

February 10, 2015



**Amarantus**  
BioScience

## **Amarantus Announces Publication in BRAIN of Eltoprazine Phase 2a Clinical Study for Treating Parkinson's Disease Levodopa-Induced Dyskinesia**

- *Eltoprazine demonstrated significant beneficial anti-dyskinesia effect at 5 and 7.5 mg doses, with no reduction of levodopa efficacy*
- *Eltoprazine was well tolerated at all dose levels, with no major adverse effects reported*
- *Results support advancing eltoprazine into Phase 2b chronic dosing, clinical studies, as a treatment for patients with Parkinson's disease levodopa-induced dyskinesia*

SAN FRANCISCO and GENEVA, Feb. 10, 2015 (GLOBE NEWSWIRE) -- [Amarantus BioSciences Holdings, Inc.](#) (OTCQB:AMBS), a biotechnology company focused on developing diagnostics in neurology, and therapeutic products with the potential for orphan drug designation in the areas of neurology, psychiatry, ophthalmology and regenerative medicine, announced that the publication of the results of a Phase 2a study of eltoprazine in Parkinson's disease levodopa-induced dyskinesias (PD-LID). The paper titled, "Eltoprazine Counteracts L-DOPA-induced Dyskinesias in Parkinson's Disease: A Dose-Finding Study," has been published in [Oxford Journals](#) (Oxford University Press) [online](#) and will appear shortly in a future print edition of *BRAIN - A Journal of Neurology*.

Eltoprazine is a small-molecule 5-HT<sub>1A/1B</sub> serotonin receptor agonist, investigational drug candidate, with a well-established safety profile. A Phase 2a dose-finding study was conducted with eltoprazine to determine its effect against levodopa-induced dyskinesia, in patients with Parkinson's disease (PD). The double-blind, randomized, placebo-controlled clinical study was led by Professor Per Svenningsson, M.D., Ph.D., Centre for Molecular Medicine, Karolinska Institutet, Professor Anders Björklund, Ph.D., Faculty of Medicine at Lund University, and Professor Håkan Widner, M.D., Ph.D., Faculty of Medicine at Lund University. The study was partially supported by a grant from [The Michael J. Fox Foundation for Parkinson's Research](#).

Some researchers believe that, in the advanced stages of PD, as dopamine nerve terminals are lost, serotonergic terminals take up levodopa and convert it to dopamine instead. Unlike in dopamine nerve endings, the serotonin nerve terminals do not have a negative feedback loop, possibly causing an excessive release of dopamine and resulting in the development of abnormal involuntary hyperkinetic movements, known as levodopa-induced dyskinesias (LID). Pre-synaptic activation of serotonin receptors using a 5HT<sub>1A/1B</sub> agonist may dampen this excessive dopamine release. In animal model studies of LID previously conducted in Professor Björklund's laboratory, simultaneous activation of 5-HT<sub>1A</sub> and 5-HT<sub>1B</sub> receptors was shown to effectively block LID. The Phase 2a dosing trial with eltoprazine was

conducted as an initial clinical pharmacology study to determine if activation of 5-HT<sub>1A/1B</sub> receptors in Parkinson's disease subjects may replicate the effects of serotonin receptor activation seen in pre-clinical dyskinesia studies.

The study in 22 subjects with long standing PD-LID was a randomized, four-way crossover design in which patients received a single dose of placebo and eltoprazine, at 2.5, 5 and 7.5 mg, in combination with a challenge dose of levodopa (1.5 times usual dose), on four different days, separated by an interval of a week. Data from the study demonstrated that eltoprazine significantly reduced peak dose dyskinesia at both the 5 and 7.5 mg doses using the Combined Dyskinesia Rating Scale. The 5 mg dose also showed a significant anti-dyskinetic effect on other measures of dyskinesia, including the Rush dyskinesia rating scale. Importantly, there were no adverse effects on levodopa efficacy at any dose level as evidenced by United Parkinson's Disease Rating Scale (UPDRS Part III) observation. Additionally, all dose levels of eltoprazine were well tolerated with no major adverse effects reported.

"Eltoprazine's anti-dyskinetic effect is promising, especially given the reduction in dyskinesia following a levodopa challenge at one and a half times greater than the regular levodopa dose," said Charlotte Keywood, M.D., Chief Medical Officer at Amaranthus. "Levodopa treatment is the current standard of care for patients to manage PD motor symptoms, despite the occurrence of dyskinesia with long-term use. Thus, we were very pleased to see that normal motor responses to levodopa, measured by UPDRS III, remained unchanged in all patients treated with eltoprazine."

The Phase 2a study also included a pharmacokinetic (PK) evaluation of eltoprazine. The data show that the PK characteristics of eltoprazine in PD patients are the same as those found in healthy subjects. Given the positive PK profile in PD patients and the acute anti-dyskinesia effect seen with the 5 and 7.5 mg doses, further advancement of eltoprazine into Phase 2b chronic dosing clinical studies to treat patients with PD-LID is warranted.

"We are pleased to have the eltoprazine study results published in this prestigious peer-reviewed journal," said Dr. Keywood. "The results of this proof of concept, first trial in PD-LID patients, support the findings of the non-clinical pharmacology studies conducted using animal models of PD-LID and show the predictive value of these models in aiding human drug development."

"The data from this study show an acute antidyskinetic effect of eltoprazine with no detriment to levodopa efficacy. With these data at hand, we are confident moving forward into longer-term dosing studies to further evaluate the utility of eltoprazine as a treatment for levodopa-induced dyskinesia," concluded Dr. Keywood.

Amaranthus expects to file its Investigational New Drug Application (IND) with the U.S. Food and Drug Administration (FDA) and commence its Phase 2b study of eltoprazine in PD-LID subjects in the first quarter of 2015.

"Dyskinesia impacts quality of life of people with Parkinson's disease, and is therefore a top priority for the Foundation," commented Maurizio Facheris, M.D., M.Sc., Associate Director of research programs at The Michael J. Fox Foundation. "We are glad to see this project moving further through clinical testing and closer to patients' hands."

To access the online version of the paper titled, "Etoprazine Counteracts L-DOPA-induced Dyskinesias in Parkinson's Disease: A Dose-Finding Study," please click [here](#).

To access the Karolinska Institutet press release titled, "New therapeutic principle for Parkinsonian dyskinesia shows clinical effect," regarding the publication in *BRAIN*, please click [here](#).

## **About Etoprazine**

[Etoprazine](#) is a small molecule 5HT<sub>1A/1B</sub> partial agonist in clinical development for the treatment of Parkinson's disease levodopa-induced dyskinesia (PD-LID) and Adult Attention Deficit Hyperactivity Disorder (ADHD). Etoprazine has been evaluated in over 600 human subjects to date, and has a well-established safety profile. Etoprazine was originally developed by Solvay Pharmaceuticals for the treatment of aggression. Upon Solvay's merger with Abbott Pharmaceuticals, the Etoprazine program was out-licensed to PsychoGenics. PsychoGenics licensed Etoprazine to Amarantus following successful proof-of-concept trials in PD-LID and adult ADHD.

## **About Parkinson's disease and levodopa-induced dyskinesia (PD-LID)**

Parkinson's disease is a chronic, progressive neurological disorder that causes motor symptoms such as tremors, rigidity and slowed movements as well as non-motor symptoms including cognitive impairment and autonomic dysfunction. The Parkinson's Disease Foundation estimates that there are approximately one million people living with Parkinson's disease in the United States and seven to 10 million PD patients worldwide. The most commonly prescribed treatments for Parkinson's disease are levodopa-based therapies. In the body, levodopa is converted to dopamine to replace the dopamine loss caused by the disease. As dopamine neurons in the brain are lost the therapeutic efficacy of levodopa attenuates, and increased use is associated with a side effect of dyskinesias. These are involuntary, uncontrollable and often exaggerated and jerky movements. They are distinct from the static, rhythmic tremor as a symptom of Parkinson's disease. Levodopa-induced dyskinesia can be severely disabling, rendering patients unable to perform routine daily tasks.

## **About Amarantus BioScience Holdings, Inc.**

Amarantus BioScience Holdings (AMBS) is a biotechnology company focused on developing diagnostics in neurology, and therapeutic products with the potential for orphan drug designation in the areas of neurology, psychiatry, ophthalmology and regenerative medicine. AMBS has licensed Etoprazine, a Phase 2b ready small molecule indicated for Parkinson's disease Levodopa-induced dyskinesia and adult ADHD. AMBS has an exclusive worldwide license to the Lymphocyte Proliferation test, (LymPro Test<sup>®</sup>), which was developed by Prof. Thomas Arendt, Ph.D., from the University of Leipzig, for Alzheimer's disease and owns the intellectual property rights to a therapeutic protein known as mesencephalic-astrocyte-derived neurotrophic factor ("MANF") and is developing MANF-based products as treatments for brain and ophthalmic disorders. AMBS also owns intellectual property for the diagnosis of Parkinson's disease (NuroPro) and the discovery of neurotrophic factors (PhenoGuard<sup>™</sup>).

In November 2014, AMBS entered into an exclusive option agreement with Lonza Walkersville, Inc., a subsidiary of Lonza Group Ltd., to acquire Cutanogen Corporation, a

subsidiary of Lonza Walkersville, to develop Engineered Skin Substitute (ESS-W), an autologous skin replacement product for the treatment of Stage 3 and Stage 4 intractable severe burns.

On January 12, 2015, AMBS announced the acquisition of DioGenix, Inc., a specialized neuro-diagnostics company, and owns the rights to MSPrecise<sup>®</sup>, a proprietary next-generation DNA sequencing (NGS) assay for the identification of patients with relapsing-remitting multiple sclerosis (RRMS) at first clinical presentation. On January 15, 2015, AMBS executed a one-year exclusive option agreement with Georgetown University to enter into a license for the patent rights related to certain blood based biomarkers for memory loss and Alzheimer's disease jointly owned by Georgetown University and University of Rochester. For further information please visit [www.Amarantus.com](http://www.Amarantus.com), or connect with the Company on [Facebook](#), [LinkedIn](#), [Twitter](#) and [Google+](#).

### **About Our Collaboration Partners**

[Karolinska Institutet](#) is one of the world's leading medical universities. Its vision is to significantly contribute to the improvement of human health. Karolinska Institutet accounts for over 40 percent of the medical academic research conducted in Sweden and offers the country's broadest range of education in medicine and health sciences. The Nobel Assembly at Karolinska Institutet selects the Nobel laureates in Physiology or Medicine.

[The Faculty of Medicine at Lund University](#) works to understand, explain and improve human health. As a part of Lund University we create unique interdisciplinary collaborations for scientific breakthroughs and innovations. Lund University was founded in 1666 and is consistently ranked among the world's top 100 universities.

### **Forward-Looking Statements**

Certain statements, other than purely historical information, including estimates, projections, statements relating to our business plans, objectives, and expected operating results, and the assumptions upon which those statements are based, are forward-looking statements. These forward-looking statements generally are identified by the words "believes," "project," "expects," "anticipates," "estimates," "intends," "strategy," "plan," "may," "will," "would," "will be," "will continue," "will likely result," and similar expressions. Forward-looking statements are based on current expectations and assumptions that are subject to risks and uncertainties which may cause actual results to differ materially from the forward-looking statements. Our ability to predict results or the actual effect of future plans or strategies is inherently uncertain. Factors which could have a material adverse effect on our operations and future prospects on a consolidated basis include, but are not limited to: changes in economic conditions, legislative/regulatory changes, availability of capital, interest rates, competition, and generally accepted accounting principles. These risks and uncertainties should also be considered in evaluating forward-looking statements and undue reliance should not be placed on such statements.

CONTACT: Investor and Media Contact:

Jenene Thomas

Jenene Thomas Communications, LLC

Investor Relations and Corporate Communications Advisor

T: (US) 908.938.1475

E: [jenene@jenenethomascommunications.com](mailto:jenene@jenenethomascommunications.com)

Source: Amaranthus BioScience Holdings, Inc.