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Amarantus Announces a New Eltoprazine Publication Confirming the Long-Term Efficacy and Elucidating the Mechanism of Action in PD-LID

- *Latest preclinical data in the peer-reviewed journal 'Movement Disorders' support previous nonclinical and clinical findings that eltoprazine is effective against Parkinson's Disease L-dopa induced dyskinesia (PD-LID)*
- *Eltoprazine treatment attenuates the development and expression of PD-LID by regulating neurochemical circuitry involved in motor control, but does not compromise the efficacy of levodopa therapy*
- *Data further support the design and dose selection of the ongoing Phase 2b clinical study*

SAN FRANCISCO and GENEVA, Aug. 5, 2015 (GLOBE NEWSWIRE) -- [Amarantus BioScience Holdings, Inc.](#) (OTCQX:AMBS), a biotechnology company developing therapeutic and diagnostic product candidates in orphan indications and neurology, announced the publication of preclinical model data demonstrating that eltoprazine prevents L-dopa induced dyskinesias. The paper entitled, "[Eltoprazine Prevents Dyskinesias by Reducing Striatal Glutamate and Direct Pathway Neuron Activity](#)," from groups including the National Institute of Neuroscience in Italy, has been published in [Movement Disorders](#), a journal of the [International Parkinson and Movement Disorder Society \(MDS\)](#).

[Eltoprazine](#) is a small molecule 5HT_{1A/1B} partial agonist in Phase 2b clinical development for the treatment of [Parkinson's disease levodopa-induced dyskinesia](#) (PD-LID). PD-LID is an abnormal involuntary, movement disorder resulting from prolonged levodopa-based therapy, the most commonly prescribed treatment for Parkinson's disease. PD-LID occurs in approximately 60-80% of Parkinson's disease (PD) patients and is one of the most difficult problems facing people with the disease. This dyskinesia can be severely disabling and impact quality of life by prohibiting the ability to perform routine daily functions.

"I am very excited by these new results, as they not only confirm the anti PD-LID activity of eltoprazine in another laboratory, but the authors also provide important evidence concerning the neurochemical mechanisms and pathways underlying eltoprazine's positive effects in PD-LID," stated David A. Lowe, Ph.D., member of the Board of Amaranthus BioScience Holdings, Inc. "Additionally this study further validates the [Phase 2a clinical data published earlier this year in the journal BRAIN](#) showing that eltoprazine

has a significant beneficial anti-dyskinesia effect with no reduction of levodopa efficacy. Furthermore, the doses used in this preclinical study are highly supportive of those being studied in the ongoing Phase 2b trial of eltoprazine."

Previous preclinical and clinical evidence shows that eltoprazine, a mixed 5-HT_{1A} /5-HT_{1B} receptor agonist, is effective in inhibiting PD-LID in experimental animals and parkinsonian patients. The new eltoprazine study published in *Movement Disorders* was conducted using a 6-hydroxydopamine-hemilesioned rat model of Parkinson's disease to investigate the mechanisms underlying the therapeutic effect of eltoprazine in PD-LID.

The data demonstrated that eltoprazine reduced the development and expression of PD-LID with maintenance of motor coordination. Correspondingly, eltoprazine reduced the rise of two important transmitter substances (GABA and Glutamate) as well as other relevant biochemical signals induced by L-Dopa in the striatum and substantia nigra, two brain areas involved in motor control. Importantly, there was no evidence of a detrimental effect on the levodopa-induced increase in striatal dopamine, indicating that the levodopa efficacy, so important in the treatment of PD, is not compromised by long-term treatment with eltoprazine.

Dr. Lowe added, "Levodopa treatment is an effective standard of care treatment for patients to manage PD motor symptoms, despite the occurrence of dyskinesia with its long-term use. The fact that eltoprazine prevents PD-LID and has no adverse effect on the efficacy of levodopa treatment is very important to improving quality of life in PD. We believe eltoprazine has the potential to be an impactful synergistic therapy for individuals with Parkinson's disease on levodopa-based regimens."

Amarantus has [initiated a multi-center, 60-subject Phase 2b study of eltoprazine in individuals with PD-LID](#). The study is a double-blind, placebo-controlled, four-way crossover, dose range finding clinical trial designed to evaluate dose response effect of repeated eltoprazine dosing on safety, tolerability and dyskinesia severity using state-of-the-art rating scales, diaries and motion sensors. For patients and physicians interested in enrollment information for the Phase 2b clinical study with eltoprazine for the treatment of PD-LID please visit clinicaltrials.gov and use identifier: NCT02439125. The Company expects to report top-line results from the eltoprazine Phase 2b study in the first half of 2016.

For online access to the abstract, "*Etoprazine Prevents Dyskinesias by Reducing Striatal Glutamate and Direct Pathway Neuron Activity*," please click <http://ow.ly/QbZB6>.

About Etoprazine

[Etoprazine](#) is a small molecule 5HT_{1A/1B} partial agonist in clinical development for the treatment of Parkinson's disease levodopa-induced dyskinesia (PD-LID), adult attention deficit hyperactivity disorder (ADHD) and Alzheimer's aggression. Etoprazine has been evaluated in over 680 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 eltoprazine program was out-licensed to PsychoGenics. PsychoGenics licensed eltoprazine 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 (PD) is a chronic, progressive neurodegenerative disorder that causes motor symptoms such as tremors, rigidity and slowed movements as well as non-motor symptoms including cognitive impairment, mood disorders 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 Amaranthus BioScience Holdings, Inc.

Amarantus BioScience Holdings (OTCQX:AMBS) is a biotechnology company developing treatments and diagnostics for diseases in the areas of neurology and orphan diseases. AMBS' Therapeutics division has development rights to eltoprazine, a small molecule currently in a Phase 2b clinical program for Parkinson's disease levodopa-induced dyskinesia with the potential to expand into adult ADHD and Alzheimer's aggression. The Company has an exclusive worldwide license to intellectual property rights associated to Engineered Skin Substitute (ESS), an orphan drug designated autologous full thickness skin replacement product in development for the treatment of severe burns currently preparing to enter Phase 2 clinical studies. AMBS owns the intellectual property rights to a therapeutic protein known as mesencephalic-astrocyte-derived neurotrophic factor (MANF) and is developing MANF as a treatment for orphan ophthalmic disorders, initially in retinitis pigmentosa (RP). AMBS also owns the discovery of neurotrophic factors (PhenoGuard™) that led to MANF's discovery.

AMBS' Diagnostics division owns the rights to MSPrecise®, a proprietary next-generation DNA sequencing (NGS) assay for the identification of patients with relapsing-remitting multiple sclerosis (RRMS), and has an exclusive worldwide license to the Lymphocyte Proliferation test (LymPro Test®) for Alzheimer's disease, which was developed by Prof. Thomas Arendt, Ph.D., from the University of Leipzig, and owns further intellectual property for the diagnosis of Parkinson's disease (NuroPro®).

For further information please visit www.Amarantus.com, or connect with the Company on [Facebook](#), [LinkedIn](#), [Twitter](#) and [Google+](#).

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.

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