Researchers in the Department of Neuroscience are not far off a Phase I clinical trial of a new therapy for spinal muscular atrophy (SMA). This rare neurodegenerative disease affecting babies and children is caused by mutations to a single gene (SMN), which cause motor neuron injury leading to serious muscle weakness and respiratory problems. Half of children with SMA die by the age of two.

Professor Mimoun Azzouz, Chair of Translational Neuroscience at the Sheffield Institute of Translational Neuroscience (SiTraN), has been investigating a gene therapy for SMA for over twelve years. Recent research data has provided promising proof of concept for Resagen, a potential gene therapy product for patients with SMA. Applying this research could lead to a safe and effective treatment, but further studies are needed before starting clinical trials.

Pre-clinical work

Using a modified virus as a vehicle for delivery, Resagen restores the missing survival motor neuron protein. It is given intravenously and crosses the blood–brain barrier.
barrier to reach the affected cells in the spinal cord. Studies with mice have proved the concept – mice with the genetic mutation can survive for only two weeks, but after the therapy they can survive for over 200 days. The model can be translated to humans.

**Orphan designation**

Because spinal muscular atrophy is such a rare condition, it was important for the potential therapy to secure ‘orphan drug designation’ from the European Medicines Agency. This status allows investigators to benefit from EU incentives, such as reduced fees and protection from competition, designed to encourage the development of medicines for rare diseases.

**MRC funding**

Support from the Medical Research Council’s Developmental Pathway Funding Scheme is enabling the team to continue the pre-clinical development of Resagen. Lasting two years, the funding will help them develop a protocol for manufacture, as well as conducting toxicity and safety studies.

Both the orphan designation and the MRC funding are key to smoothing the path towards clinical trials. Healthcare Gateway Business Managers Martin Whitaker and Susan Smith have supported the SITraN team with the applications.

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**Next steps**

Once data from the safety studies has been collected, the teams will start preparing a dossier of evidence for a licence for clinical applications. Professor Azzouz hopes that a Phase I clinical trial of Resagen will begin in the third quarter of 2014, although further financial backing will be needed and more partners will be sought.

**Future potential**

If SMA is caught early, this therapy has the potential to stop the progress of the disease. Replacing levels of the survival motor neuron protein will greatly improve chances of prolonging life. Proving that the virus vehicle works for gene therapy could also have implications for other inherited monogenetic disorders.

Professor Azzouz is encouraged by recent results: “The data is promising, and now we need to take it to the next step. It would be fantastic for us to translate this programme to human applications in SMA patients. It’s a long process but the important thing is to make sure that something comes out of it.”