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MANF Therapeutics Announces Independent Publication of Positive Data for MANF in Traumatic Brain Injury Animal Model

NEW YORK, June 11, 2018 (GLOBE NEWSWIRE) -- *via OTC PR WIRE*--MANF Therapeutics, Inc., a wholly-owned subsidiary of Amarantus Bioscience Holdings, Inc. (OTCPK:AMBS) in pre-clinical development advancing the orphan-drug designated therapeutic protein mesencephalic astrocyte-derived neurotrophic factor (MANF) as a disease-modifying treatment for orphan ophthalmological conditions, Glaucoma and Parkinson's disease, today announced the publication of a scientific article entitled "MANF prevents traumatic brain injury in rats by inhibiting inflammatory activation and protecting Blood Brain Barrier" in World Neurosurgery that describes positive effects of MANF in an animal model of acute traumatic brain injury. The work was published by researchers at Anhui Medical University and University of Science & Technology of China Hefei.

The data demonstrated that acute delivery of a high dose of recombinant human MANF(20 g/20 L) significantly increased the modified Garcia score, and reduced brain water content (BWC) as well as cerebral edema volume in Magnetic Resonance Imaging (MRI). Furthermore, MANF alleviated not only the blood-brain barrier(BBB) permeability, but also the expressions of IL-1 and TNF- mRNA and protein. The activation of P65 was also inhibited. These results suggest that MANF provides neuroprotective effect against acute brain injury after TBI, via attenuating BBB disruption and intracranial neuroinflammation, while the inhibition of NF-B signaling pathway could be a potential mechanism.

It is estimated there are over 2,000,000 acute TBIs in the United States annually.The global traumatic brain injuries treatmentmarket stood at $112B in 2017 and is expected to reach $156 billion by 2024, according to Energias Market Research Pvt. Ltd. An effective therapy that could improve functional outcomes for patients in response to a severe TBI event is expected to generate over $1B in annual in sales. Based on the results of the study published in World Neurosurgery, MANF has the potential to be developed as a treatment for post-stroke recovery.

MANF Therapeutics is preparing to restart IND-enabling development of MANF in 2018, initially in ophthalmology. MANF has therapeutic potential across multiple orphan ophthalmological conditions such as RAO and retinitis pigmentosa, where MANF has already received orphan drug designations from the FDA, as well as in larger indications such as Glaucoma, Parkinson's, Alzheimer's, diabetes and in cardiovascular disease, such as stroke and myocardial infarction. MANF Therapeutics is the front-runner and primary worldwide intellectual property (IP) holder for MANF-based therapies including protein therapy, gene therapy and cell therapy. The Company owns rights to composition of matter patents for

MANF and owns, or has licenses to, method of use patents covering the use of MANF in ophthalmology, neurology and diabetes.

ABSTRACT

Background

Our previous studies have shown that MANF provides neuroprotective effect against ischemia/reperfusion injury and is also involved in inflammatory disease models. This work investigates the potential role and mechanism of MANF in acute brain damage after traumatic brain injury (TBI).

Methods

The model of TBI was induced by Feeney free falling methods with male Sprauge-Dawley rats. The expression of MANF, 24 hrs after TBI, was detected by the immunohistochemistry, immunofluorescence, Western blot and Reverse transcription PCR(RT-PCR) techniques. After treatment with recombinant human MANF following TBI, assessment was conducted - 24 hrs later for brain water content(BWC), cerebral edema volume in MRI, neurobehavioral testing and Evans blue extravasation. Moreover, by the techniques of Western blot and RT-PCR, the expression of inflammatory cytokines(IL-1, TNF-) and P65 was also analyzed to explore the underlying protective mechanism of MANF.

Results

At 24 hrs after TBI, we found that endogenous MANF was widely expressed in the rat's brain tissues and different types of cells. Treatment with high dose of recombinant human MANF(20 g/20 L) - significantly increased the modified Garcia score, and reduced BWC as well as cerebral edema volume in MRI. Furthermore, MANF alleviated not only the blood-brain barrier(BBB) permeability, but also the expressions of IL-1 and TNF- mRNA and protein. Besides, the activation of P65 was also inhibited.

Conclusions

These results suggest that MANF provides neuroprotective effect against acute brain injury after TBI, via attenuating BBB disruption and intracranial neuroinflammation, while the inhibition of NF-B signaling pathway might be a potential mechanism.

About MANF Therapeutics, Inc.

MANF (mesencephalic-astrocyte-derived neurotrophic factor) is believed to have broad potential because it is a naturally-occurring protein produced by the body to reduce/prevent apoptosis (cell death) in response to injury or disease, via the unfolded protein response. By administering exogenously produced MANF 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's lead indication is retinitis pigmentosa, and additional indications including Parkinson's disease, diabetes and Wolfram's syndrome are envisioned. Further applications for MANF may include Alzheimer's disease, traumatic brain injury, myocardial infarction,

antibiotic-induced ototoxicity and certain other orphan diseases.

In April 2017, Amarantus incorporated the wholly-owned subsidiary MANF Therapeutics, Inc. to focus on progressing preclinical and clinical development of MANF.

About Amarantus Bioscience Holdings, Inc.

Amarantus Bioscience Holdings (AMBS) is a JLABS alumnus biotechnology company developing treatments and diagnostics for diseases in the areas of neurology, regenerative medicine and orphan diseases through its subsidiaries. AMBS' wholly-owned subsidiary Elto Pharma, Inc. has development rights to eltoprazine, a Phase 2b-ready small molecule indicated for Parkinson's disease levodopa-induced dyskinesia, Alzheimer's aggression and adult attention deficit hyperactivity disorder, commonly known as ADHD. AMBS acquired the rights to the Engineered Skin Substitute program, a regenerative medicine-based approach for treating severe burns with full-thickness autologous skin grown in tissue culture that is being pursued by AMBS' wholly-owned subsidiary Cutanogen Corporation. AMBS' wholly-owned subsidiary MANF Therapeutics, Inc. owns key intellectual property rights and licenses from a number of prominent universities related to the development of the therapeutic protein known as mesencephalic astrocyte-derived neurotrophic factor ("MANF"). MANF Therapeutics, Inc. is developing MANF-based products as treatments for brain and ophthalmic disorders. MANF was discovered by the Company's Chief Scientific Officer John Commissiong, PhD. Dr. Commissiong discovered MANF from AMBS' proprietary discovery engine PhenoGuard. The Company also re-acquired rights to the Alzheimer's blood diagnostic LymPro Test , MSPrecise and NuroPro.

For further information please visit www.Amarantus.com, or connect with the Amarantus on Facebook, LinkedIn, Twitter and Google+.

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