

October 1, 2015



# Amarantus to Focus Near-Term Development Efforts on Engineered Skin Substitute for Indications in Rare Pediatric Diseases

*Company is Currently Evaluating Human Clinical Data From Previous Studies Supporting Clinical Development Program Expansion Beyond Treatment of Adult Burns Into Pediatric Burns*

*Published Data Support Development Expansion Into Congenital Giant Hairy Nevus*

SAN FRANCISCO and GENEVA, Oct. 1, 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 Company's intention to strategically focus the majority of its resources on the development of Engineered Skin Substitute (ESS) for the treatment of rare pediatric diseases, including the treatment of pediatric severe burns and Congenital Giant Hairy Nevus. Management believes the ESS program represents a vast commercialization opportunity and its near term advancement is critical to the Company's overall business strategy. Additionally, treatments in development for rare pediatric diseases in the United States are eligible to receive Rare Pediatric Disease Designation (RPDD). The Sponsor of a treatment that is approved by the US Food and Drug Administration (FDA) under the RPDD pathway is entitled to receive a Priority Review Voucher (PRV).

"With the integration of the Cutanogen acquisition now complete, we have unearthed powerful human clinical data that validates the significant potential for the ESS program beyond the areas of adult and pediatric severe burns and into Congenital Giant Hairy Nevus," said Gerald E. Commissiong, President & CEO of Amaranthus. "It is important for us to now focus the majority of our resources over the next several months on the ESS program. Upon completion of our review of the long-term longitudinal data, we intend to work closely with the FDA in an effort to establish a shortened clinical development pathway to approval via the RPDD pathway."

In the scientific publication [Plastic and Reconstructive Surgery. 2004;114\(6\):1523-1528](#) entitled "Autologous cultured skin substitutes conserve donor autograft in elective treatment of congenital giant melanocytic nevus," the authors reported on the treatment of two (2) cases of Congenital Giant Hairy Nevus.

ABSTRACT

This report presents a series of two patients having giant congenital nevi (400 to 650 cm<sup>2</sup>) treated by excision and grafting with autologous cultured skin substitutes prepared from less than 20 cm<sup>2</sup> of donor skin autograft. Nevi were excised to fascia and grafted with cadaveric allograft for 1 week, followed by removal of the allograft and grafting with cultured skin substitutes. The mean ratio of closed to donor areas was 26. In comparison to sheet split-thickness skin grafting, cultured skin substitutes exhibited comparable cosmesis, pliability, and durability while reducing the donor-site area by approximately one order of magnitude.

"Each approved treatment under the RPDD pathway is entitled to receive a PRV that may be sold to other companies. Two PRVs have been sold in the last 6 months for an aggregate of \$595 million to major pharmaceutical companies. The proceeds from the sale of a PRV are in addition to any potential revenues that could be generated from the commercial sales. We believe ESS has the potential for an accelerated regulatory pathway to market in multiple rare and ultra-rare pediatric diseases based on the data we have seen in our preliminary review of the ESS program post-acquisition. Given that the majority of the ESS-related expenses are fixed costs associated with GMP manufacturing, we believe that we gain economies of scale by accelerating the regulatory and clinical development of ESS for the treatment of rare and ultra-rare pediatric diseases."

## **Updated Portfolio Strategy**

### *ESS*

ESS development will become the primary clinical development focus for Amaranthus in the immediate future. After a thorough review of the timeline for GMP-ready material, the Company believes that it will achieve full GMP status in the fourth quarter of 2015, and initiate the pending adult severe burn clinical study with the US Army in the fourth quarter of 2015, or the first quarter of 2016. During the fourth quarter of 2015 and first quarter of 2016, Amaranthus intends to engage the FDA in the filing of applications for rare pediatric disease designation, fast-track designation, orphan drug designation (ODD) and breakthrough designation pathways, as well as other pathways designed to accelerate time to approval. In parallel, the Company will also be aggressively pursuing non-dilutive funding.

### *Eltoprazine*

Amarantus will pause enrollment for its Phase 2b clinical study of Eltoprazine due to this internal prioritization of the ESS program into multiple indications. There is no pre-clinical, safety, or other activity concern about the use of Eltoprazine that was involved in this decision. Amaranthus anticipates restarting enrollment in 2016 and will evaluate various options for Eltoprazine for the treatment of Parkinson's disease Levodopa Induced Dyskinesia (PD LID). Given the recent acceptance by the FDA of PD LID as an indication eligible for the ODD pathway, the Company believes it may be able to accelerate the commercialization pathway for Eltoprazine and will use this period of enrollment pause to explore this potential. Management will accelerate the preparation of clinical development programs for Eltoprazine in Alzheimer's aggression and adult ADHD, as well as renew initiatives to obtain non-dilutive funding to accelerate program development in PD LID.

## *MANF*

MANF development will continue as planned. The majority of expenses for MANF are related to GMP manufacturing, and the company will continue to make progress in the months ahead, although the rate of progress towards the clinic may be slowed somewhat due to the Company's focus on ESS. Given recent positive developments for the MANF program with the issuance of a US patent covering synthetic MANF and receipt of orphan drug designation for MANF in retinal artery occlusion, the Company will continue to invest resources to shepherd MANF towards first-in-man studies. The Company will also renew its focus for obtaining non-dilutive funding to accelerate development in the areas of ophthalmology and Parkinson's disease.

## *Amarantus Diagnostics*

The Company is currently evaluating potential strategic transactions for the commercialization of our diagnostic assets. Amarantus remains focused on completing at least one strategic transaction in this division in the fourth quarter of 2015.

## **About Engineered Skin Substitute (ESS)**

Engineered Skin Substitute (ESS) is a tissue-engineered skin prepared from autologous (patient's own) skin cells. It is a combination of cultured epithelium with a collagen-fibroblast implant that produces a skin substitute that contains both epidermal and dermal components. This model has been shown in preclinical studies to generate a functional skin barrier. Most importantly, self-to-self skin grafts for autologous skin tissue are less likely to be rejected by the immune system of the patient, unlike with porcine or cadaver grafts in which immune system rejection is a possibility. ESS has been used in an investigator initiated clinical setting in over 130 human subjects, primarily pediatric patients, for the treatment of severe burns up to 95% total body surface area.

## **About Eltoprazine**

[Eltoprazine](#) 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), adult attention deficit hyperactivity disorder (ADHD) and Alzheimer's aggression. Eltoprazine has been evaluated in over 680 human subjects to date, and has a well-established safety profile. Eltoprazine 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 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 (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 (IP) around MANF, and is initially focusing on the development of MANF-based protein therapeutics. MANF's lead indications are retinitis pigmentosa (RP) and retinal artery occlusion (RAO), and additional indications including Parkinson's disease, diabetes and Wolfram's syndrome are currently pursued. Further applications for MANF may include Alzheimer's disease, traumatic brain injury (TBI), myocardial infarction, antibiotic-induced ototoxicity and certain other rare orphan diseases currently under evaluation.

### **About MSPrecise<sup>®</sup>**

MSPrecise<sup>®</sup> is a proprietary next-generation DNA sequencing (NGS) assay for the identification of patients with relapsing-remitting multiple sclerosis (RRMS) at first clinical presentation. MSPrecise utilizes next-generation sequencing to measure DNA mutations found in rearranged immunoglobulin genes in immune cells initially isolated from cerebrospinal fluid. MSPrecise would augment the current standard of care for the diagnosis of multiple sclerosis by providing a more accurate assessment of a patient's immune response to a challenge within the central nervous system. This novel method of measuring changes in adaptive human immunity may also be able to discern individuals whose disease is more progressive and requires more aggressive treatment.

### **About LymPro Test<sup>®</sup>**

The Lymphocyte Proliferation Test (LymPro Test<sup>®</sup>) is a diagnostic blood test that determines the ability of peripheral blood lymphocytes and monocytes to withstand an exogenous mitogenic stimulation that induces them to enter the cell cycle. It is believed that certain diseases, most notably Alzheimer's disease, are the result of compromised cellular machinery that leads to aberrant cell cycle re-entry by neurons which then leads to apoptosis. LymPro is unique in the use of peripheral blood lymphocytes as a surrogate for neuronal cell function, suggesting a common relationship between peripheral blood lymphocytes and neurons in the brain.

### **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. 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 and 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<sup>™</sup>) that led to MANF's discovery.

AMBS' Diagnostics division 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, has an exclusive worldwide license to the Lymphocyte Proliferation test (LymPro Test<sup>®</sup>) 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](http://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.

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: Amarantus BioScience Holdings, Inc.