PRODUCT PROFILE

Innurex®
A Gene-based Neural Cell Regeneration Therapeutic

PRODUCT DESCRIPTION
Innurex is a novel gene-based therapeutic for nerve repair. Oxford BioMedica's LentiVector® technology is the most versatile technology currently available for delivering genes to cells of the central and peripheral nervous system. Innurex is a product that uses this technology to deliver a gene that induces neurons to produce neurite outgrowths. This strategy opens the possibility of creating new nerve connections to repair spinal injury.

MARKET
Spinal cord injuries affect approximately 40 people per million per annum, with a total prevalence of 750 per million. At the time of injury the average age of patients is 32, 55% are aged 16-30 and 80% are male. Most injuries occur as a result of trauma, with motor vehicle accidents (44%), acts of violence (24%) and falls (22%) being the most common causes. The cost of care varies in the first year from about £150,000 to £350,000 depending upon the severity of the injury (paraplegia vs. quadriplegia) and then ranges from £20,000-£75,000 per annum for subsequent years. Spinal cord injuries are devastating and, while survival is good (85% of patients who survive the first 24 hours are alive after 10 years), prognosis for significant functional recovery is poor. Market estimates for Europe and the USA range from US$0.5-2.0 billion.

PRODUCT RATIONALE
The effects of injuries to the central nervous system are devastating and often permanent (Figure 1). Stumps of transected axons will completely fail to regenerate and as neurons are unable to divide, they cannot produce daughter cells to replace old or dying cells in a similar manner to the rest of the body. Current therapies are limited. Clinical management of spinal cord injury in the immediate aftermath of an injury aims to stabilize the spinal cord, to treat and inhibit the onset of inflammation (and thus relieve spinal cord compression) and to limit necrotic and apoptotic cell death. The success rate is low.

Treatment strategies under development at Oxford BioMedica include seeking to initiate regenerative processes by stimulating axonal growth with neurotrophins that may additionally act as neuroprotective agents, promoting new growth through substrate or guidance molecules, or blocking molecules that inhibit regeneration. The RAR?2 gene used in Innurex is a subtype of the retinoic acid receptor (RAR). These receptors are ligand-activated nuclear transcription factors and addition of RA (the biologically active derivative of vitamin A) to cells expressing these receptors induces transcription of neurotrophin genes. These, in turn, stimulate neurite outgrowth and, potentially, the establishment of new connections and nerve maintenance and repair.

PRODUCT
Innurex: A gene-based product for nerve repair in spinal injury.

INDICATION
Traumatic spinal injuries.

MARKET
Estimated worldwide market of US$0.5-2.0 billion.

TECHNICAL DESIGN
LentiVector delivering the human RARß2 gene, a proprietary nuclear retinoic acid receptor gene, to induce neurite outgrowth in damaged nerves.

CLINICAL STATUS
Preclinical proof-of-concept successfully completed. Clinical plan is being defined.

COMMERCIALISATION STRATEGY
Commercial partners sought for clinical development and marketing.

PARTNERS/FUNDING
King's College London, UK
The Christopher Reeve Paralysis Foundation, USA (grant awarded to King's College)

DEVELOPMENT STATUS

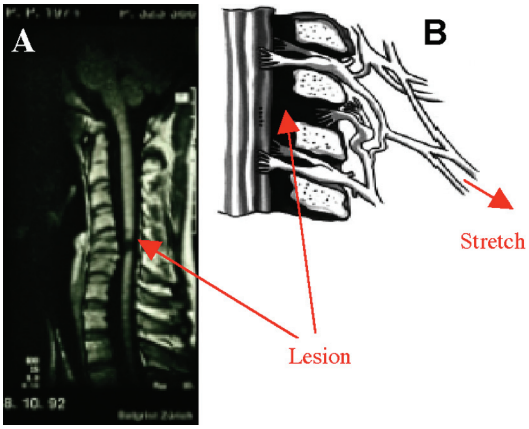
- *In vitro* studies with Innurex have shown expression of RARß2 and substantial neurite outgrowth from adult spinal cord (Figure 2). Similar data were obtained in dorsal root ganglia.
- Avulsion injury preclinical studies with Innurex have shown regeneration of neurons from the dorsal root ganglia back into the spinal cord and also the restoration of function to damaged limbs.
- A placebo-controlled preclinical model of spinal cord injury with Innurex showed statistically significant improvements in both sensory and motor function. The data were presented at the ASGT annual meeting in June 2005 and published in Nature Neuroscience in February 2006.
- These data suggest that Innurex may be useful in the clinical treatment of both stretch injury and also spinal cord damage.
- Further preclinical studies are being conducted and a clinical plan for initial trials of Innurex is being defined.

PARTNERSHIP OPPORTUNITIES

Oxford BioMedica is seeking partners for development of Innurex, and is particularly

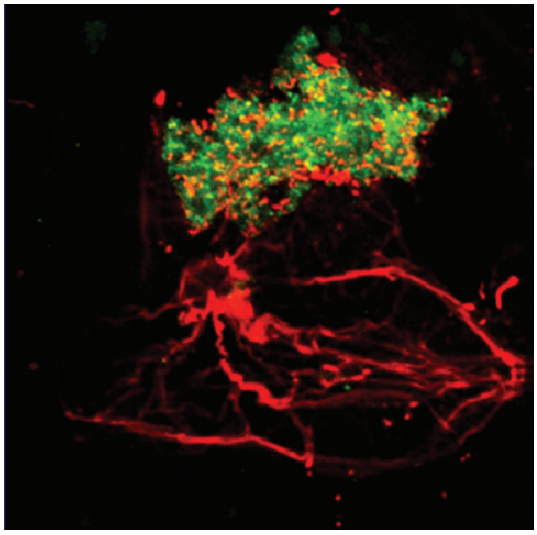
interested in companies with existing programmes in nerve regeneration, or those wishing to establish a market position based on this novel product.

FIGURE 1: THERAPEUTIC TARGETS



(A) Complete spinal cord lesion as indicated by the arrow. (B) An example of spinal root avulsion that may be caused by over-stretching peripheral nerves.

FIGURE 2: NEURITE OUTGROWTH STIMULATED BY INNUREX



Adult spinal cord explant transduced with Innurex. Cells transduced with RARß2 are labelled with an anti-Flag antibody (green) and neurite outgrowth is visualized with an anti-neurofilament antibody (red). These data show for the first time neurite outgrowth from a spinal cord explant.

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