Serina Therapeutics

Randall Moreadith, MD, PhD President and CEO

SER-214

POZ-Rotigotine

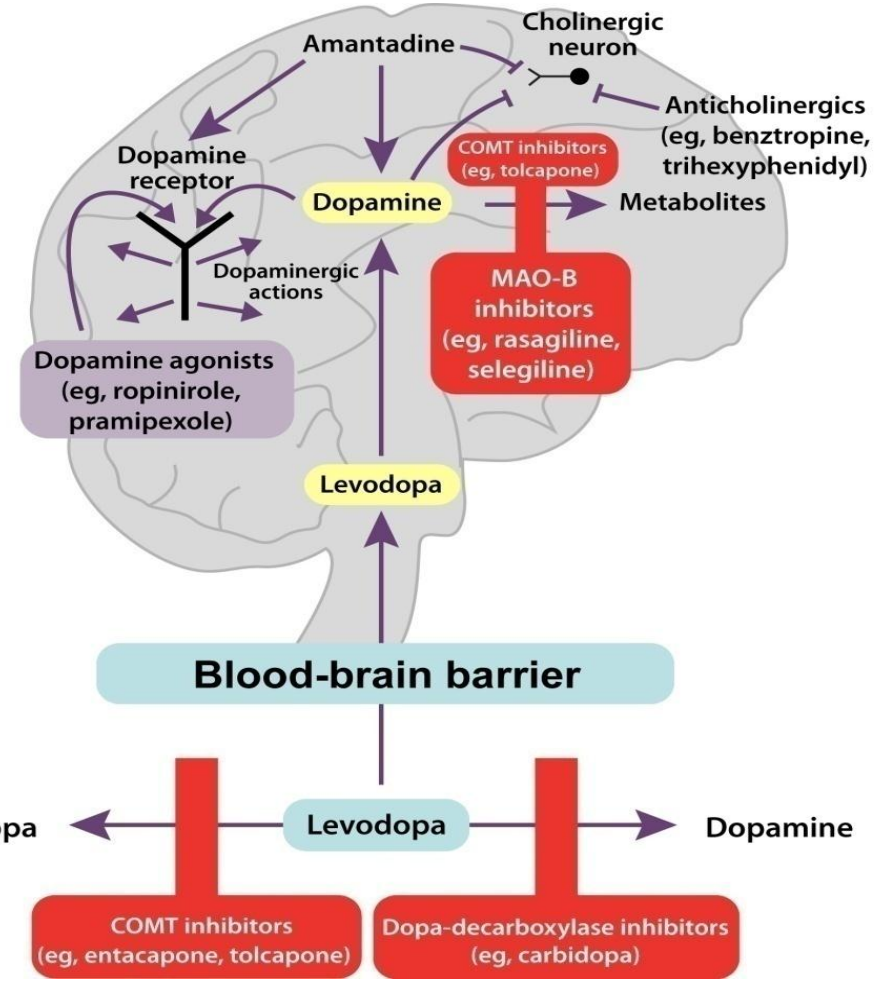
A Once-per-week SC Injection that Provides Continuous Drug Delivery

Parkinson's Disease

"Do you think you could use your polymer technology to develop a drug to treat Parkinson's disease ?"

Serina shareholder and patient with Parkinson's disease

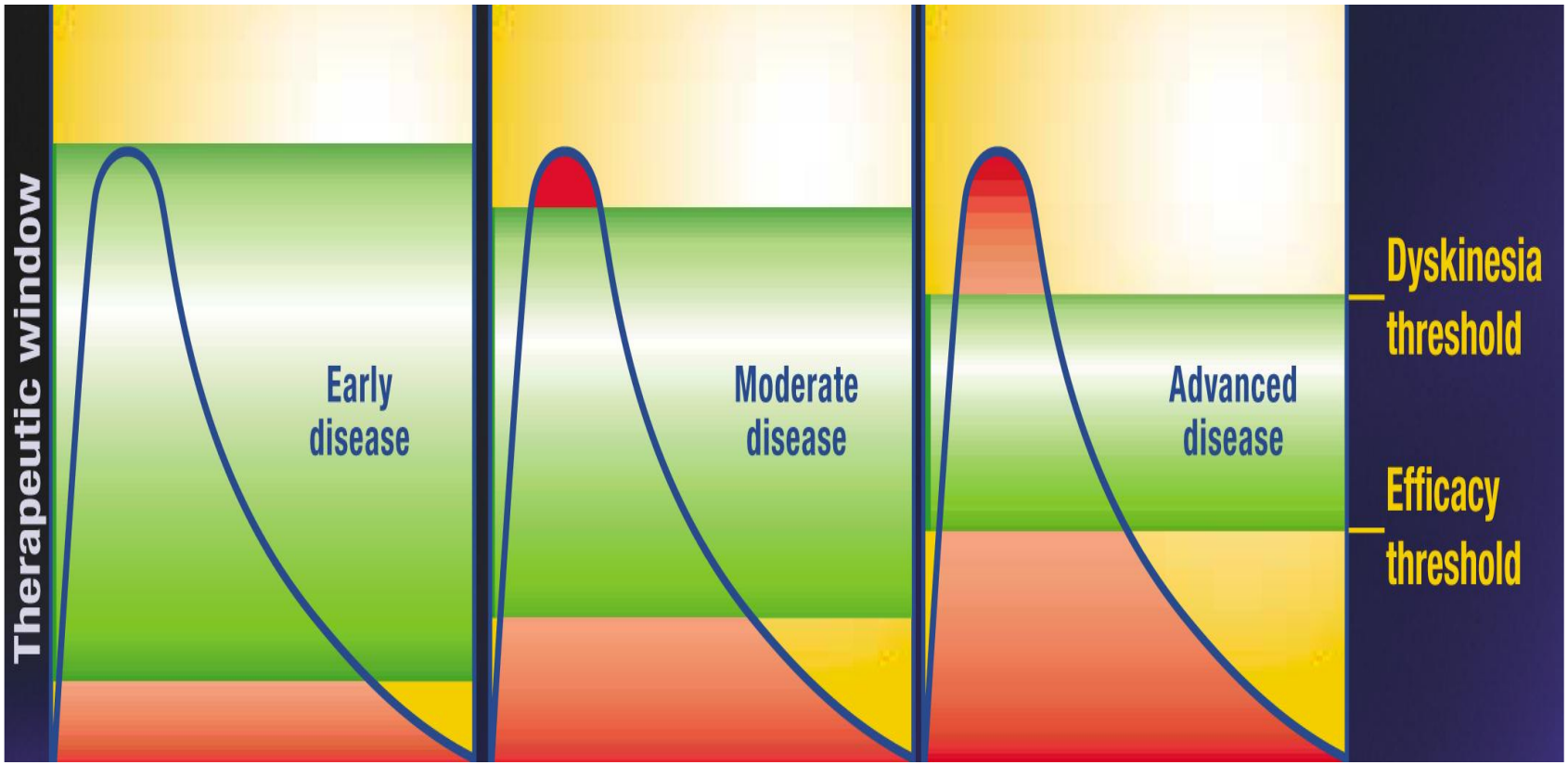
Parkinson's Disease



Of the current drugs for Parkinson's disease the dopamine agonists had some attractive features for a POZ conjugate approach …

The "Therapeutic Window" For Treatment of Parkinson's Disease

Current Drugs – "wearing off" and dyskinesia



Adapted from: Stocchi F, et al. *Eur Neurol*, 1996.

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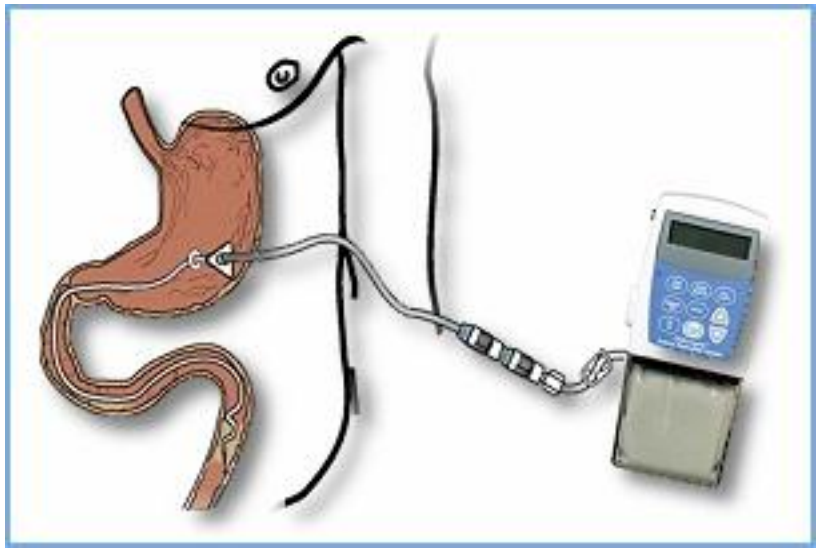
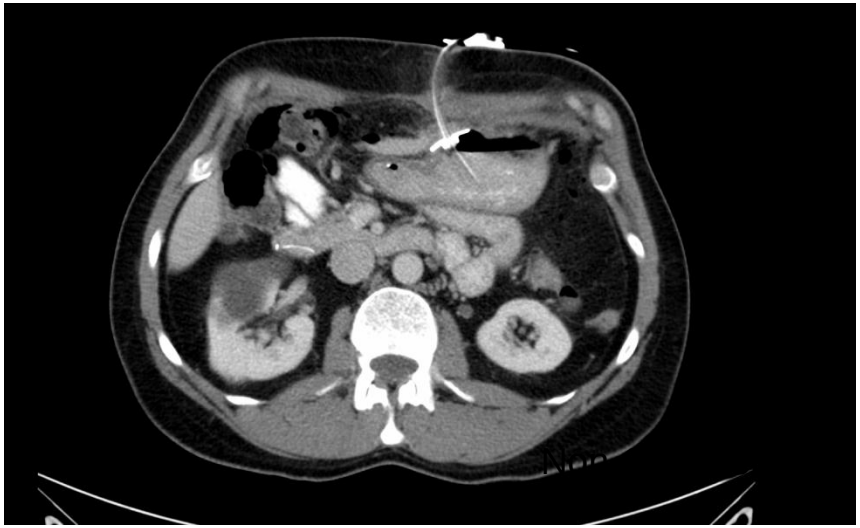
None of the approved drugs for PD deliver CDS … but would it work ?





Summary

- **Study Design**
  - Double-blind, double-dummy trial of levo-dopa gel infusion (37 patients) versus levo-dopa sustained release capsules (34 patients) *
  - Endpoint was reduction in "off" time and corresponding increase in "on" time (without troublesome dyskinesia) during 12 weeks of administration
  - **Results :**
    - *Mean "off" time decreased by 4 hrs – $p < 0.0015$ – compared to capsules*
    - *Mean "on" time increased by 4.1 hrs – $p < 0.0059$ – compared to capsules*
  - Expert Commentary
    - *"This study shows that levo-dopa gel infusion provides a definite advantage in patients with advanced Parkinson's disease … and the results appear similar to those obtained with deep brain stimulation," Dr. Stanley Fann*

**** Principal Investigator C. Warren Olanow, MD, Serina Clinical Advisory Board. This is the only study of its kind in the Parkinson's literature. It is being developed by AbbVie.***

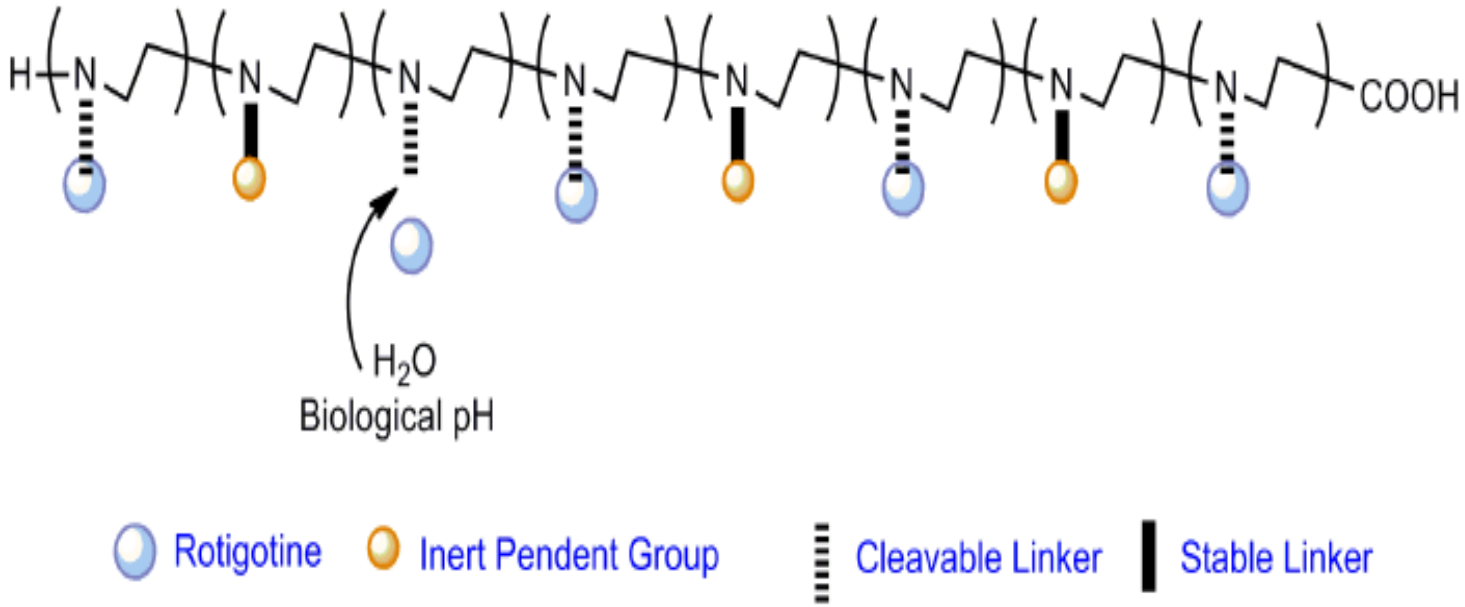
SER-214

Product Concept

- **Target Product Profile**
  - Subcutaneous delivery ***once a week*** in a standard insulin or tuberculin syringe (injectate ~ 0.5-1 cc)
  - Prompt onset of dopaminergic "tone" (within 20-30 min)
  - Steady-state levels of dopamine agonist within a relatively narrow therapeutic window
  - Sustained levels of dopamine agonist for approximately one week ("continuous dopaminergic stimulation")
  - Consistent levels of dopamine agonist upon repeat dosing
    - *Week-to-week drug exposure and half-life do not vary widely, and do so within the therapeutic window for control of symptoms*

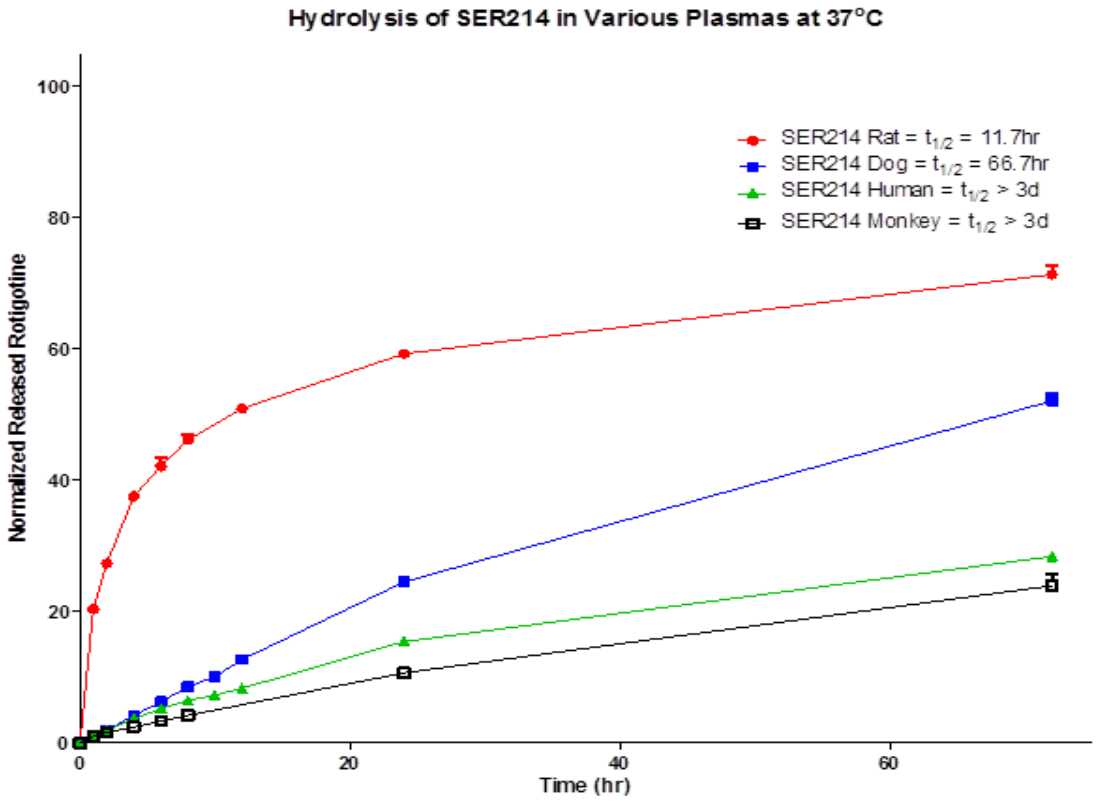
SER-214

20 kDa POZ polymer with 10 rotigotine molecules



PK Profiles in Plasma

SER-214 "slow release"

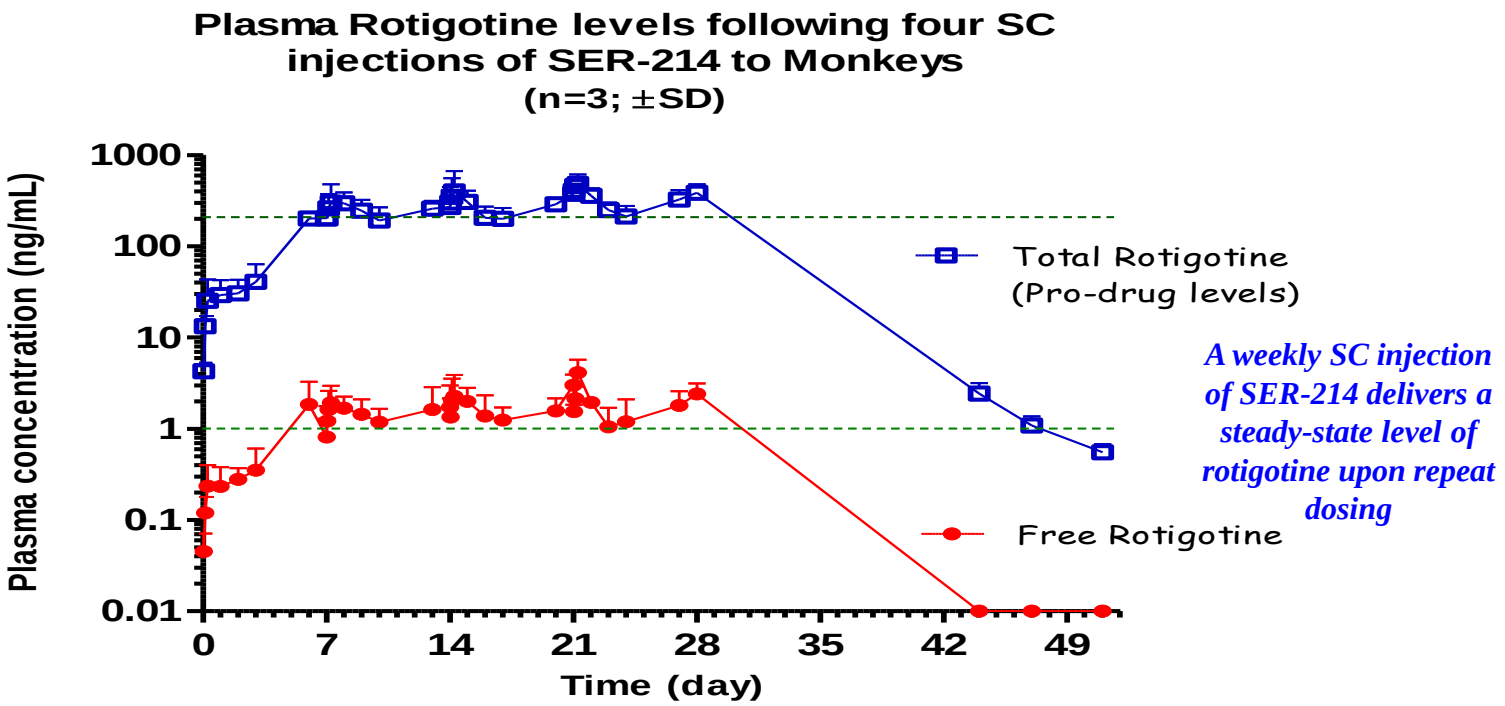


SER-214 showed a marked difference in release rates, with a half-life of ~ 11 hours in the rat and > 3 days in monkey and human (the same linker:drug attached to PEG or polydextrans releases completely in < 10 minutes)

MPTP Monkey Model
Study Design

- The study is a twelve week PK and PD study to assess the efficacy and safety of a weekly SC injection of SER-214 versus a twice daily oral dose of L-DOPA versus polymer alone
- Adult monkeys (6-7 YOA) were treated with daily MPTP for several months
  - MPTP is a mitochondrial toxin that disrupts the electron transport chain
  - Progressive exposure to MPTP results in a profound state of "Parkinsonism" in monkeys due to selective degeneration of the pre-synaptic dopaminergic neurons in the *substantia nigra*
  - This has served as the non-human primate model for every drug that has been approved for Parkinson's disease
  - ***The results are …***

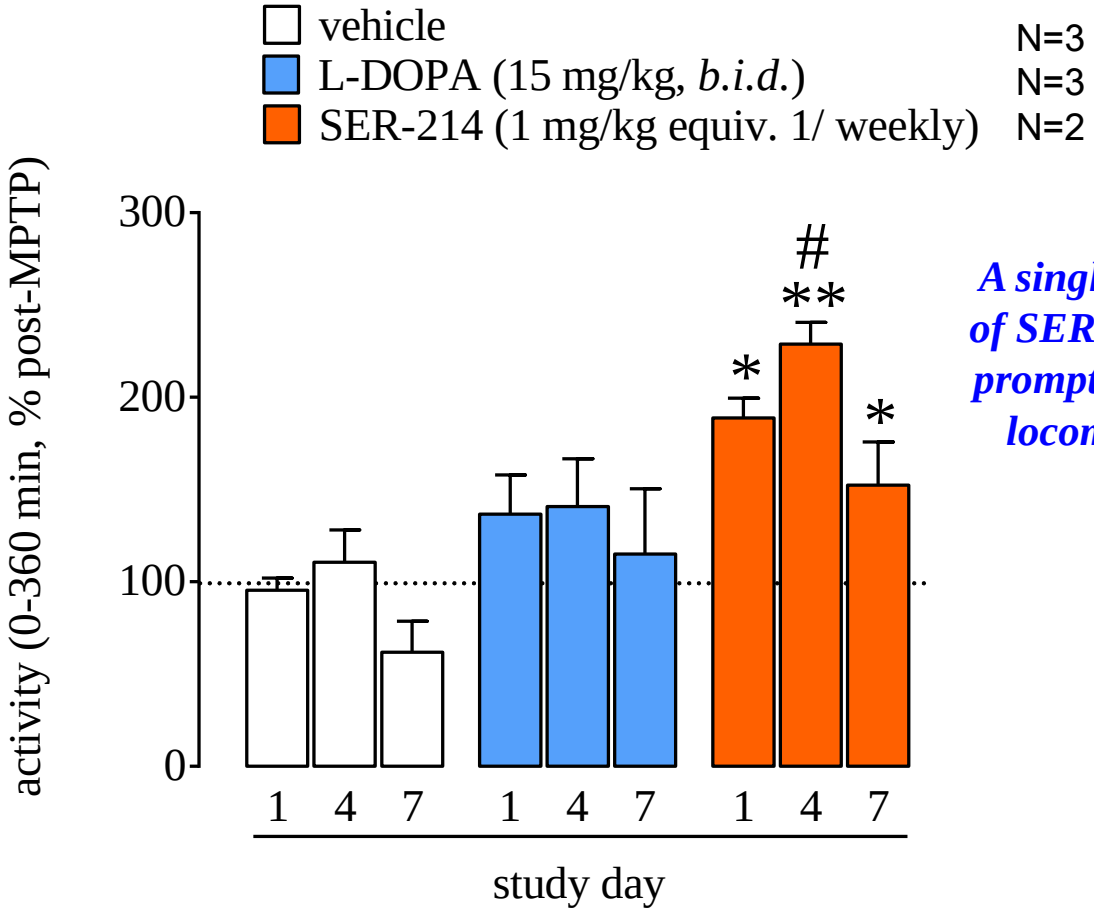
Preliminary Results
PK Profiles



A weekly SC injection of SER-214 delivers a steady-state level of rotigotine upon repeat dosing

Total rotigotine refers to total amount of rotigotine released by alkaline hydrolysis

Preliminary Results (Week Two)

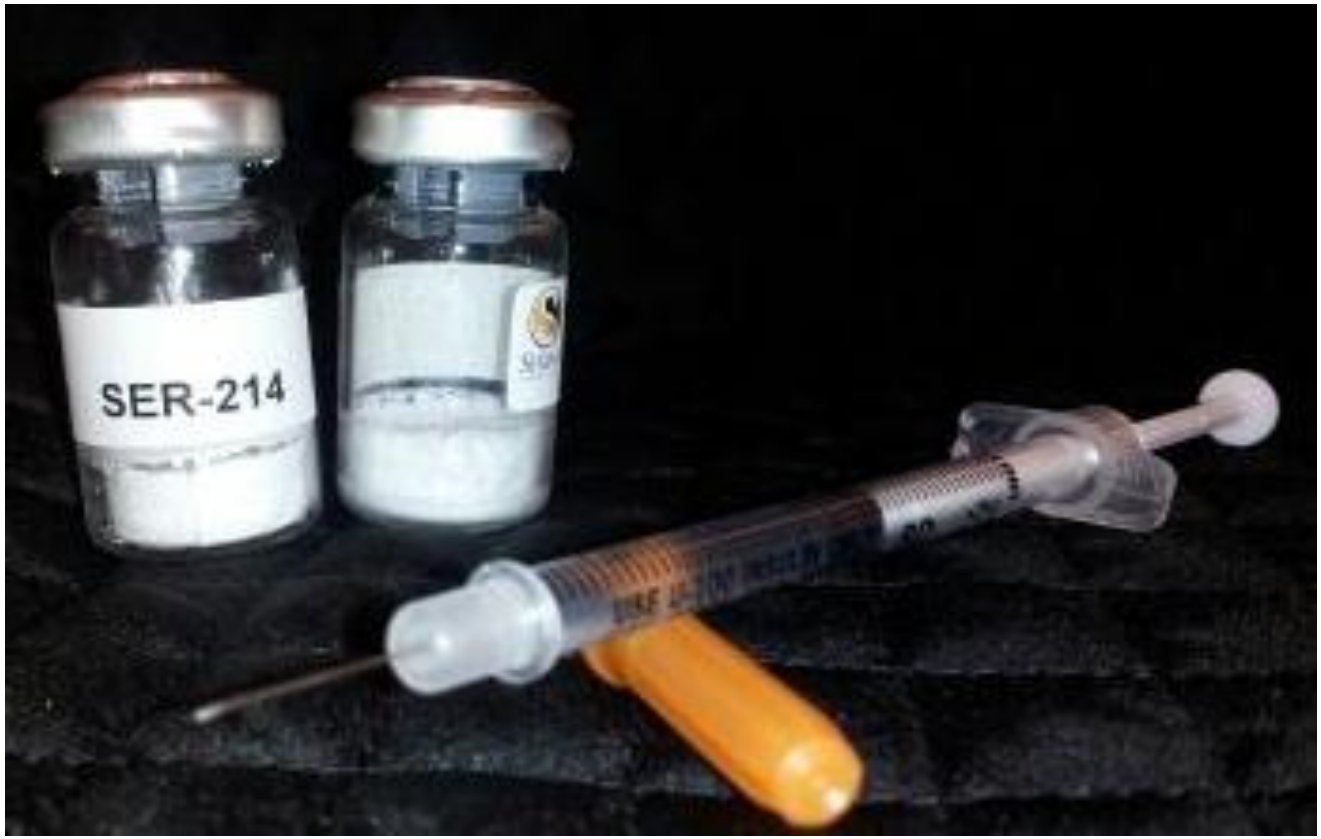


A single SC injection of SER-214 promotes prompt and sustained locomotor activity

Preliminary Results

- SER-214 appears to be safe – no adverse events reported in the monkeys to date
  - Polymer control is safe, and shows no evidence of efficacy
- L-DOPA twice daily promotes prompt, but non-sustained locomotor activity (as expected for this model)
  - ***Monkeys in the L-DOPA group have all developed dyskinesia***
- SER-214 promotes prompt, sustained locomotor activity in severely impaired MPTP-lesioned monkeys
  - ***None of the SER-214 treated monkeys have developed dyskinesia <u>after 12 weeks of dosing</u>***
- Plasma PK profile (first four weeks) demonstrates continuous drug delivery with steady-state levels of plasma rotigotine in the therapeutic window for CDS

Formulation



Development Milestones And Timelines

- IND-enabling Toxicology
  - *In vitro* Metabolite Profiles (GLP) – ***Complete***
  - Rat single dose MTD and PK (GLP) - ***Complete***
  - Dog single dose MTD and PK (GLP) - ***Complete***
  - Rat 6 week and 12 week PK (non-GLP) - ***Complete***
  - Rat Chronic Dose 3 Month Study (GLP) - ***Complete***
    - Observed effect identified, and NOAEL identified
  - Rat ADME Study
    - QWBA – ***Complete***
  - Rat 6-OHDA Efficacy – ***Complete (Published)***
  - ***Planned pre-IND Meeting with the Agency in June***
- cGMP Campaign
  - Underway - ***Demo Batches Complete***

Strong IP Position

Issued on SER-214

- **US 8,383,093 B1 – Issued February 26, 2013**
- **US 8,597,633 B2 – Issued December 3, 2013**
  - ***Subcutaneous delivery of poly(oxazoline) conjugates***
  - ***"… a heterofunctional POZ of a general formula containing a dopamine agonist (all dopamine agonists)"***
  - Composition of matter on SER-214
    - Which includes controlled release of the attached dopamine agonist
    - Covers all classes of dopamine agonists and some other classes of drugs
  - Method of treating a disease with a heterofunctional POZ-dopamine agonist where the disease is a dopamine-responsive disorder
  - Subcutaneous delivery of POZ-therapeutics
  - Specifically covers Parkinson's disease

Summary

- ***SER-214***
  - Target Product Profile achieved
  - Parkinson's disease models (rat and monkey)
    - At least as efficacious as levo-dopa in MPTP monkey model (Week 2)
    - ***All*** monkeys in levo-dopa:carbidopa cohort have developed dyskinesias
    - ***None*** of the monkeys in the SER-214 cohort have developed dyskinesias
- ***Market Research (100 Neurologists – movement disorder specialists)***
  - Twice market share of Neupro in un-blinded product profile
  - Would be used as first-line therapy in new onset patients as a levo-dopa sparing strategy
  - Transition therapy for patients experiencing "wearing off" and early dyskinesias
- ***Executed partnership with AstraZeneca in January 2013***
- ***Executed partnership for development of polymer-ADCs with Scripps 2013***
- ***Exclusive license to "click chemistry" to POZ***
  - Unlimited right to sublicense

Acknowledgements

The Serina Team

Our Shareholders

Dr. David Standaert

Chairman, Division of Neurology, UAB

Dr. Warren Olanow

Chairman Emeritus, Mt Sinai Medical Center

The Atuka Team

Montreal, Canada