Cynapsus Therapeutics Inc.
Lead PI: Albert Agro

Organization and Team Overview

Cynapsus is a specialty pharmaceutical company developing a convenient and easy to use sublingual (oral) thin film strip for the acute rescue of "off" motor symptoms of Parkinson’s disease.

Anthony Giovinazzo is a Director, President and Chief Executive Officer of the Cynapsus. He is an experienced Biopharma CEO with more than 20 years of experience in international pharmaceutical drug development, private and public financings, and M&A transactions. He has identified, licensed, and overseen the development of eight biotech drug development candidates, pre-clinical to Phase 3, for the treatment of Parkinson’s, Alzheimer’s, anxiety, neuropathic pain and nausea. Mr. Giovinazzo led the sale of Nova Molecular Diagnostics to Variagenics Inc. through the public listing of Variagenics. As CEO, he also led the acquisition of Cita Neuropharmaceuticals by Vernalis Plc. He is one of the inventors of the original APL-130277 intellectual property that was acquired by Cynapsus.

Dr. Albert Agro joined Cynapsus as Chief Medical Officer in August 2010. Prior to this role, Dr. Agro was Senior Vice President, Drug Development of TransTech Pharma (2007-2009). From 2003 to 2007, he was a Partner at Axon Medical Communications that helped build the Clinical Research arm of the business (2005-2007), as well as Vice President, Medical and Scientific Affairs at Axon (2003-2005). Dr. Agro served as Director, National Medicine, as well as Director, Immunology, Virology and Respiratory Medicine, at Boehringer Ingelheim (2000-2003). Dr. Agro also worked at Bayer Inc., as Associate Director, Cardiopulmonary Medicine (1998-2000). Dr. Agro is also assistant professor, Department of Pathology and Molecular Medicine at McMaster University in Hamilton, Ontario.

Opportunity Overview

Cynapsus’ drug candidate, APL-130277, is an easy-to-administer, fast-acting reformulation of apomorphine, which is the only approved drug in the United States, Europe, Japan and other countries, to rescue patients from “off” episodes experienced with Parkinson’s disease. APL-130277 is a unique, patented thin-film product. The product is easy to self-administer under the tongue and dissolves in less than 2 to 3 minutes. The in-situ reaction allows for fast and reliable uptake of the drug and pharmacokinetics that closely mimic the injection, but without the needle.

Apomorphine, a potent dopamine agonist with a unique mechanism of action, is the only drug approved specifically for the treatment of acute motor fluctuations/hypomobility (freezing or “off” episodes) in patients with advanced Parkinson's disease. Presently, apomorphine is administered by intermittent subcutaneous injection usually via a pre-filled injection pen, or, in some cases outside the United States, by continuous infusion pump. Drawbacks associated with subcutaneous injection therapy for patients and caregivers include aversion to needles, the need for multiple injections, which can be painful and are often associated with irritation and inflammation at the injection site, and the requirement for a degree of manual dexterity that some Parkinson’s patients find difficult.

With the completion of 4 pilot clinical trials demonstrating favourable PK characteristics, Cynapsus plans to move forward with a registration program using the 505(b)(2) regulatory pathway with a focus on efficacv.

For additional information, please contact: ResearchPartnerships@michaeljfox.org
Details of MJFF Grant

The Michael J. Fox Foundation awarded a new grant of US$500,000 to support clinical studies to develop APL-130277. This second MJFF grant will be used to fund the Company’s CTH-105 clinical study. The MJFF previously awarded Cynapsus an initial grant of US$947,925 to complete a comparative study of APL-130277 versus subcutaneous injection (CTH-103). The results of CTH-103 were announced on January 13, 2014.

CTH-105 is a Phase 2 clinical study of APL-130277. APL-130277 will be studied in 16 patients with Parkinson’s disease who are naïve to the use of apomorphine and who experience at least one daily “off” episode, with a total duration of “off” in any 24-hour period of at least 2 hours. The first patients are expected to enter the screening phase before the end of July. This open-label study will examine the effect of APL-130277 on relieving “off” episodes over a single day, with dose-titration used to determine dose strengths necessary for future clinical development.

Results and Potential Next Steps

For development of APL-130277 in the United States, the Corporation will follow the 505(b)(2) regulatory pathway. In the next 2 years, the Corporation expects to complete the following clinical studies:

1. **CTH-200 Bridging Study.** A single dose, crossover comparative bioavailability and PK study in healthy volunteers. This study is designed to provide the clinical “bridge” to the FDA's finding of safety and efficacy for the Reference Listed Drug (s.c. Apomorphine). The CTH-200 Bridging Study is expected to begin in Q4 2014 subsequent to completion of CTH-105. This study is expected to be complete by end of Q4 2014.

2. **CTH-300a Efficacy Study in apomorphine naïve patients.** A double-blind, placebo-controlled, parallel-design study with Parkinson’s patients who have at least one “off” episode every 24 hours, with total “off” time of at least 2 hours. The primary end point will be the change in the UPDRS III score.

3. **CTH-301 Safety Study.** A long-term safety study in apomorphine naïve Parkinson’s patients who have at least one “off” episode every 24 hours, with total “off” time of at least 2 hours. The Safety Study is expected to start in early 2015 and be completed by the end of 2015. The study will look at the safety and tolerability of the new delivery route over a minimum period of 16 weeks.

Upon completion of the efficacy and safety studies, as well as the CMC section, the Corporation expects it will begin preparation of a FDA 505(b)(2) NDA in 2016.

Intellectual Property Status

For APL-130277, the patent portfolio owned by Cynapsus covers all major developing markets and emerging markets. The Corporation’s patent portfolio consists of three patent applications that provide a range of broad and specific claims: (1) A pioneer patent application (U.S. Application 12/813,820) filed in June 2009; (2) A follow-on patent was filed in December 2010 (U.S. Application 13/445,656). The application was extended to a PCT and to corresponding National Phase applications (U.S. Pub 20120195955 and WO 2012/083269); and (3) A fast-track USPTO patent application was filed in April 2012 (U.S. App 13/445,656) using the Track 1 procedure. In April 2013, the USPTO granted the patent (U.S.

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