

Amarantus BioScience Holdings, Inc.

(AMBS-OTCQB)

**AMBS: ESS will be near term priority---
Buy**

Current Recommendation	Buy
Prior Recommendation	Sell
Date of Last Change	07/12/2015
Current Price (03/07/16)	\$0.12
Target Price	\$1.00

UPDATE

Despite what we believe is aggressive discounting and downward adjusting of our models based on overly pessimistic probability assumptions, we are still arriving at a target price of \$1.00 per share. The current market capitalization is only \$2 million. Our target is far more consistent with that we see as a peer-valuation for similar-stage NASDAQ listed companies. We believe several pending catalysts over the next 15 months, including the AMDX sales / spin-off, starting human clinical trials with MANF, reporting results from the eltoprazine Phase IIb data, and the ESS Phase IIa data should allow for the realization of a significantly higher stock price.

SUMMARY DATA

52-Week High	\$11.94
52-Week Low	\$0.10
One-Year Return (%)	-98.85
Beta	-1.22
Average Daily Volume (sh)	1,939,638

Shares Outstanding (mil)	14
Market Capitalization (\$mil)	\$2
Short Interest Ratio (days)	0.02
Institutional Ownership (%)	N/A
Insider Ownership (%)	N/A

Annual Cash Dividend	\$0.00
Dividend Yield (%)	0.00

5-Yr. Historical Growth Rates	
Sales (%)	N/A
Earnings Per Share (%)	N/A
Dividend (%)	N/A

P/E using TTM EPS	N/A
P/E using 2015 Estimate	N/A
P/E using 2016 Estimate	N/A

Risk Level	Ultra High / Speculative
Type of Stock	Small-Growth
Industry	Biotech

ZACKS ESTIMATES

Revenue

(In millions of \$)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2014	0.0 A				
2015	0.0 A	0.0 A	0.0 A	0.2 E	0.2 E
2016					1.0 E
2017					3.5 E

Earnings per Share

(EPS is operating earnings before non-recurring items)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2014	-\$1.32 A	-\$0.82 A	-\$0.86 A	-\$1.95 A	-\$5.19 A
2015	-\$0.96 A	-\$1.08 A	-\$0.98 A	-\$0.59 E	-\$3.53 E
2016					-\$2.23 E
2017					-\$2.10 E

WHAT'S NEW

Update on Diagnostics Business

The Merger Deals

On Jan 19, Amaranthus and **Avant Diagnostics** (AVDX) announced they have entered into a Letter of Intent to merge an Amaranthus wholly-owned subsidiary, Amaranthus Diagnostics, into Avant Diagnostics. Under the terms of the LOI, upon execution of definitive merger agreements, Avant shall issue to Amaranthus **80 million** shares of common stock of Avant Diagnostics, representing approximately 45% of Avant's post-merger common stock, and **10 million** additional shares of common stock upon achievement of certain sales milestones. Amaranthus shall have the right to appoint two directors to the Avant Board of Directors, and will assist Avant in bolstering its product development and commercialization resources to accelerate the further development of the combined company's product pipeline.

On March 7, 2016, Avant Diagnostics and Amaranthus announced that the two companies jointly entered into a letter of intent for Avant to acquire assets and certain liabilities of **Theranostics Health**.

Under the terms of the letter of intent, Avant shall issue to THI **25 million** shares of its common stock upon the closing. Amaranthus BioScience has provided a convertible note of \$400,000 to THI to facilitate the transaction that will be assumed by Avant upon closing of the transactions. As previously disclosed, Avant plans to issue 80 million shares of its common stock to Amaranthus Biosciences upon completion of its merger with Amaranthus Diagnostics. The Transactions are expected to close in the first half of 2016.

Post-Merger Avant Pipeline/Products

OvaDx® (from Avant): immuno-oncology diagnostic assay is a protein-based test, potentially representing a significant improvement in the screening and diagnosis for **ovarian cancer**. OvaDx offers the possibility to make a clear improvement to the current diagnostic standard by substantially improving the accuracy of diagnosis, and allowing for a more effective therapeutic triaging and intervention strategy. Longer term, the assay could become a much-needed early screening tool for all women as part of a standard screening paradigm. Current market size for ovarian cancer testing is about \$2 billion, and it is estimated that the market opportunity for OvaDx is \$50M annually as a diagnostic test for ovarian cancer, and that this opportunity could expand to over \$2B annually if it were to be approved as a generalized screening and/or monitoring tool.

MSPrecise® (from Amaranthus): neuroimmunology-based next-generation sequencing diagnostic assay for multiple sclerosis (MS) offers a potentially highly accurate and actionable result that will substantially improve upon the high mis-diagnosis rate of this degenerative disease. More specifically, MS has an approximately 40% misdiagnosis rate, meaning that improving diagnostic accuracy will be a key driver to adopt more effective therapeutic strategies that will reduce costs for payers and improve outcomes for patients. The potential market opportunity for MSPrecise as a diagnostic for multiple sclerosis is over \$200M annually, and could increase to over \$1B if it were to be approved as a monitoring tool to measure the efficacy of drug treatment.

LymPro Test® (from Amaranthus): neuroimmunology-based flow cytometry assay for Alzheimer's Disease (AD), offers an early, accurate, and scalable diagnostic result for physicians seeking to provide the best information and treatment plan for patients from the earliest stages of this devastating disease. AD diagnosis has an approximately 30% misdiagnosis rate. The estimated market opportunity for LymPro is over \$3B in a commercial setting as a generalized screening test for patients at their initial Medicare enrollment visit.

TheraLink® Assay (from Theranostics): This assay includes phospho-activation markers for known drug targets of over 30 approved molecular targeted therapies for treating breast cancer patients. In addition, the TheraLink® Assay panel includes other biomarkers that have utility in directing patients to clinical trials involving new investigational agents. Research programs and clinical trials are underway at leading institutions to validate the TheraLink® Assay panel for managing cancer treatment decision-making in other clinically significant areas such as colorectal, lung, pancreatic and ovarian cancer.



The Implications for Amaranthus

We welcome the deals as these mergers will accelerate the development of Amaranthus' diagnostic pipeline. In January 2015, Amaranthus did two deals to greatly enhance its **diagnostic business**. The company acquired **MSPrecise** from DioGenix and entered into a one-year, exclusive option agreement to exclusively conduct research and negotiate with Georgetown University on its **Alzheimer's biomarker** assay.

With MSPrecise, Amaranthus has the ability to offer a CLIA lab a "commercial ready" product to launch into a well-established and under-served market. With the Georgetown asset, Amaranthus has the ability to package the AD assay in with LymPro and enhance the suite of "biomarker services" they are currently offering to the investigational use only (IUO) market.

It's our belief that the combination with Theranostics and Avant Diagnostics will accelerate the development of Amaranthus' pipeline and generate the economies of scale.

Also the deals will help Amaranthus manage its balance sheet. Under the terms of the agreement, upon closing, Avant will issue 80 million common shares to Amaranthus, which has a market value of about \$48 million. Also Avant will issue additional 10 million shares to Amaranthus upon achievement of certain sales milestones, which represents another market value of \$6 million as of this writing. Amaranthus could sell these shares to fund its operations.

Near-Term Development Effort Is Focused on ESS for Indications in Rare Pediatric Diseases

In early October, 2015, Amaranthus announced the Company's intention to strategically focus the majority of its resources on the development of Engineered Skin Substitute (**ESS**) program with a focus on 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 FDA under the RPDD pathway is entitled to receive a Priority Review Voucher (PRV) that may be sold to other companies.

We noticed that recent two PRVs have been sold for an aggregate of \$595 million to major pharmaceutical companies. In May 2015, Retrophin sold its PRV to Sanofi for total of \$245 million and in August 2015, United Therapeutics sold its PRV to Abbvie for total of \$350 million.

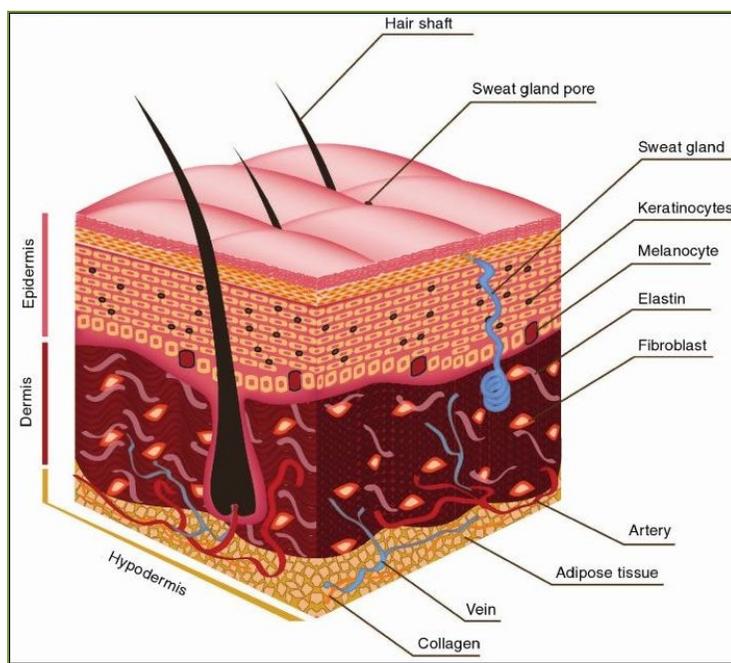
The proceeds from the sale of a PRV are in addition to any potential revenues that could be generated from the commercial sales of the company's diagnostics products. Considering the company's current financial situation, we believe this non-dilutive financing makes a lot of sense to boost its balance sheet without diluting existing shareholder base.

Further, 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 preliminary review of the ESS program post-acquisition of **Cutanogen** Corporation. Given that the majority of the ESS-related expenses are fixed costs associated with GMP manufacturing, the company could gain economies of scale by accelerating the regulatory and clinical development of ESS for the treatment of rare and ultra-rare pediatric diseases.

A Brief Review of the Skin Structure

Skin is the largest organ of the body, serving primarily as a protective barrier against the environment. It also helps to prevent body dehydration and constitutes a physical barrier, limiting the penetration of potentially harmful agents to internal organs.

The human skin has a **three-layer structure** composed of epidermis, dermis and hypodermis. The epidermis is mainly composed of keratinocytes but also contains other cell types, such as Langerhans cells and melanocytes, providing a barrier against infection and moisture loss. The dermal layer, situated below the epidermis, is responsible for the elasticity and mechanical integrity of the skin. It contains vascularized extracellular matrix (ECM) rich in collagen, elastin and glycosaminoglycans. The cellular components of the dermal layer include fibroblasts, endothelial cells, smooth muscle cells and mast cells. The hypodermis, located below the dermis, is mainly composed of adipose tissue and collagen, and mainly acts as an energy source.



Skin damage is very common and can be caused by burn, chronic wounds, excision of skin, tumors and other dermatological conditions. According to WHO, 300,000 deaths are annually attributed to burn injuries, while 6 million patients worldwide suffer from burns every year. Additionally, more than 6 million individuals suffer from

chronic skin ulcers. In the USA alone, more than 3 million patients suffer from chronic wounds (*Am. J. Surg.*193(2),213–218, (2007)).

Treatment of Skin Lesions

The treatment of skin lesions is a critical issue in healthcare, requiring the need to consider several parameters affecting the healing process, such as the wound type, the wound depth, the patient's health and the level of the exudate. Currently, a great variety of wound-care products are available for the treatment of different types of skin lesions (*Adv. Drug Deliv. Rev.*63(4–5),352–366 (2011)).

Treatment of skin lesions	Advantages	Limitations
Autografts	'Golden standard' in skin regeneration; good adhesion to the wound bed; provides pain relief; reduced rejection	Limited availability of donor sites; induce scar formation; patient morbidity; lengthy hospital stays
Allografts	Temporary prevention of wound dehydration and contamination; incorporate into deep wounds	Limited availability; may lead to immune rejection; transmission of diseases
Creams, solutions and ointments	Ease of use; provide disinfection, cleaning and debridement; not expensive in general	Limited skin regeneration; short residence time on the wound (require frequent administrations)
Traditional dressings	Not expensive; provide a protective barrier against the penetration of exogenous microbes	High absorption capacity; do not provide a moist environment; adhere to the wound bed; may inhibit the healing process
Modern dressings	Create and maintain a moist wound environment; can be made from a wide range of materials with different properties; ability to hydrate the wound and remove excess exudate	More expensive; low adhesion to the wound bed; inability to promote the regeneration of lost skin, in particular the dermal layer
Tissue-engineered skin substitutes	Promote the regeneration of dermis and epidermis; prevent fluid loss and provide protection from contamination; may deliver extracellular matrix components, cytokines, growth factors and drugs to the wound bed, enhancing the healing process; can be used in combination with autografts	High manufacturing costs; difficult handling; poor adhesion to the wound bed; possibility of immune rejection and transmission of diseases (allogeneic skin cells); inability to promote the regeneration of full-thickness wounds; poor vascularization; impossibility of reproducing skin appendages
<i>In situ</i> biofabrication of skin substitutes	Provide immediate and effective relief to the patient; enable the direct fabrication of skin substitutes fitting to the anatomical shape of the defect; allow the controlled deposition of cells and biomaterials; may eliminate the use of bioreactors for growing and maturing the tissue <i>ex vivo</i> ; may solve the need for vascularization through the controlled deposition of endothelial cells	Biofabrication techniques need to be adapted for <i>in situ</i> biofabrication; may require integration with imaging techniques to print the skin substitute with appropriate anatomical shape; requires the use of printable materials exhibiting adequate biological and mechanical properties

Tissue-Engineered Skin Substitutes

Tissue-engineered skin substitute (ESS) has emerged as a **new and promising field** for the treatment of skin lesions, combining scaffolds, cells and biomolecular signals, such as growth factors.

Despite recent developments in manufacturing processes and biomaterials, both autografts/allografts and wound dressings have significant limitations for skin regeneration. The main drawbacks of wound dressings are the low adhesion to the lesion, impossibility of reproducing skin appendages and the inability to replace the lost tissue, particularly the dermis, after severe burns. In order to address these limitations and solve the problem of the donor graft shortage, both cellular (e.g., Apligraf™; Organogenesis, MA, USA) and acellular (e.g., Alloderm™; Biohorizons, AL, USA) tissue-engineered skin substitutes were developed. Skin regeneration is, in fact, among the few fields where tissue engineering commercial products are already available and under clinical utilization.

Acellular constructs are made of natural or synthetic biomaterials, and can be used in combination with autografts. Cellular constructs contain biomaterials and cells, obtained from different origins including autologous, allogenic or xenogeneic. Clinically available skin substitutes can be broadly divided into epidermal, dermal and dermoepidermal constructs. However, available skin substitutes often suffer from a range of problems including poor integration due to inadequate vascularization, inefficient adhesion to the wound bed, scarring at graft margins or the lack of skin appendages.

Substitute	Product	Graft type	Cell source	Manufacturer
Epidermal substitutes	Epicel®	Cell based	Autologous keratinocytes	Genzyme Biosurgery (MA, USA)
▪	CellSpray®	Cell based	Autologous keratinocytes	Avita Medical (Perth, Australia)
▪	Myskin™	Scaffold containing cells	Autologous keratinocytes	CellTran Ltd (Sheffield, UK)
▪	Laserskin®	Scaffold containing cells	Autologous keratinocytes	Fidia Advanced Biopolymers (Abano Terme, Italy)
▪	ReCell®	Autologous epidermal cell suspension	Autologous keratinocytes	Avita Medical
Dermal substitutes	Integra®	Cell free	–	Integra NeuroSciences (NJ, USA)
▪	AlloDerm®	Cell free	–	LifeCell Corp. (NJ, USA)
▪	Hyalomatrix PA®	Cell free	–	Fidia Advanced Biopolymers
▪	Dermagraft®	Scaffold containing cells	Neonatal allogeneic fibroblasts	Advanced BioHealing (CT, USA)
▪	TransCyte®	Scaffold containing cells	Neonatal allogeneic fibroblasts	Advanced BioHealing
▪	Hyalograft 3D™	Scaffold containing cells	Autologous fibroblasts	Fidia Advanced Biopolymers
Dermoeipidermal substitutes	OrCel®	Natural-based scaffold containing cells	Allogeneic keratinocytes and fibroblasts	Ortec International (GA, USA)
▪	Apligraf®	Natural-based scaffold containing cells	Allogeneic keratinocytes and fibroblasts	Organogenesis Inc. (MA, USA)
▪	PolyActive®	Synthetic scaffold containing cells	Autologous keratinocytes and fibroblasts	HC Implants BV (Leiden, The Netherlands)

Amarantus ESS Program

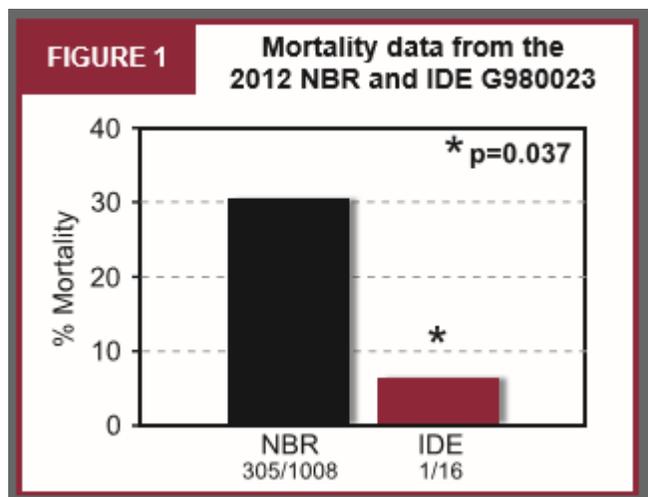
Amarantus' engineered skin substitute (ESS) is a full thickness skin replacement product prepared from autologous (patient's own) tissue-engineered skin cells in development for the treatment of **severe burns**. It is a combination of cultured epithelium with a collagen-fibroblast implant that produces 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.

In July, 2015, Amarantus completed the acquisition of **Cutanogen** Corporation from Lonza Walkersville, Inc. a subsidiary of Lonza Group Ltd. Cutanogen has an exclusive worldwide license to intellectual property rights associated with ESS. With this acquisition, Amarantus has engaged Lonza via a long-term services agreement to manufacture ESS under Good Manufacturing Practices (GMP) for human clinical trials, and subsequent commercial distribution.

To acquire the rights to ESS, Amarantus paid Lonza Group a fee of \$3.15 million in cash. In return, Lonza has committed to spending "a good portion" of the payment on preparing the initiation of the **Phase II** clinical study. We note that the first institutional review board (IRB) approval came earlier in May 2015. Besides the upfront payments, Amarantus has also agreed to pay milestones to Lonza of \$1.0 million for a successful clinical trial and \$4.0 million upon the filing of a Biologic License Application (BLA). Lonza is also entitled to 2% royalties on future commercial sales. Amarantus has also settled all outstanding litigation on the product with Regenicin, paying the company a total of \$3.6 million in cash and stock between November 2014 and February 2015.

Amarantus 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 and [initial data on ESS](#) looks outstanding.

In one clinical study with 16 pediatric subjects treated with ESS (IDE G980023), 15 subjects survived for an overall mortality rate of 6.25% (1/16). This mortality rate is statistically lower ($p=0.037$; one-sample z-test) than the average rate of 30.3% (305/1008) reported in the National Burn Repository (NBR) for patients of comparable age and magnitude of injury.



ESS also demonstrated impressive data in the treatment of congenital giant melanocytic nevus (*Plastic and Reconstructive Surgery*. □ 2004;114(6):1523-1528).

ESS Development Plan

Based on the compelling data of ESS for the treatment of severe burn and congenital giant melanocytic nevus, ESS development will become the primary clinical development focus for Amaranthus in the immediate future.

Amarantus plans to initiate the pending **Phase II** adult severe burn clinical study with the US Army in the first quarter of 2016.

The planned Phase II study will enroll 10 adult patients. This study is designed to evaluate the safety and efficacy of ESS compared to conventional split-thickness AG for the treatment of extensive, deep partial- and full-thickness thermal burns. A matched and randomized burn site format will be used to evaluate the successful graft take on excised deep partial- and full-thickness burns when grafted with either 1) unmeshed ESS or 2) meshed AG (the current standard treatment of split thickness AG).

This research study is divided into five study periods: (1) Screening Period of up to one week and (2) Pre-Grafting Period, which will last approximately 35-45 days, (3) Grafting Day(s), which are the day(s) on which grafts are applied (i.e., First Graft: Day 0 and the optional subsequent Grafting Day i.e., Second Graft: Day 0), (4) Post Grafting Observation Period, which begins with 28 days follow-up after each Grafting Day(s), and continues till Post-Operative Month (POM) 6 from the last Grafting Day, and (5) Anecdotal Observation Period.

In early August, 2015, the company signed a Cooperative Research and Development Agreement (CRADA) with the U.S. Army Institute of Surgical Research (USAISR) and Rutgers University to expand the development of ESS for the treatment of deep partial- and full-thickness burn wounds in adult patients.

During the 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.

The market for severe intractable severe burns is wide open, as there is truly no effective standard-of-care.

ESS has already been granted Orphan Drug designation by the U.S. FDA for the treatment of hospitalized patients with deep partial and full thickness burns requiring grafting. We believe positive Phase II data on ESS, likely to be reported in 2016, is another major potential valuation inflection for the company.

Update on cGMP Manufacturing Technical Transfer

On Feb 22, 2016, Amaranthus provided an update on the status of its cGMP manufacturing technical transfer for producing ESS at Lonza Walkersville, Inc., a premier contract manufacturer providing cell and tissue-based products for clinical development.

The company announced that it has successfully completed the growth and testing components of its confirmatory engineering run in February 2016, and is now finalizing the documentation, sterilization validation, and auditing that is required to complete the technical transfer. Once the technical transfer is finished, which is expected to be in the first quarter of 2016, Amaranthus will be operationally ready to supply ESS for the planned Phase II clinical study for the treatment of full thickness thermal burns covering over 50% of the body with the US Army.

Amarantus is planning three distinct clinical development programs for ESS, all of which have the opportunity to gain rapid market approval in various orphan dermatologic conditions:

1. Adult severe burns: Initiating a 10-patient Phase II clinical development program with US Army study under CRADA at ISR and two additional leading civilian burn centers
2. Pediatric severe burns: Evaluating Phase III development program designs with leading pediatric burn center(s) in the United States
3. Giant Congenital Melanocytic Nevi (GCMN): Evaluating pivotal Phase III development program designs with leading dermatology center(s) in the United States

Amarantus Plans to Restart Enrollment of Phase IIb Trial of Eltoprazine for PD-LID

On February 10, 2016, Amaranthus announced that it has received **orphan drug designation** (ODD) from the US FDA for **Eltoprazine** in the treatment of Parkinson's disease levodopa-induced dyskinesia (**PD-LID**), which provides for a seven year marketing exclusivity and that it plans to **restart the enrollment of the Phase IIb** trial for PD-LID.

Background of Eltoprazine

Eltoprazine is a small molecule 5HT1A/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. 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 Amaranthus following successful proof-of-concept trials in PD-LID and adult ADHD.

Development Plan for Eltoprazine

In May 2015, Amaranthus entered into an [agreement with Chiltern](#) International, a leading global contract research organization (CRO) to manage the clinical research and monitoring program for a **Phase IIb** study, which commenced to enroll patients in early June 2015. First patient was enrolled in mid-July.

The multi-center, 60-subject Phase IIb study in patients with Parkinson's disease is a double-blind, placebo-controlled, four-way crossover design. The purpose of the study is to assess the safety and tolerability of various doses of eltoprazine over longer-periods of time, as well as investigate the effects on dyskinesia and akinesia using various motor scoring scales recorded by motion sensors and patient diaries. Secondary goals will include finding the minimal efficacious and maximum tolerated doses, as well as to help define the statistical analysis plan for the Phase III trial.

However, in early October, 2015, due to the shift of the company's development resources to its ESS program, Amaranthus **paused enrollment** for the **Phase IIb** clinical study then. There is no pre-clinical, safety, or other activity concern about the use of Eltoprazine that was involved in this decision. Given the approval of ODD for Eltoprazine, Amaranthus plans to **restart enrollment** in 2016 and will evaluate various options for Eltoprazine for the treatment of PD LID. 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.

The Implication

Based on the positive **Phase IIa** data, we believe the Phase IIb has a high probability to succeed. Amaranthus recently published the Phase IIa data in BRAIN in February 2015 and highlighted the publication of two independent peer-reviewed scientific publications describing the mechanism of action of eltoprazine for the treatment of PD-LID in [August of 2015](#) and [December 2015](#).

We noticed that positive Phase IIb data is often the catalyst for significant valuation inflection in CNS assets. It is also often what opens the doors to potential licensing agreements with larger organizations. It is also important to note that Amaranthus just received a notice of allowance for a U.S. patent application covering both methods of administration and composition in the treatment of Parkinson's disease for eltoprazine in May 2015.

With the re-enrollment of the Phase IIb, we believe Eltoprazine, together with ESS, will become the primary driver of valuation inflection at Amaranthus. The key to creating that valuation inflection will be the release of **Phase IIb** data hopefully by the end of the year.

We also note that Amaranthus plans to expand the clinical investigation of eltoprazine outside of PD into potentially larger areas, including adult ADHD and Alzheimer's disease aggression, which will further expand the Eltoprazine franchise. The company recently announced positive data for Eltoprazine in a Phase II clinical trial of elderly patients with Alzheimer's dementia who are aggressive.

MANF

MANF development will continue as planned. 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.

Although development with MANF remains pre-clinical, Amaranthus added significant value to the program by filing two Orphan Drug applications, one already granted in both [in the U.S.](#) and [in the EU](#) in Retinitis Pigmentosa (RP) and another in central retinal artery occlusion (RAO) granted by the FDA. We anticipate another Orphan Drug application to go under review for Wolfram's Syndrome in the near future.

In the meantime, the company is currently conducting preclinical IND-enabling studies with MANF, with a goal of filing the U.S. IND application in early 2016. MANF has yet to enter clinical testing, so we believe that Amaranthus must demonstrate acceptable PK/PD profiles in healthy patients; however, because MANF is a naturally-occurring protein we do not anticipate any significant safety or tolerability issues.

As such, we believe the asset becomes highly attractive to potential partners based on the Orphan Drug indications and potential for non-dilutive funding for Phase I and Phase II programs in 2016 and 2017. We note that Amaranthus recently signed an [agreement with Catalent Biologics](#) for the production of MANF for human clinical studies in 2016.

MANF recently received a Notice of Allowance for the U.S. , EU and China patent application covering compositions of matter and methods of use related to proprietary manufacturing processes for synthetic MANF and its administration for protein therapy and cell therapy.

Valuation and Recommendation

We maintain our Buy rating for Amaranthus shares and our new price target is \$1.00 per share.

Amaranthus is a biotech company with two business divisions: A **Diagnostic** division with two commercially ready assets and a **Therapeutic** division with three candidates in different stages of development targeting different indications, including PD-LID, severe skin burn, adult ADHD and Parkinson's disease. With the merger of its diagnostics business with Avant, the company will be focused on the therapeutics business going forward.

Program	Preclinical	Phase 1	Phase 2	Phase3	Next step
ESS Pediatric 50%+ TBSA Stage 3&4 Burns	[Progress bar: Preclinical to Phase 2]				1. FDA Meeting: pivotal design 2. RPDD + ODD
ESS Congenital Giant Hairy Nevus	[Progress bar: Preclinical to Phase 2]				1. FDA Meeting: pivotal study 2. RPDD + ODD
ESS Adult 50%+ TBSA Stage 3&4 Burns	[Progress bar: Preclinical to Phase 1]				Phase 2 Clinical Trial w/ US Army
Eloprazine Adult ADHD	[Progress bar: Preclinical to Phase 2]				FDA Meeting: pivotal design
Eloprazine Parkinson's L-Dopa induced Dyskinesia	[Progress bar: Preclinical to Phase 1]				1. FDA Decision on ODD Application 2. Phase 2b results
Eloprazine Alzheimer's Aggression	[Progress bar: Preclinical to Phase 1]				FDA Meeting on Phase 2 clinical study design

It is understandable why the shares have been under pressure lately. The company has to raise money to fund its operations on a regular basis and has to continuously dilute existing shareholder base. However, money raising is not necessarily a bad thing, especially for a development stage company like Amaranthus. These small cap companies need the cash to move their pipeline forward and generate meaningful clinical data. We believe data is the ultimate driver of valuation, and we believe once the ESS and eltoprazine trials get underway, institutional interest in the company will become significant. We noted two examples of companies with similar late-stage CNS assets, Acadia Pharmaceuticals with pimavanserin and Auspex Pharmaceuticals with SD-809. Six months following positive Phase III data, these stocks were up 700% and 733%, respectively. However, what investors may not know is that their respective share counts were also up 45% and 33% during that same time period of six months before to six months after data. In this regard, we encourage Amaranthus investors to focus on the pipeline and what the core assets might be worth if successful.

With respect to valuation, we admit that it's always difficult to get an accurate value for a development stage small biotech company. Amaranthus is no exception. According to current market data and our experience, most small cap development stage biotech companies are valued from \$50 million to \$2 billion in market cap based on how advanced the pipeline is and the market potential of the candidates.

Currently, Amaranthus shares are trading at about \$0.12 per share, which values the company at roughly \$2 million in market cap based on outstanding shares of 14 million. We think this is a huge discount when compared to its peers. Amaranthus is a mid-stage biotech company with two candidates in Phase II trials. We estimate ESS will be approved by the FDA in mid-2019. The company's diagnostics may generate revenue in 2016. If everything goes Amaranthus' way, combined revenue from the diagnostics and therapeutics will reach \$80 million in 2020 with an EPS of \$0.12 per share. Currently, the biotech industry is trading at a 25 x P/E multiple, which also is appropriate for Amaranthus. If we use the 25x P/E ratio, discount at 25% for 4 years, we come up with the fair value of \$1.00 per share for Amaranthus. Our target price values the company at \$14 million in market cap which is still conservative in our view. As long as management can execute on its growth strategy, the price target is achievable.

Our target is far more consistent with that we see as a peer-valuation for similar-stage NASDAQ listed companies. We believe several pending catalysts over the next 15 months, including the AMDX sales / spin-off, starting human clinical trials with MANF, reporting results from the eltoprazine Phase IIb data, and the ESS Phase IIa data should allow for the realization of a significantly higher stock price.

Cash burn is our chief short term concern when the company needs to raise new money to fund its operations. Longer term, we are more than willing to focus on the clinical advancement and potential commercial opportunity for its diagnostic business. Volatility in the broad market will also impact the company's share price performance. But overall, Amaranthus is an interesting name for investors with a long term investment horizon and high risk tolerance.

INCOME STATEMENT

Amarantus (\$ mm, except for share data)	2014 A	Q1 A	Q2 A	Q3 A	Q4 E	2015 E	2016 E	2017 E	2018 E	2019 E	2020 E
Therapeutics	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$5	\$50
<i>YOY Growth</i>	-	-	-	-	-	-	-	-	-	-	900.0%
Diagnostics	\$0	\$0	\$0	\$0.0	\$0.2	\$0.2	\$1.0	\$3.5	\$7.5	\$15.0	\$30.0
<i>YOY Growth</i>	-	-	-	-	-	-	400.0%	250.0%	114.3%	100.0%	100.0%
Total Revenues	\$0	\$0	\$0	\$0.0	\$0.2	\$0.2	\$1.0	\$3.5	\$7.5	\$20.0	\$80.0
<i>YOY Growth</i>	-	-	-	-	-	-	400.0%	1650.0%	650.0%	471.4%	966.7%
CoGS	\$0	\$0	\$0	\$0.0	\$0.1	\$0.1	\$0.2	\$0.7	\$1.5	\$4.0	\$16.0
<i>Product Gross Margin</i>	-	-	-	-	75.0%	75.0%	80.0%	80.0%	80.0%	80.0%	80.0%
R&D	\$13.8	\$2.5	\$2.3	\$1.5	\$2.0	\$8.2	\$12.5	\$15.0	\$17.0	\$20.0	\$24.5
SG&A	\$7.6	\$4.1	\$3.3	\$2.0	\$2.5	\$11.9	\$13.5	\$17.5	\$21.5	\$23.0	\$30.0
Operating Income	(\$21.4)	(\$6.5)	(\$5.6)	(\$3.6)	(\$4.4)	(\$20.0)	(\$25.2)	(\$29.7)	(\$32.5)	(\$27.0)	\$9.5
<i>Operating Margin</i>	-	-	-	-	-	-	-	-	-	-	-
Interest & Other Income	(\$5.9)	(\$0.0)	(\$0.1)	(\$1.9)	(\$0.5)	(\$2.6)	(\$2.0)	(\$2.0)	(\$2.0)	(\$2.0)	(\$2.0)
Pre-Tax Income	(\$27.3)	(\$6.6)	(\$5.7)	(\$5.4)	(\$4.9)	(\$22.6)	(\$27.2)	(\$31.7)	(\$34.5)	(\$29.0)	\$7.5
Taxes	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0
<i>Tax Rate</i>	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
Preferred Stock Dividends	\$0	\$0.8	\$3.2	\$2.4	\$1.0	\$7.4	\$4.0	\$4.0	\$4.0	\$4.0	\$4.0
Net Income	(\$27.3)	(\$7.4)	(\$8.9)	(\$7.8)	(\$5.9)	(\$30.0)	(\$31.2)	(\$35.7)	(\$38.5)	(\$33.0)	\$3.5
<i>Net Margin</i>	-	-	-	-	-	-	-	-	-	-	-
Reported EPS	(\$5.19)	(\$0.96)	(\$1.08)	(\$0.98)	(\$0.59)	(\$3.53)	(\$2.23)	(\$2.10)	(\$1.93)	(\$1.32)	\$0.12
<i>YOY Growth</i>	-	-	-	-	-	-	-	-	-	-	-
Basic Shares Outstanding	5.3	7.7	8.2	8.0	10.0	8.5	14.0	17.0	20.0	25.0	30.0

Source: company filings and Zacks estimates

HISTORICAL ZACKS RECOMMENDATIONS



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