

**About PMD**

PMD (Pelizaeus-Merzbacher Disease) is a degenerative disorder caused by a mutation in the gene controlling the production of proteolipid protein (PLP), which is integral to the formation of myelin. Myelin is the substance that surrounds nerve fibers (axons) and provides the insulation necessary for proper transmission of electrical signals. Without myelin, nerve impulses are disrupted, resulting in deteriorating coordination, motor control and intellectual function.



The gene for producing PLP is found on the X chromosome. So males (who have just one X chromosome) are more likely to inherit the condition than females, who may inherit a normal X chromosome to offset the mutation in the other.

PMD symptoms typically appear in early childhood. Individuals with the milder form may have nearly normal life spans, but suffer from a decline in neurological function. The more severe form, congenital PMD, usually becomes apparent in the first few months of life. Early symptoms are often nystagmus (jerky side-to-side eye movement) and hypotonia (floppy muscle tone). Seizures and spasticity may develop as neurological function deteriorates. Severe neurological impairment, resulting in abnormal mental and physical development, is followed by premature death.

While symptoms may be mediated by medication for movement disorders, there is currently no standard course of treatment, nor is there a cure.

**The Bigger Picture**

The dysmyelinating neurodegenerative disorders known as leukodystrophies, of which PMD is just one, are relatively rare. Demyelinating disorders, in which once-healthy myelin is damaged or destroyed, are far more common, with multiple sclerosis and spinal cord injury each estimated to affect over 2 million people worldwide. Transverse myelitis and a certain type of cerebral palsy are other disorders in which disturbances of myelination play a key role. The potential of a cell-based therapy to treat myelin deficiencies represents hope for patients with these debilitating or fatal conditions.

**Milestones**

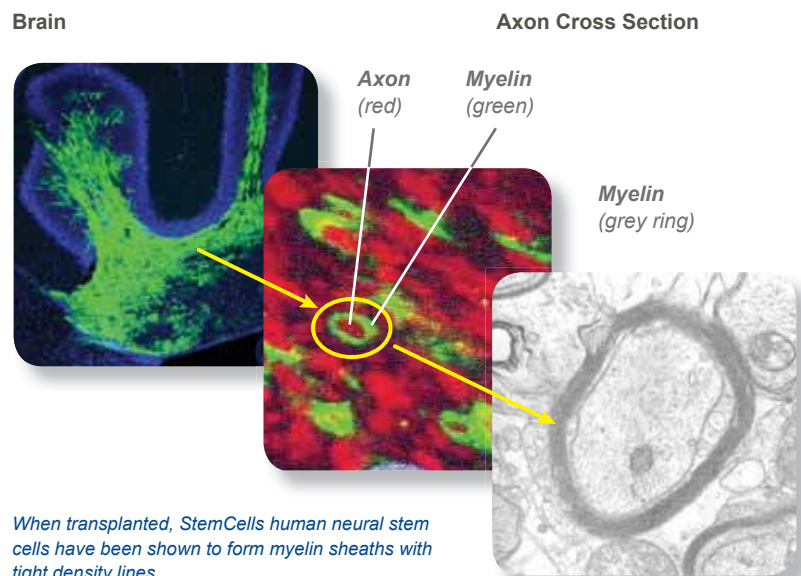
**StemCells, Inc. is conducting a Phase I clinical trial in PMD — the first ever neural stem cell trial in a myelination disorder.**

- ▶ **August 2005:** Initial preclinical myelination data published in the *Proceedings of the National Academy of Science* (Cummings, et al. 2005)
- ▶ **June 2008:** Additional preclinical myelination studies presented at the International Society of Stem Cell Research (ISSCR) *Annual Meeting*
- ▶ **December 2008:** Clearance received from the U.S. Food and Drug Administration (FDA) for an Investigational New Drug application (IND) to conduct a clinical trial of the StemCells HuCNS-SC product candidate in patients with PMD
- ▶ **November 2009:** Phase I clinical trial initiated at UCSF Children’s Hospital to evaluate safety and preliminary efficacy of HuCNS-SC human neural stem cells as a treatment for PMD
- ▶ **February 2011:** Enrolled and dosed fourth and final patient in Phase I clinical trial

**Preclinical Proof of Concept**

Preclinical studies performed by StemCells and its collaborators provide a rationale for potential therapeutic use of the Company’s HuCNS-SC product candidate in myelination disorders. StemCells has demonstrated that, when transplanted into an animal model of hypomyelination (shiverer mouse), its neural stem cells engraft and differentiate into mature oligodendrocytes and form myelin sheaths around host nerve fibers. StemCells is using this same approach to treat spinal cord injury, which is often associated with neuron loss and demyelination. Preclinical studies have shown that when transplanted into the spinal cord of injured mice, StemCells neural stem cells form myelin around the damaged nerve axons and restore lost motor function.

**Neural stem cells restore myelin in animal model of hypomyelination (shiverer mouse).**

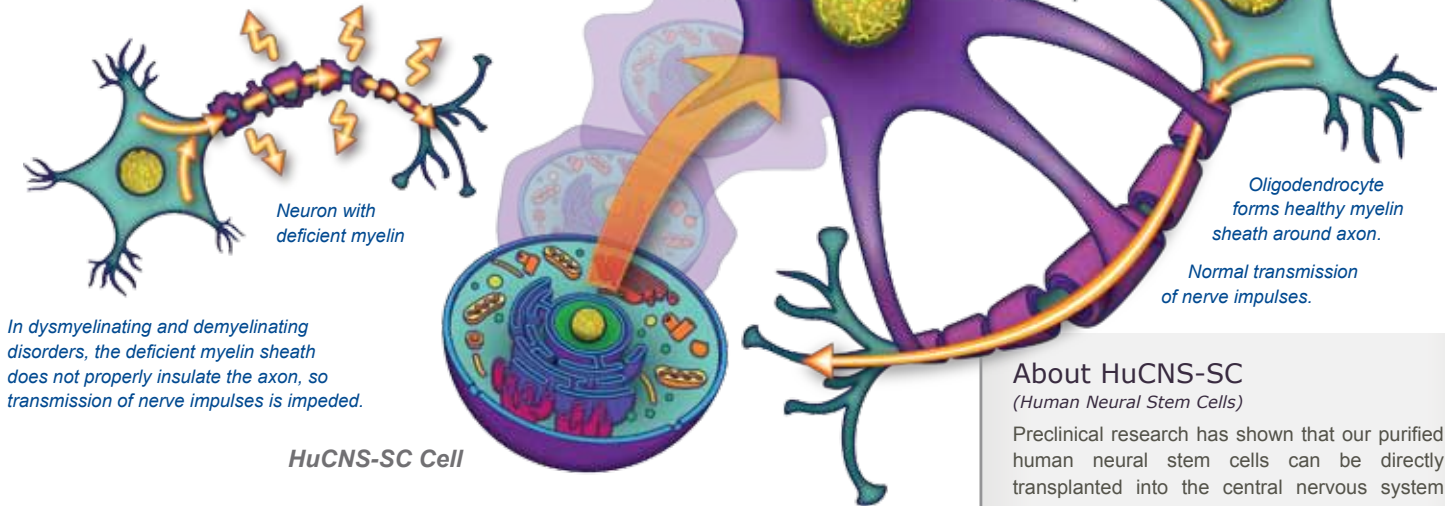


*When transplanted, StemCells human neural stem cells have been shown to form myelin sheaths with tight density lines.*

## Pelizaeus-Merzbacher Disease (PMD)

Oligodendrocytes develop appendages that wrap around the axons of nearby neurons, providing the insulation (myelin) needed for proper transmission of nerve impulses.

Myelin, comprised of fats, cholesterol and protein, is critical to healthy functioning of the central nervous system. The gene mutations responsible for PMD result in improperly produced or too much proteolipid protein (PLP), which proves toxic to the oligodendrocyte cells that make myelin.



In dysmyelinating and demyelinating disorders, the deficient myelin sheath does not properly insulate the axon, so transmission of nerve impulses is impeded.

**HuCNS-SC Cell**

### The StemCells Approach: Myelin Production to Protect Nerve Cells

When StemCells neural stem cells are transplanted, they migrate to the sites where myelin is deficient. They differentiate into oligodendrocytes and form healthy myelin sheaths to protect axons, helping nerve cells communicate with each other.

### Phase I Trial in PMD

In November 2009, StemCells, Inc. initiated a Phase I clinical trial of its HuCNS-SC human neural stem cells in PMD at the University of California, San Francisco (UCSF) Benioff Children's Hospital, one of the leading medical centers in the United States for neonatology, pediatric neurology and neurosurgery. In February 2010, the HuCNS-SC product candidate was used to treat the first patient enrolled in the trial, marking the first time that human neural stem cells have been transplanted as a potential treatment for a myelination disorder. In February 2011, the fourth and final patient was enrolled and dosed. Results of the trial will be reported in early 2012.

This is the second clinical trial of StemCells HuCNS-SC human neural stem cells. The first study, a Phase I Clinical Trial in NCL (neuronal ceroid lipofuscinosis), often referred to as Batten disease, was completed in January 2009. Data from the NCL trial demonstrated a favorable safety profile, along with evidence of engraftment and long-term survival of the HuCNS-SC cells.

The Phase I PMD trial is designed to assess the safety and preliminary efficacy of the HuCNS-SC product candidate in four patients with congenital PMD, the most severe form of the disease. While the primary focus in this trial is safety, StemCells will also be looking for evidence of new myelin formation in the patients' brains following transplantation, as well as any signs of improved neurological function. All patients were transplanted with HuCNS-SC cells, and will be immunosuppressed for nine months. Following transplantation, the patients will be evaluated regularly over a 12-month period in order to monitor and evaluate the safety and tolerability of the HuCNS-SC product candidate, the surgery and the immunosuppression. In addition, MRI examination of the brain post-transplant may enable the measurement of new myelin formation. StemCells plans to follow the effects of this therapy long-term so, as with its Phase I NCL trial, this trial will also be followed by a separate, four-year observational study.

### About HuCNS-SC

(Human Neural Stem Cells)

Preclinical research has shown that our purified human neural stem cells can be directly transplanted into the central nervous system (CNS), after which they engraft, migrate and differentiate into neurons, astrocytes and oligodendrocytes, surviving long-term with no sign of tumor formation or adverse effects. This suggests the possibility of a durable clinical benefit following a single transplantation. In 2009, data from our first clinical trial demonstrated the safety and tolerability of our HuCNS-SC product candidate and the transplantation process. Additional data reported in 2011 provides evidence that HuCNS-SC cells persist long after immunosuppression is discontinued. We are currently developing our HuCNS-SC product candidate for the treatment of several indications including:

- Spinal cord injury (Ph. I/II trial underway)
- PMD (Ph. I trial underway)
- Retinal disorders (Ph. I trial targeted for 2012)
- Alzheimer's disease and stroke (preclinical)

Processed in compliance with cGMP standards, our HuCNS-SC cells can be expanded, cryopreserved and then stored in banks for future use as "stem cells in a bottle."

### About StemCells, Inc.

Driven by nearly 20 years of pioneering research and innovation, StemCells, Inc. is applying its scientific and industry leadership in stem cell biology to discover, develop and commercialize novel therapeutics and enabling tools and technologies for use in stem cell-based research and drug discovery.

#### USA

7707 Gateway Blvd.  
Suite 140  
Newark, CA 94560  
T +1 (510) 456-4000

#### EUROPE

Minerva Building 250  
Babraham Research Campus  
Cambridge CB22 3AT UK  
T +44 (0) 1223 499161

[www.stemcellinc.com](http://www.stemcellinc.com)