SpineThera, Inc.
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Novel 'micro-suspension' drug for epidural injection

SpineThera is developing a sustained-release injectable drug for back pain with the aims of improving safety and reducing the need for repeated epidural injections of corticosteroids.

Epidural steroid injections have been used for decades to treat back pain. In the United States, for example, where the US Food and Drug Administration (FDA) has not approved any corticosteroid product for injection into the epidural space of the spine, 7 million such injections are given every year. An analysis of US healthcare-claims data shows that 40% of these are repeat procedures given within 90 days of the first injection, suggesting a limited duration of pain relief from a single injection of currently available corticosteroids.

A risk of serious neurologic events has been reported with such treatments, particularly when corticosteroid suspension formulations are used. These suspensions may be linked to an increased risk of embolism after inadvertent injection into a spinal artery[1]. In 2014, the FDA issued a class warning statement that injection of corticosteroids into the epidural space of the spine may result in rare but serious adverse events, including loss of vision, stroke, paralysis and death[2].

"At SpineThera, we are developing a long-acting injectable corticosteroid that is intended to reduce the need for repeat injections and also address the risk of serious adverse events," said Jeff Missling, founder and CEO of SpineThera. By designing a sustained-release drug formulation that meets the unique safety requirements of a transforaminal epidural injection to treat lumbar radiculopathy, the company aims to improve on the health outcomes currently achieved with off-label use of generic corticosteroids.

Founded in 2012 and based in Plymouth, Minnesota, USA, SpineThera is a privately held, preclinical-stage pharmaceutical company that operates under a semi-virtual model. A team of four employees at the company's clean-room pilot plant focuses on developing and making the sustained-release formulations, and analytical testing is outsourced. SpineThera is leasing space and has a shared services agreement with an established contract manufacturing organization to minimize overhead costs. It works with consultants to access specialist advice and has also established a medical advisory board, which includes leading physicians who routinely perform epidural steroid injections and conduct research in the field of pain medicine.

Injectable micro-suspension

SpineThera's lead drug product candidate, SX600, is currently in preclinical development. The active ingredient, dexamethasone acetate, has been reformulated into an injectable micro-suspension containing microspheres that are much smaller than the particles in a standard corticosteroid suspension. The active drug is encapsulated within these tiny biodegradable microspheres, which provide sustained release. SpineThera can optimize its patent-protected formulations for different applications by altering the properties of these microspheres.

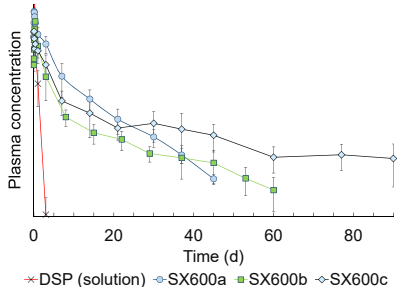

Figure 1: A preclinical canine epidural study demonstrated 45, 60 or 90 days of *in vivo* corticosteroid exposure, depending on the formula, after a single epidural injection of SpineThera's sustained-release micro-suspension drug. SX600a, SX600b and SX600c are three different formulations that demonstrate SpineThera's ability to tune and control the sustained-release profile. Dexamethasone sodium phosphate (DSP) solution provided only 3 days of exposure.

In order to achieve sustained drug release from the microspheres, SpineThera has overcome an important formulation challenge. "Of course, the smaller you make the microspheres, the harder it is to obtain a long-term sustained release from them because the main mechanism for that is diffusion of the drug out of the microsphere," said Missling. "A bigger microsphere has a longer diffusion path length, and the drug will be released more slowly."

SpineThera has also addressed the safety concerns associated with epidural administration of corticosteroid suspensions by making the SX600 microspheres smaller than a red blood cell. "We believe these non-aggregating microspheres are small enough to pass through a capillary bed if inadvertently injected into a spinal artery, thereby minimizing the risk of serious adverse events, such as paralysis," said Missling.

Pharmacokinetic results from a preclinical canine epidural study reveal a promising sustained-release profile, which could minimize the need to administer repeated injections of corticosteroids. The canine plasma concentration of dexamethasone was cleared completely within 3 days after a single epidural injection of dexamethasone solution (which has not been implicated in cases of paralysis)[1], whereas it remained detectable for 45, 60 or 90 days when three different SpineThera micro-suspension formulations were injected (**Fig. 1**).

"We have shown that we can achieve sustained-release and long-term drug exposure from a single epidural injection," said Missling. "Our hypothesis is that if we can deliver the drug for 45 to 90 days, patients should get pain relief for that period of time or beyond."

Multiple benefits

By reducing or eliminating the need for repeated epidural corticosteroid injections, SX600 has the potential to improve treatment outcomes, reduce the risk of adverse events and yield more manageable overall treatment costs compared with currently available options.

Patients could not only gain a long-term therapeutic benefit from fewer injections, but also benefit from a reduced risk of infection or other adverse events associated with the transforaminal injection procedure. Physicians could potentially treat more patients successfully, which could be beneficial whether payments are made through a fee-for-service model or under an accountable care organization (ACO) model for outcomes in a patient population. If SX600 received FDA approval, physicians would also finally have access to an FDA-approved corticosteroid product for injection into the epidural space of the spine.

The preclinical development program for SX600 is continuing in preparation for early-stage clinical trials.

SpineThera has already raised $4 million from angel investors, plus an additional $300,000 in nondilutive government funding, and is open to partnering opportunities.

"We believe that our preclinical development program will put SpineThera in a good position to develop future products for spine-related diseases that may use different active ingredients, as well as apply our existing product to other disease states," said Missling.

1. Racoosin, J.A. *et al. N. Engl. J. Med.* **373**, 2299–2301 (2015).
2. US FDA. Drug Safety Communication. http://www.fda.gov/Drugs/DrugSafety/ucm394280.htm (2014).

contact
Jeff Missling, Founder & CEO
SpineThera, Inc.
Plymouth, Minnesota, USA
Tel: +1-612-508-4795
Email: jmissling@spinethera.com