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SAFETY AND EFFICACY DATA PUBLISHED FOR ONASEMNOGENE ABEPARVOVEC (SPINAL MUSCULAR ATROPHY GENE THERAPY) FOR PRESYMPTOMATIC INFANTS AT RISK FOR SMA TYPES 1 OR 2

STRASBURG, PA – Recently published companion papers detail the safety and efficacy of onasemnogene abeparvovec, a gene replacement therapy for spinal muscular atrophy (SMA), for presymptomatic infants with two or three copies of *SMN2* at risk for developing SMA type 1 or 2, respectively. Together, these papers summarize the final results of SPR1NT, a Phase III study focusing on newborns administered one-time intravenous *SMN* gene replacement therapy before six weeks of age. SMA is a devastating genetic disorder that leads to progressive degeneration of spinal motor neurons that control movement, swallowing, and breathing. Untreated infants with SMA Type 1 do not achieve independent sitting or other advanced motor milestones and 100% die or require permanent ventilation by two years of age. Infants with untreated SMA Type 2 sit independently but do not walk, and develop debilitating musculoskeletal and respiratory complications with advancing age. The companion papers, divided into *SMN2* two-copy (n=14) and three-copy (n=15) cohorts, were recently published in the journal *Nature Medicine*. Dr. Kevin A. Strauss, Medical Director at the Clinic for Special Children, served as first author.

In the first paper, focused specifically on children at risk for SMA Type 1, 14 infants received gene therapy at a median 21 days of life, before the onset of overt signs of disease. Notably, all 14 children (100%) sat independently by 18 months of age. The majority, 11 of 14 children (79%), stood alone within the normal developmental window. Nine of 14 children (71%) walked alone. The therapy had a significant impact on quality of life; all 14 (100%) children in the two-copy cohort were alive and free of permanent

ventilation as well as non-oral or mechanical feeding support by 14 months of age, and their status did not change through the end of the study.

The second study focused upon children with three *SMN2* copies at high risk for SMA type 2. Fifteen children received gene therapy at a median 32 days of life, before disease onset. All 15 children (100%) sat independently by 24 months of age. Notably, 14 of the 15 children (93%) walked independently by 24 months of age. Like the SMA Type 1 study, all 15 (100%) children were alive and free of permanent ventilation, non-oral feeding, and mechanical support of any kind by 14 months of age, maintained through the end of the study.

Both studies demonstrated a favorable safety profile of the therapy in newborns, and underscore the importance of delivering the therapy to infants before the overt onset of disease, which can result in normal or nearly normal patterns of growth and neuromuscular development. According to Dr. Strauss, lead author for both papers, "two decades following completion of the human genome project, onasemnogene abeparvovec delivers on the promise of that great undertaking, demonstrating the transformative potential of gene-based therapies for previously intractable hereditary disorders in children. SPR1NT provides an example of what can be achieved when newborn screening is combined with safe and effective disease-modifying therapy. It represents remarkable evolution in the SMA standard of care, from a reactive to a proactive stance; from a focus on *patients* who survive to *children* who thrive. At the Clinic for Special Children, we are committed to applying this preemptive model to other life-threatening conditions enriched in the populations we serve, and deeply value the community's partnership in that endeavor."

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The research was conducted by a team including the study's first author Kevin A. Strauss from the Clinic for Special Children, Strasburg, PA, USA, Penn Medicine-Lancaster General Hospital, Lancaster, PA, USA, and Departments of Pediatrics and

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About the Clinic for Special Children

The Clinic for Special Children (CSC) is a non-profit organization located in Strasburg, PA, which provides primary care and advanced laboratory services to children and adults who live with genetic or other complex medical disorders. Founded in 1989, the organization provides services to over 1,200 individuals and is recognized as a world-leader in translational and precision medicine. The organization is primarily supported through community fundraising events and donations. For more information, please visit www.ClinicforSpecialChildren.org