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Amarantus BioSciences Announces Landmark MANF Genomics Publication

SUNNYVALE, Calif., Oct. 1, 2012 /PRNewswire/ -- Amarantus BioSciences, Inc. (OTCBB: AMBS), a biotechnology company developing new treatments for brain-related disorders including Parkinson's disease and Traumatic Brain Injuries (TBI) centered on its proprietary anti-apoptotic therapeutic protein known as MANF, today announced the publication of a landmark research paper on MANF, Amarantus' lead development program. The studies were conducted at the University of Helsinki, a research institution based in Helsinki, Finland, performing groundbreaking neuroscience research based in its' Department of Biosciences and Institute of Biotechnology. This research paper, published by Palgi et al., from Dr. Tapio Heino's laboratory at the University of Helsinki in the peer-reviewed journal BMC Genomics is entitled "Gene expression analysis of *Drosophila Manf* mutants reveals perturbations in membrane traffic and major metabolic changes," in which researchers describe the critical role MANF plays in the endoplasmic reticulum, the unfolded protein response (UPR), and dopaminergic neurons which are affected by Parkinson's Disease. http://www.ncbi.nlm.nih.gov/pubmed/22494833.

"This publication marks a significant advancement in our understanding of how the MANF molecule works in improving overall cellular function," said Dr. John W. Commissiong, Founder & Chief Scientist at Amarantus. "This could be very significant as the MANF Program is advanced for Parkinson's disease"

The MANF-family (MANF and CDNF) of proteins are remarkably conserved in evolution in multicellular organisms. Previous studies in Dr. Heino's laboratory carried out by Palgi *et al.* demonstrate that fruit fly, *Drosophila melanogaster, Manf* (DmMANF) is a true orthologue to mammalian MANF, meaning that the proteins have similar biological functions in the two systems. This was most clearly demonstrated by the observation that the lethal effects of the absence of DmMANF observed in *Manf* mutant flies are fully rescued by human MANF (hMANF). This gene orthology makes *Drosophila* a powerful genetic model that can be used to study MANF signaling pathways. Furthermore, DmMANF is specifically required for the maintenance of dopaminergic neurites because in *Manf* mutant embryos and larvae, dopaminergic neurites degenerate and dopamine levels are extremely low. Still, despite these important observations, little is known about the mechanism of action, and about the molecules that interact with the MANF/CDNF proteins.

Dr. Heino's research group has performed an extensive microarray analyses and report interesting genome-wide differences in gene expression between wild type flies, *Manf* mutant flies, and flies overexpressing *Manf*. The data obtained from functional annotation clustering, which provides information about biological pathways influenced by these genetic differences, revealed statistically significant enrichment of genes related to metabolism and membrane transport. The observed changes at the gene expression level were further supported by ultrastructural studies of the mutants, which revealed accumulation of vesicles

and a structurally disorganized endoplasmic reticulum (ER). Altogether more than 40% of the known *Drosophila* genes related to the ER and the unfolded protein response (UPR) showed altered expression levels in the mutants. The researchers were also able to demonstrate that lack of *DmMANF* results in activation of UPR *in vivo*. Overexpression of *DmMANF* resulted in upregulation of genes involved in oxidation reduction, an important process that protects dopamine neurons from oxidative stress. Thus, the results support the previously reported findings in mammalian cells that upregulation of MANF is important in the UPR and is protective for the cell. The UPR has been implicated in several human neurodegenerative diseases.

Dr. Mari Palgi, the lead author on the study observed that, "Additionally, this microarray study in *Drosophila* revealed several other genes and processes implicated in the pathology of Parkinson's disease such as mitochondrial Htra2 and DJ-1, oxidative phosphorylation, and protein ubiquitination. Interestingly, despite the very low dopamine levels in *Manf* mutants, the genes involved in dopamine synthesis and metabolism showed clear upregulation."

About Amarantus BioSciences, Inc.

Amarantus BioSciences, Inc. is a development-stage biotechnology company founded in January 2008. The Company has a focus on developing certain biologics surrounding the intellectual property and proprietary technologies it owns to treat and/or diagnose Parkinson's disease, Traumatic Brain Injury and other human diseases. The Company 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 disorders. The Company also is a Founding Member of the Coalition for Concussion Treatment (#C4CT), a movement initiated in collaboration with Brewer Sports International seeking to raise awareness of new treatments in development for concussions and nervous-system disorders. For further information please visit www.Amarantus.com.

Forward Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Such statements include, but are not limited to, statements about the possible benefits of MANF therapeutic applications and/or advantages presented by Amarantus' PhenoGuard technology, as well as statements about expectations, plans and prospects of the development of Amarantus' new product candidates. These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including the risks that the anticipated benefits of the therapeutic drug candidates or discovery platforms, as well as the risks, uncertainties and assumptions relating to the development of Amarantus' new product candidates, including those identified under "Risk Factors" in Amarantus' most recently filed Annual Report on Form 10-K and Quarterly Report on Form 10-Q and in other filings Amarantus periodically makes with the SEC. Actual results may differ materially from those contemplated by these forward-looking statements Amarantus does not undertake to update any of these forward-looking statements to reflect a change in its views or events or circumstances that occur after the date of this presentation.

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