest that early drug intervention is required for greatest efficacy in SMA.

Natural history data indicates that there's only a small opportunity for intervention in the most common and severe form of SMA type 1. Dr. Kathryn Swoboda of the University at Mass General Hospital has shown that type 1 infants demonstrate normal motor neuron innervation during the presymptomatic phase of the disease, but suffer rapid and severe loss of motor units in the early perinatal period during the first 3 months of life. This can result in the loss of more than 90% of motor units within 6 months of age. Moreover, a recent multi-center natural history study conducted by the NINDS NeuroNEXT clinical trial network in infants under six months of age with genetically confirmed SMA has shown significant differences between the SMA and control infants at the baseline visit for in motor function tests, suggesting very early motor neuronal deficits.

Preliminary data in human and mice models also indicate that presymptomatic drug intervention is more effective than postsymptomatic, with the results being remarkably consistent, using genetic means, gene therapy vectors, and antisense oligonucleotides to increase SMN levels. All have shown the best results when the drugs are given as early possible with little drug effect after the first week of life in severe mouse models of SMA.

Secondary to this, studies have also shown that proactive treatment in the first few weeks to months of life prolongs survival and improves quality of life. The increasing survival in the type I infants related to proactive respiratory and nutritional modalities has been increasingly well-documented. However, in the current environment in the absence of newborn screening, these interventions remain predominantly reactive to medical crises. In fact, diagnostic delay is very common in SMA. A recent systematic literature search showed that the mean ages of onset for SMA types I, II, and III, were 2.5, 8.3, and 39.0 months respectively, while the weighted mean ages of confirmed spinal muscular atrophy genetic diagnosis were 6.3, 20.7, and 50.3 months.

In addition to the aforementioned items, the case for implementing universal newborn screening for SMA is made more convincing by the fact that the technology exists and has been successfully utilized in several ongoing pilot newborn screening programs, namely in New York State and Taiwan.

In conclusion, the SMA community strongly urges the advisory committee to take up renewed consideration of the forthcoming SMA nomination with concerted focus on the availability of a treatment for SMA in the very near future, the success of the technology in screening for SMA, and the demonstrated benefits of early intervention. I thank the committee for the opportunity to testify.