

**Cynapsus Therapeutics Inc.
Albert Agro, PhD (Lead PI)****Organization and Team Overview**

Cynapsus is a specialty pharmaceutical company developing the only oral (sublingual) delivery of the only approved drug (apomorphine) to be used as a rescue therapy for “off” motor symptoms of Parkinson’s disease (PD).

Anthony Giovinazzo is a Director and the President and Chief Executive Officer of the Corporation. He is an experienced Biotech CEO with more than 18 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 PD, Alzheimer’s, anxiety, neuropathic pain, and nausea. He is a co-inventor of the APL-130277 technology and a patent holder. Mr. Giovinazzo led the sale of Nova Molecular Diagnostics to Variagenics Inc. through the public listing of Variagenics that resulted in significant above-average returns to investors. As CEO, he also led the acquisition of Cita Neuropharmaceuticals by Vernalis Plc.

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 and 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 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.

Dr. Nathan Bryson was named Chief Scientific Officer of Cynapsus in May 2009. He has contributed significantly to the drug formulation work for APL 130277 drug candidate, the development and execution of intellectual property strategy, and towards the development of clinical and regulatory plans. Dr. Bryson draws from more than 18 years of experience in pharmaceutical development, having held scientific and executive management level positions at Flamel Technologies, Inc., Bionisis SA and Matrogen Corp. Dr. Bryson has a strong knowledge of early-stage drug product development and formulation and has co-authored more than 20 patents.

Opportunity Overview

Cynapsus’ drug candidate, APL-130277, is an easy-to-administer, fast-acting, thin film strip reformulation of apomorphine, being developed to rescue patients from “off” episodes. Apomorphine is currently available only as a subcutaneous injection. It is not only difficult for a patient to self-administer, but results in scarring and nodules. A thin film strip formulation will be easier for patients to self-administer. As a reformulation of an approved drug, an abbreviated development pathway is available through section 505(b)2 of the US Food and Drug Act.

The pharmacokinetics and safety/tolerability of APL-130277 were demonstrated in 2 human volunteer studies. The first study included 15 healthy volunteers with 12 of 15 subjects receiving drug product and 3 subjects receiving placebo. Pharmacokinetic parameters mirrored those seen with a subcutaneous injection of apomorphine after an expected dose adjustment. The study showed that APL-130277 was safe and showed good local tolerability (no irritation). All adverse effects were typical of those commonly observed with apomorphine injection.

In August 2012, Cynapsus announced the results of a second human volunteer pilot proof-of-concept clinical trial (CTH-102) of APL-130277. The first dose evaluated in the study was deemed to be dose proportional to the dose evaluated in the CTH-101 clinical pilot study. It achieved a pharmacokinetic profile (Cmax, AUC and Tmax) that was sufficiently similar to subcutaneous injectable apomorphine and reached therapeutic levels. Management decided that it was unnecessary to proceed with a second dose, and then began preparations for a Comparative Biostudy (CTH-103) to be funded by the MJFF.

Details of MJFF Grant

Cynapsus Therapeutics Inc. was awarded a grant of USD\$947,925 to support clinical studies to develop APL-130277, a sublingual (oral) thin film strip reformulation of apomorphine. Apomorphine is an approved drug in the US, Europe and several other countries as a subcutaneous injection or infusion for PD patients experiencing daily "OFF" or motor fluctuation episodes. APL-130277 is potentially the only oral formulation of Apomorphine, and as such will provide patients with a convenient and more tolerable alternative to multiple daily injections.

The grant was awarded under the Foundation's The Edmond J. Safra Core Programs for PD Research, Clinical Intervention Awards, aimed at supporting human clinical trials testing promising Parkinson's therapies that may significantly and fundamentally improve treatment for people with PD. The grant directly supports the CTH 103 comparative biostudy.

"Improved methods of delivery for apomorphine, which has been shown to effectively treat 'off-episodes' in motor fluctuation, have been a goal of pharmaceutical research for at least a decade," says Maurizio Facheris, MD, MSc, Associate Director of Research Programs at MJFF. "Preliminary data around Cynapsus' novel formulation (APL-130277) show promise for a more frequent and effective use of this dopaminergic drug. We are hopeful that these clinical studies will support this promise, and drive APL-130277 further along the pipeline of therapeutic development."

CTH-103 will be a placebo-controlled, randomized cross-over Phase 1 trial in healthy volunteers to examine the pharmacokinetic profile of three dose strengths of APL-130277 as compared to equivalent doses of apomorphine subcutaneous injection. The objective of this study is to directly compare the pharmacokinetic profile of APL-130277 to subcutaneous apomorphine in healthy subjects to more precisely design the subsequent bio-equivalent registration trial to support an FDA 505(b)(2) NDA in 2015.

Results and Potential Next Steps

CTH 103 is expected to report results in October 2013.

Pharmacokinetics Bioequivalence Study: CTH201 (Pivotal Registration)

- IND-sponsored, healthy volunteer study, N= 108
- 2mg, 3mg and 4mg Apokyn® crossover with equivalent dose of APL-130277 (dose values based on results from CTH103, if needed)
- First data: Q-1 2014

Safety/Tolerability Study: CTH301 (Pivotal Registration)

- 150 – 200 apomorphine naïve patients, 25 to 30 centers, primarily in US
- Placebo controlled vs. APL-130277 (dose titrated to effect)
- At least 12 weeks in duration (confirmed at pre-IND)
- Primary endpoint: local tolerability (potential other safety measures)
- Secondary endpoints: UPDRS motor function, length of OFF, time to ON, PK, use of L-dopa

Cynapsus is seeking a partner or acquirer to sell APL-130277 on a world-wide basis, undertake a NDA submission in the US and complete development and regulatory submissions in the EU and other territories.

Intellectual Property Status

Anticipated commercial products are protected by US 8,414,922.

The sub-lingual thin film strip is a system of apomorphine and functional constituents which comprise a solid dosage form that maintains stable drug, dissolves in less than 2 minutes, promotes absorption of drug, and minimizes or eliminates tissue irritation. The claims also include minimum blood concentrations of apomorphine within critical time constraints to achieve the fast on required for a rescue therapy.