Fact Sheet on SER-214

This fact sheet briefly describes Serina Therapeutics' experimental drug candidate SER-214, and how we are planning to use this to treat patients with Parkinson's disease.

What is a "POZ polymer conjugate" ?

Polymers of poly(2-ethyl-oxazoline), the chemical "building block" of our proprietary polymer, are referred to as POZ. POZ polymers can be made in many different sizes and architectures (branched, linear, pendent). We have developed methods for attaching a drug to POZ, as in the case of SER-214, and we refer to that as a POZ polymer conjugate.

What is SER-214 ?

SER-214 is a POZ polymer conjugate that is 20,000 daltons in molecular size with ten pendent rotigotine molecules attached to it. Rotigotine is a potent dopamine agonist that can replace the missing chemical in the brain known as dopamine. Serina chemists have developed chemical linkers to attach rotigotine to the polymer backbone, and one of those chemical linkers was found to precisely control the rate of release of rotigotine from the polymer so that it could be administered once a week in a standard insulin-type syringe by subcutaneous injection. We developed this drug candidate to treat patients with Parkinson's disease.

What is Parkinson's disease ?

Approximately 500,000 to 1,000,000 people in the US and as many as 7 million people worldwide suffer from Parkinson's disease (PD). The average age of onset is approximately 62 years. It is the second most common neurodegenerative disease after Alzheimer's. There is no cure or therapy that slows disease progression. PD is characterized clinically by both motor and non-motor symptoms. Motor symptoms include tremor, rigidity, slow movement (bradykinesia), and loss of the ability to initiate movement (akinesia) (collectively,

the “off” state). Pathologically, the disease is characterized by degeneration of dopamine-producing nerve cells in the substantia nigra pars compacta, and this degeneration of the dopamine centers in the brain leads to deficiency of dopamine. Thus, therapies are often aimed at providing dopamine-like drugs, such as rotigotine, to the patient so it can get to the brain and restore function.

Why develop a drug like SER-214 ?

SER-214 was developed as an approach to treat patients with Parkinson’s disease. Many of the drugs used to treat PD have to be taken several times a day, and none of the current therapies deliver a “steady-state” level of the drug – which is what the brain normally does when it generates its own dopamine. Thus, many of the drugs used to treat PD are prone to “wearing off” - they simply don’t work as well over time and you have to keep escalating the doses, or they induce dyskinesia - involuntary motor movements that result from long-term use of some of the PD drugs like levo-dopa / carbidopa combinations.

SER-214 was designed to release the attached drug rotigotine in a continuous manner so that each weekly injection of SER-214 results in a steady-state level of rotigotine in the blood. SER-214 itself does not cross the blood brain barrier and get into the brain; instead, Serina scientists believe an enzyme in the blood “clips” the rotigotine from the polymer as it circulates in the blood and this releases the rotigotine into the plasma. The rotigotine is then taken up directly by the brain, and replaces the deficiency of dopamine in the brain. Rotigotine is in a class of drugs known as “dopamine agonists” – that means it acts like dopamine in the brain and restores normal function to certain parts of the brain. In this manner, patients with PD who have significant motor fluctuations can restore those motor functions closer to normal.

In experimental studies Serina scientists have shown that SER-214 provides continuous drug delivery of rotigotine, and that results in what we refer to as “continuous dopaminergic stimulation” (CDS) – a long-sought clinical strategy that mimics what occurs normally in the brain.

Does SER-214 work ?

In experimental studies conducted by Serina scientists SER-214 was found to reverse the motor fluctuations that are characteristic of PD in animal models of this disorder. You may find some publications on this by visiting www.serinatherapeutics.com.

Is SER-214 an approved drug ?

SER-214 is not yet approved for prescription use in PD patients. Serina Therapeutics has received approval from the Food and Drug Administration (FDA) to begin a clinical study in PD subjects in late 2015. That study is called a Phase I study, as it will be aimed primarily at determining if SER-214 is safe, tolerable and provides pharmacokinetic results similar to what was observed in experimental animals. Subjects who enroll in the SER-214 Phase I study will undergo informed consent to participate in an experimental study of this nature, and assessments of safety, tolerability and plasma levels of the drug will be determined. Serina Therapeutics expects to enroll approximately 20 subjects in this study by the end of 2016.

Can SER-214 be used to treat other disorders ?

SER-214 may be useful in other disorders of dopamine insufficiency. One such disorder is known as restless leg syndrome (RLS). Patients with RLS have been shown to respond to the same drug that is attached to SER-214 – namely rotigotine. Serina believes SER-214 would be useful in RLS as well, but at this time Serina Therapeutics has no plans to begin such a study.

If I am a patient with Parkinson's disease, how do I find out more about this study ?

If you are a patient with PD you and your physician can find more information on the Phase I SER-214 study by visiting ClinicalTrials.gov at this link – https://clinicaltrials.gov/show/NCT02579473, or the Michael J Fox Foundation website at https://foxtrialfinder.michaeljfox.org/trial/4237/.