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Amarantus Announces Publication of Study on Targeted Delivery of MANF to Brain Areas Associated With Parkinson's Disease

- Renishaw plc's convection-enhanced delivery device results in accurate targeting and distribution of MANF to Parkinson's disease-associated brain areas -

- Study confirms the potential of convection-enhanced delivery of MANF as a novel treatment strategy for Parkinson's disease -

- Results support the co-infusion of gadolinium as a proxy measure of MANF distribution in future clinical studies -

SAN FRANCISCO and GENEVA, Oct. 06, 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 a study demonstrating the targeted delivery of mesencephalic-astrocyte-derived neurotrophic factor (MANF) to brain regions associated with Parkinson's disease in a porcine model. The paper entitled, *"*Convection-enhanced delivery of MANF – volume of distribution analysis in porcine putamen and substantia nigra[1]*,"* from the collaboration with Renishaw plc's (LON:RSW) Neurological Applications Department and the Functional Neurosurgery Research Group at the University of Bristol, was published in the Journal of the Neurological Sciences.

The publication reports for the first time the distribution of MANF in putamen and substantia nigra following convection-enhanced delivery (CED) in a large animal model and confirms the potential of targeted infusion of MANF as a novel treatment strategy for PD. The study demonstrates that: (i) MANF can successfully be delivered to the porcine putamen and substantia nigra, the brain areas centrally involved in PD, and (ii) that pharmacologically meaningful volumes of distribution of MANF can be achieved using Renishaw's convection-enhanced delivery device currently in human clinical development.

"Our decades-long human experience with convection-enhanced delivery of protein therapeutics taught us that the therapeutic potential of neurotrophic factor treatment of PD is heavily dependent on the ability to accurately and effectively target the affected brain regions," said Prof. Steven Gill, MB, FRCS, MS, honorary professor of neurosurgery at the University of Bristol. "These published data confirm the translational potential of CED of MANF as a novel treatment strategy in PD."

"We now have definitive confirmation that MANF can be precisely and accurately delivered

to specific sites in the brain that are affected by Parkinson's disease. Moreover, MANF can be distributed via CED in a volume thought to elicit a therapeutic effect," said Gerald E. Commission, President & CEO of Amarantus. "The availability of an accurate and effective targeting method to deliver MANF to the brain is an important step for the development of MANF in PD. We believe these data provide a firm basis for studies in non-human primates as well as subsequent human clinical trials."

Study Summary

The porcine model is increasingly being used in neuroscience research as the large brain volume and similarity of cortical and subcortical anatomy to the human brain may offer increased translational relevance over rat and non-human primate models. The aims of this recently published study using convection enhanced delivery (CED) in pig brains were two-fold: (1) To assess the targeting and to determine distribution volumes of MANF in porcine putamen and substantia nigra and (2) to correlate the distribution volumes of MANF with co-infused gadolinium-DTPA.

Using a recessed-step catheter design it was possible to achieve reflux-free infusions in both putamen and substantia nigra. The volumes of distribution of gadolinium-DTPA and MANF were determined by real-time magnetic resonance imaging (MRI) and immunohistochemical analysis, respectively. The authors concluded that the distributions of gadolinium-DTPA and MANF correlated well and that co-infusion of gadolinium as a proxy measure of MANF distribution in future clinical studies is supported by these data.

CED of MANF resulted in an effective distribution within the target regions of the brain as evidenced by immunohistochemical staining. Comparison of the MANF diffusion (Vd) and infusion (Vi) volumes indicated an approximate (Vd:Vi) ratio of 3 in the putamen and 2 in the substantia nigra. The volume of the substantia nigra pars compacta (SNpc) in patients with PD has recently been reported as less than 120 mm^3. An extrapolation of the results from this present study indicates that with a single catheter targeted to the human SNpc and assuming a Vd:Vi ratio of 2, it may be possible to distribute MANF throughout this target in approximately 30 minutes using a maximum infusion flow rate of 5 ml/min. Similar considerations apply to the delivery of MANF to the human putamen. Infusion times in the range of 30 to 120 minutes are likely to be acceptable to patients and reports are emerging of using faster flow rates safely in the human putamen which would further reduce the infusion time. Moreover, pre-clinical data from a rat PD disease model suggests that only a fraction of the striatal volume needs to be targeted to elicit a pharmacological effect.

The abstract, *"Convection-enhanced delivery of MANF – volume of distribution analysis in porcine putamen and substantia nigra*," may be accessed online via the *Journal of the Neurological Sciences* at http://www.jns-journal.com/article/S0022-510X(15)00477-3/abstract.

[1]N.U. Barua, A.S. Bienemann, M. Woolley, M.J. Wyatt, D. Johnson, O. Lewis, C. Irving, G. Pritchard, S.Gill, Convection-enhanced delivery of MANF – volume of distribution analysis in porcine putamen and substantia nigra, *Journal of the Neurological Sciences*(2015), doi: 10.1016/j.jns.2015.08.003.

About Parkinson's Disease

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 PD in the United States and seven to ten million PD patients worldwide. The most commonly prescribed treatments for PD are levodopa-based therapies. There is currently no cure available for Parkinson's disease.

About Mesencephalic-Astrocyte-derived Neurotrophic Factor (MANF)
MANF (mesencephalic-astrocyte-derived neurotrophic factor) is believed to have broad potential because it is a naturally-occurring protein produced by the body for the purpose of reducing and preventing apoptosis (programmed cell death) in response to injury or disease, via the unfolded protein response. By manufacturing MANF and administering it to the body, Amarantus is seeking to use a regenerative medicine approach to assist the body with higher quantities of MANF when needed. Amarantus is the front-runner and primary holder of intellectual property around MANF, and is initially focusing on the development of MANF-based protein therapeutics. MANF was discovered utilizing Amarantus' proprietary PhenoGuard™ Protein Discovery Engine.

MANF's lead indication is retinitis pigmentosa, and additional indications including Parkinson's disease, diabetes and Wolfram's syndrome are currently being pursued. Further applications for MANF may include Alzheimer's disease, traumatic brain injury, myocardial infarction, antibiotic-induced ototoxicity and certain other rare orphan diseases currently under evaluation.

About Amarantus 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. 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 adult severe burns currently preparing to enter Phase 2 clinical studies. The Company is currently evaluating human clinical data from previously conducted studies in pediatric severe burns and Congenital Giant Hairy Nevus to support clinical development expansion into those areas. AMBS also 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. 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) and retinal artery occlusion (RAO). 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) at first clinical presentation, 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 intellectual property for the diagnosis of Parkinson's disease (NuroPro).

For further information please visit www.Amarantus.com, or connect with the Company on

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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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