EDISON

Amarantus BioScience

Initiation of coverage

Building up therapeutics assets

Pharma & biotech

Amarantus has acquired several pre-commercial therapeutic assets in recent years, and intends to create value by furthering their development before out-licensing or commercialising them. The firm recently acquired ESS-W, which can shorten the time needed to treat severe burns. Eltoprazine aims to reduce involuntary movements associated with long-term levodopa therapy in Parkinson's disease. These candidates provide long-term potential, and drive our $76m rNPV.

Year end	Revenue ($m)	PBT* ($m)	EPS* ($)	DPS (p)	P/E (x)	Yield (%)
12/13	0.0	(8.3)	(2.76)	0.0	N/A	N/A
12/14	0.0	(22.0)	(4.36)	0.0	N/A	N/A
12/15e	0.0	(14.3)	(1.87)	0.0	N/A	N/A
12/16e	0.0	(17.2)	(1.68)	0.0	N/A	N/A

Note: *PBT and EPS are normalised, excluding intangible amortisation, exceptional items and share-based payments.

ESS-W and Eltroprazine target unmet needs

Amarantus recently acquired ESS-W from Lonza. ESS-W is a cell therapy full-thickness skin replacement treatment for severe burns, prepared from a small sample of the patient's own skin, which has the potential to significantly reduce hospital stays and risk of complications. Eltoprazine recently began a Phase IIb study for the reduction of involuntary jerky movements associated with prolonged levodopa treatment for Parkinson's disease. This candidate is also being developed as a non-stimulant adult ADHD therapy.

Diagnostics division primed for divestiture

Amarantus Diagnostics contains the LymPro and MSPrecise assays, which aim to improve the diagnostic capabilities of clinicians in Alzheimer's disease (AD) and multiple sclerosis (MS), respectively. LymPro is aimed as a blood test to improve non-invasive investigation, whereas MSPrecise intends to improve accuracy in borderline cases to ensure appropriate treatment. Amarantus plans to divest or spin out the Diagnostics division to strengthen its focus on its therapeutics programmes and potentially generate additional funding.

Valuation: rNPV of $76m, multiple shots on goal

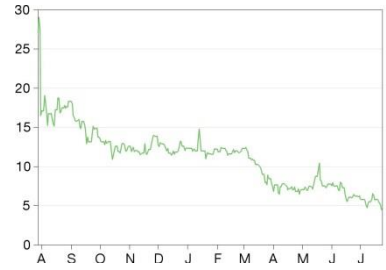
We value Amarantus using a risk-adjusted net present value (rNPV) model, with a 12.5% cost of capital. Our valuation of $76m ($8.18/share) includes the prospects of ESS-W and eltroprazine, but does not include the Diagnostics division, or for the firm's preclinical-stage MANF. MANF has shown some benefits in sparing retinal cells in preclinical models of retinitis pigmentosa (RP), an orphan indication. MANF advancement or an Amarantus Diagnostics divestiture could provide further upside. The company completed a 150:1 share consolidation in July 2015 and is seeking to uplist its shares to NASDAQ. The uplisting may accompany a fund-raising programme for its development projects. We estimate that significant development risks remain and the company will require access to repeat funding to support its development projects. We anticipate ESS-W could be the earliest programme to reach the market, in the 2018-19 time frame.

27 July 2015

Price	**US$4.72**
Market cap	**US$34m**

Net debt ($m) at Q115	2.5
Shares in issue (Q115)	7.2m
Free float	95%
Code	AMBS
Primary exchange	OTC
Secondary exchange	N/A

Share price performance



%	1m	3m	12m
Abs	(26.8)	(30.5)	(78.6)
Rel (local)	(25.8)	(29.3)	(79.5)
52-week high/low		$29.025	$4.50

Business description

Amarantus BioScience is a San Francisco-based life sciences firm developing therapeutics in multiple indications. Eltoprazine is in Phase IIb trials for Parkinson's disease, levodopa-induced dyskinesia (PD-LID). The company' Diagnostics subsidiary targets unmet need in neurology.

Next events

Q215 results	August 2015
Begin ESS-W Phase II study	H215

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Investment summary: Multiple assets to drive value

Company description: Assets secured, focus on execution

Founded in 2008, San Francisco-based Amarantus BioScience has acquired several unique therapeutic assets in recent years and is focused on advancing their development. The firm recently completed its acquisition of ESS-W, which has the potential to sharply reduce recovery times for severe burn victims. Eltoprazine has shown early efficacy in levodopa-induced dyskinesia (LID) associated with Parkinson's disease (PD-LID), and ADHD, and recently started a 60-patient Phase IIb study in PD-LID. It has also developed MANF, a preclinical-stage asset under investigation for retinitis pigmentosa (RP) and potentially other conditions given its propensity to reduce apoptosis (cellular death). Amarantus is working to sell or spin out its Diagnostics subsidiary, which includes proprietary products designed to address unmet need in the diagnosis of chronic neurological diseases. A successful transaction could potentially generate funding to support the firm's therapeutic programmes.

Exhibit 1: Product pipeline

Product	Description	Stage	Acquisition/in-licensing highlights
Therapeutics			
ESS-W	Intractable severe burns	Phase II (planned H215)	Obtained option to acquire in Nov 2014 from Lonza (Lonza to provide manufacturing); exercised in July 2015 for $4.0m upfront, plus up to $5.0m in regulatory milestones ($4m on BLA submission), and 2% royalties on future net sales. Amarantus paid $3.6m to privately held Regenicin (a holder of IP involving ESS-W) and 0.25m shares* to resolve infringement litigation case against Lonza.
Eltoprazine	Parkinson's disease (PD) Levodopa-induced dyskinesia (LID)	Phase IIb	Acquired in Jan 2014 from PsychoGenics for $0.1m upfront, $0.65m in R&D reimbursements, plus up to $4m in development milestones, and single-digit royalties on future net sales.
MANF	Retinitis pigmentosa (RP)	Preclinical	Developed internally, but also entered various intellectual property agreements with the universities of Massachusetts and Miami.
Diagnostics assays (Amarantus Diagnostics)			
LymPro test	Alzheimer's disease (AD) diagnosis	Early commercialisation exploration (for investigational use market)	Acquired from MemoryRx in Dec 2012 for issue of 0.013m shares* ($5.93/share), plus 0.043m shares* in mid-2014; 9% royalty payable on future net sales.
MSPrecise diagnostics	Multiple sclerosis diagnosis	Regulatory preparations (CLIA)	Acquired in Jan 2015 for issue of 0.66m shares* ($13.50/share), plus up to $2m in milestones; low single-digit royalty payable on future net sales.

Source: Company reports. Note: *Share count and pricing adjusted for the 150:1 reverse consolidation (from June 2015).

Valuation: rNPV of $76m reflects sum of diverse assets

Our rNPV of $76m (or $8.18 per share) applies a 12.5% cost of capital and assumes probability-weighted assumptions for the company's development assets (excluding MANF given its early development stage). This is higher than the current c $37m EV.

Financials: Further capital required in 2015 and 2016

Amarantus had $2.5m net debt on 31 March 2015 and a trailing 12-month burn rate of $18.1m. We forecast 2015 and 2016 burn rates of $15.5m and $17.1m, respectively, with expenditures largely directed towards advancing eltoprazine and ESS-W. We assume the firm will use the remaining $14.5m of its existing equity line of credit by mid-2016 and raise an additional $11m in funds by year end 2016 which, for illustrative purposes, we assign to long-term debt.

Sensitivities: Funding, development risks, partnerships

In addition to development and regulatory risk, a key challenge will be sustaining access to capital at favourable terms to fund its multiple development projects. The firm will also be reliant on its relationships with third parties, as it seeks potential partners or licensees for the neurodiagnostics business and for its therapeutic assets in the future following further clinical development. There is a risk the eltoprazine-use patents could be challenged and thus limit its market exclusivity duration.

Outlook: Developing a pipeline of treatment assets

Amarantus has acquired, in-licensed or entered transactions to acquire diverse development-stage therapeutic assets in recent years. It sought therapeutic assets that were relatively inexpensive (possibly due to prior development challenges) with the goal of addressing any hurdles, advancing products through human trials and then explore sale/out-licensing options. It has also built a Diagnostics division by in-licensing strategic neurodiagnostics assets. The January 2015 DioGenix acquisition strengthened the neurodiagnostics subsidiary and helped better position its diagnostics division for a possible out-licensing, sale or spin-out, which could help generate capital and enable the firm to focus its resources on advancing its therapeutics assets.

ESS-W engineered skin substitute

Amarantus entered into an option agreement to purchase ESS-W from Lonza in November 2014, and completed the acquisition in July 2015 (terms included $4m upfront, up to $5m in milestones and 2% royalties on future sales). It will retain Lonza for manufacturing. ESS-W is a cell therapy full-thickness replacement treatment for Stage 3 and Stage 4 (severe) burns. Skin grafting is the current treatment approach for burns. Mild- to moderate-stage burns may only require split-thickness grafts (comprising the epidermis and part of the dermis) and often heal more quickly (and with fewer adverse events) than full-thickness grafts. Full-thickness grafts may be needed for more severe burns and carry higher auto-rejection and infection risks, and longer recovery times. ESS-W treatment is a tissue-engineered skin substitute (ESS), which is prepared from a small sample of the patient's own skin cells whereby an absorbable collagen and glycosaminoglycan (C-GAG) matrix is populated with the patient's epidermal keratinocytes and dermal fibroblasts at a central laboratory and then surgically transplanted. ESS-W can potentially facilitate more complete and lasting wound closure than existing grafting methods (such as autograft, where the patient's own skin on a different area of the body is used for grafting to the injured site).

Over $18bn is spent per year on the treatment of severe burns in the US alone,[1] about 100,000 moderate to severe burn injuries requiring hospitalisation occur each year in the US, and about 5,000 die per year from complications.[15] The National Center for Injury Prevention and Control estimates that 500-2,000 patients pa present with severe burns requiring hospitalisation. Patients can stay up to 80-120 days in an intensive care unit (ICU) to heal (>$10,000/day cost). An average of $1.6m is spent per patient for those without complications. Amarantus previously estimated a US market opportunity of $500m for severe burns, and we forecast over $240m in global peak sales.

Engineered skin substitutes (ESS) might be less likely to be rejected by the immune system of the patient than external source grafting such as porcine or cadaver. ESS-W, which has orphan drug designation in the US, has the potential to change the current standard of care for severe burns, demonstrating in preclinical trials the ability to generate a functional skin barrier. Under ESS-W, a skin sample from an affected patient will be sent to a central laboratory (Maryland-based) that will produce as much engineered skin as required to close a wound within c 30-35 days of sample extraction (ie a 30- to 35-day dry cell growth phase). A key value driver for ESS-W is that full wound closure could occur within 45 days of burn event, thereby potentially sparing patients more than two months' additional stay time in an ICU.

An earlier ESS-W version (PermaDerm) in a previous human study was subject to a clinical hold and study halt as a result of GMP compliance and product consistency issues (not related to manufacturing, but due to incorporation of non-standardised or animal products); Lonza rectified these issues and the clinical hold was lifted in May 2014, but a legal challenge from Regenicin persisted. Amarantus settled the dispute with Regenicin, which included a payment to Regenicin of

[1] Church D, Elsayed S, Reid O, et al. Clin Microbiol Rev. 2006 Apr; 19(2): 403–434. 10.1128/CMR.19.2.403-434.2006.

$3.6m and the equivalent of 0.25m common shares, adjusted for the 150:1 share consolidation. This paves the way for the resumption of clinical development once Amarantus completes the Lonza acquisition.The Regenicin transaction was expensed in 2014 in the firm's R&D expense line.

Phase II ESS-W Clinical trial planned for H215

Amarantus expects recruitment to start in H215 for a two- to three-site Phase I/IIa trial with an improved and better standardised version of ESS-W in 10 patients with deep partial and full-thickness burn wounds (data expected in 2016). Efficacy will be compared to that of meshed spit-thickness autograft (AG). Studies are expected to receive partial funding by a US government grant from the Armed Forces Institute for Regenerative Medicine (AFIRM); $1m has already been secured and additional funds may be available. Amarantus anticipates that total study costs will not exceed $2.5-3.0m. Subsequently, a Phase III registration study would be needed for approval (which may require less than 100 patients). The full commercialisation of the treatment could occur in 2018-19, although we believe that Amarantus plans to examine spin-off/out-licensing opportunities before then (ie potentially before or during the Phase III trial).

Exhibit 4: Competing products for skin burn treatment/replacement

Company	Product (candidate)	Description	Status
Avita Medical	ReCell Spray-on Skin	Cultured epithelial autograft/autologous suspension in spray formulation; it reduces donor skin harvesting requirements in the treatment of burn injuries.	Phase III (US), marketed EU/Other
Integra Life Science Holdings	Integra Dermal Regeneration Template	Used for full-thickness or deep partial thickness thermal injuries where sufficient autograft is not available or desirable; It provides the needed framework for blood vessels and dermal skin cells to regrow, and a thin-level epidermal skin graft can then be applied.	Marketed
Kinetic Concepts	AlloDerm Acellular allograft dermal matrix	An acellular dermal matrix derived from donated human skin that undergoes a process to remove both the epidermis and cells that can lead to tissue rejection; the purpose is to decrease the need for autograft in full-thickness wounds and burns.	Marketed
Arteriocyte	Magellan platelet gel	Gel using proprietary Magellan autologous platelet separator technology; developed as an adjunctive therapy to improving autologous skin graft adherence, acceptance and integration in second- and third-degree burn patients.	Phase I
Global Neurotech (GNT)	Neu2000	NMDA receptor NR2B selective antogonist intended to reduce damage/injury caused by burns.	Phase I
Kuros Biosurgery	I-020502, KUR-212	Fibrin sealant incorporating a variant of platelet-derived growth factor, for severe burns; adhesive agent to fixate the graft to the site of the burn, thus avoiding the use of staples and to improve the healing process.	Phase II

Source: Company reports, BioCentury

Eltoprazine

Eltoprazine is a small molecule 5HT1A/1B serotonin receptor partial agonist, which is in Phase II development for the treatment of levodopa-induced dyskinesia (LID) associated with Parkinson's disease (PD-LID) and adult attention deficit hyperactivity disorder (ADHD). It showed a favourable safety profile in more than 680 patients[2] tested across several Phase I and Phase II studies, including dosing periods of up to two years and at daily doses up to 30mg. Dose-limiting adverse events with single doses were nausea and somnolence/sedation, which decreased on repeat dosing. Eltoprazine was originally developed by Solvay (now Abbvie) and out-licensed to PsychoGenics, which subsequently licensed it on to Amarantus in January 2014.

Eltoprazine in Parkinson's disease

Levodopa is one of the most commonly used treatments for PD symptoms. LID occurs after five to 10 years of levodopa treatment and is characterised by involuntary random and jerky movements. Between 50% and 70% of levodopa-treated PD patients can develop LID. Current management includes adjusting levodopa dosing and/or adding a dopamine receptor D2-agonist to the regimen to spare levodopa. Amantadine (Symmetrel by Endo Pharmaceuticals), an NMDA receptor antagonist, is the only orally active drug on the market that can be prescribed without special

[2] Including approximately 300 healthy subjects, and more than 300 patients with aggression, ADHD, or mental disorder.

monitoring to improve PD-LID, although it can induce side effects including dizziness. Neurosurgery may also be considered.

Certain evidence supports the theory that LID is provoked by the take-up of levodopa by serotonergic terminals, which convert it to dopamine, subsequently causing abnormal involuntary movements. Amarantus believes the pre-synaptic activation of serotonin receptors using a 5HT1A/1B agonist may dampen the resulting excessive release of dopamine.

Completed Phase I/IIa shows LID reduction at 5mg dose

In a previous 22-patient, dose-ranging, double-blind, placebo-controlled Phase I/IIa study of eltoprazine as a treatment of PD-LID, the drug met its primary endpoint exhibiting a statistically significant reduction in LID vs placebo at a 5mg and 7.5mg dose after eight weeks, without adversely affecting levodopa efficacy. Patients made five dosing visits where they were exposed to placebo (twice) and all three tested eltoprazine doses (2.5, 5 and 7.5mg). During each visit, the PD-LID subjects received a suprathreshold challenge L-DOPA dose[3] (calculated as 150% of his/her regular dose, up to a 250mg maximum) and the study drug, and were observed (video filmed) for three hours. Independent ("blinded" or unbiased) observers rated, at 30-minute intervals, the patients' PD tendencies with the Unified Parkinson's Disease Rating Scale part III (UPDRS-III), as well as dyskinesia levels using the Clinical Dyskinesia Rating Scale (CDRS). The crossover study design allowed for intra-individual comparisons of placebo effects, as well as unbiased comparisons between the different doses and placebo.

Dyskinesia ratings calculated using CDRS AUC 0-3 (area under curve up to three hours post-dose) showed a significant reduction of LIDs (p=0.004) in the 5mg arm, compared to randomized placebo.

Exhibit 2: Differences between eltoprazine and randomized placebo (n=22)

Parameter	Eltoprazine 2.5mg	Eltoprazine 5.0mg	Eltoprazine 7.5mg
CDRS AUC 0-3	-0.64	-1.02	-0.043
P-value	0.065	**0.004**	0.103
Change in UPDRS	-2.52	-1.17	0.49
P-value	0.053	0.156	0.375

Source: Company reports

Post-hoc analyses also determined an estimated 15% decrease (P = 0.003) in CDRS AUC 0-3 at 5mg of eltoprazine, a 9% decrease with 7.5mg (P = 0.083) and a 6% decrease with 2.5mg of eltoprazine (P = 0.271). There were no significant differences found in UPDRS-III AUC 0-3 or maximum UPDRS-III scores three hours post-dosing between any of the treatments and placebo, which suggest there is no deterioration of the normal anti-Parkinsonian treatment effect of L -DOPA by eltoprazine co-treatment.

As eltoprazine's mechanism of action differs from amantadine, combining both drugs could potentially provide additive LID relief, and Bezard et al (2013) showed that these drugs can have additive anti-dyskinetic actions in animal LID models.

60-patient Phase IIb study started in June 2015

Amarantus initiated a multi-centre, four-way crossover, 60-patient Phase IIb study (NCT02439125) in June 2015 to assess the sustained effects of repeated eltoprazine dosing (at three dose ranges) on PD LID. Subjects with moderate to severe PD LID receiving daily levodopa doses above 300mg will be recruited to receive three-week cycles of BID doses of eltoprazine 2.5mg, eltoprazine 5.0mg, or eltoprazine 7.5mg, and placebo.

[3] The challenge L-DOPA dose was used to increase the study's sensitivity for assessing whether the study drug would worsen PD symptoms.

The primary endpoint will be the clinical impact on dyskinesia measured by total UDysRS (Unified Dyskinesia Rating Scale) score at the end of each of the four three-week treatment arms. The UDysRS scale was developed more recently than the CDRS scale used in the Phase I/IIa trial. A task force from the International Parkinson and Movement Disorder Society assessed that the UDysRS scale has excellent clinimetric properties that appear to provide a reliable and valid assessment tool of dyskinesia in PD.[4] Secondary endpoints also include measurements of PD motor symptoms using patient diaries and physiological measurements of abnormal movements as measured by motion sensors.

Partnership likely if Phase IIb data successful

The firm expects to complete the Phase II study in H116 and anticipates looking to partner the drug on positive data. Parallel Phase III studies could occur from 2016-18, leading to a potential 2021 launch. The Parkinson's Disease Foundation estimates more than one million Americans have PD and approximately six million are diagnosed worldwide, a market it expects to double by 2030. An effective LID treatment could garner much interest. We estimate that eltoprazine could be commercialised in 2021 and generate global end-user sales over $680m.

Exhibit 3: Competing products in development for PD LID

Company	Product candidate	Description	Status
Adamas Pharmaceuticals	ADS-5102 (Nurelin-amantadine)	Oral extended-release formulation of amantadine.	Phase III; possible launch 2016
Otsuka	AVP-923 (Nuedextra, dextromethorphan/ quinidine)	Combination NMDA receptor antagonist dextromethorphan with quinidine sulfate, a cytochrome P450 2D6 enzyme inhibitor.	Phase II
Laboratoires Pierre Fabre	Befiradol (generic)	Serotonin (5-HT1A) receptor agonist.	Phase II

Source: Company reports, BioCentury

Eltoprazine in adult ADHD

ADHD is characterised by persistent inattention and/or hyperactivity, poor impulse control and forgetfulness. Often considered as a disease affecting children (prevalence cited as high as 15%), ADHD can persist into adulthood and is believed to affect up to 4.4% of US adults aged 18-44.[5] Approximately 600,000 people in the US alone are currently treated for adult ADHD and with the vast majority remaining undiagnosed and untreated, there is significant opportunity for improved effective treatments. Currently, the most commonly prescribed ADHD drugs are stimulants such as methylphenidate (off-patent, although branded Concerta by J&J recorded $782m in 2013 revenue), dextroamphetamine and amphetamine (Adderall by Shire). GBI Research expects the global ADHD market to rise from $6.9bn in 2013 to $9.9bn by 2020.

In 2014, positive data were reported for eltoprazine in a 36-patient, US placebo-controlled crossover study in adults with ADHD. Significant improvements were shown with doses of 5mg and 10mg in multiple clinical measures, including the ADHD-RS-IV scale (primary endpoint), with 25% greater efficacy than placebo (p=0.003 for 5mg arm; p=0.037 for 10mg arm). Amarantus believes that eltoprazine's relative lack of stimulant properties could positively differentiate it vs stimulant ADHD drugs, which could be more prone to patient abuse/addiction. The current best-selling, non-stimulant ADHD drug is atomoxetine (Strattera, Lilly), with $738.5m in worldwide 2014 sales. As the PD-LID Phase IIb study is now underway. we believe Amarantus is assessing its next steps for advancing eltoprazine towards a potential Phase IIb adult ADHD trial.

Mesencephalic Astrocyte-derived Neurotrophic Factor

Mesencephalic Astrocyte-derived Neurotrophic Factor (MANF) is an endogenous widely expressed protein that was discovered by the company's chief scientific officer Dr John Commissiong. MANF

[4] Mov Disord. 2010 Jul 15;25(9):1131-42. doi: 10.1002/mds.23072.
[5] Kessler RC, Adler L, Barkley R, et al. American Journal of Psychiatry. 2006. 163: 724-732.

may act on multiple molecular functions, including as part of the endoplasmic reticulum stress response (ER-SR) system of the unfolded protein response (UPR). Amarantus estimates MANF can reduce and prevent apoptosis (cell death) in response to injury or disease, via the UPR. It has shown potential efficacy in various animal models for PD, retinitis pigmentosa (RP), cardiac ischemia and stroke. Amarantus is focusing its MANF development in orphan indications, and most recently has emphasized its efforts in genetically associated retinal disorders such as RP. MANF received FDA Orphan drug status in RP in late 2014.

Retinitis Pigmentosa (RP)

Retinitis pigmentosa (prevalence one in 3,000 to one in 5,000) refers to a group of inherited diseases causing gradual and cumulative damage to photoreceptors located within the retina. Patients often experience a progressive degeneration of peripheral, night and colour vision before losing central visual acuity. RP frequently leads to severe vision impairment within 10-20 years of diagnosis. There is no known cure for RP, although vitamin A supplementation is often recommended as some studies suggest it can delay blindness by up to 10 years. Preclinical studies using gene therapy (to replace damaged or defect proteins in the retina), or stem cell therapy (introduced into the eye to restore or replace dying photoreceptor cells) showed early promise.

In 2012, the University of Miami reported preclinical data on transgenic rats showing that intravitreal recombinant MANF injections protected rods and cone photoreceptors from degeneration, and Amarantus reported in 2014 that MANF injections provided functional vision benefits in a mouse RP model. Amarantus entered into an agreement with Catalent Biologics to prepare MANF for cGMP manufacturing. On completing toxicology studies, the firm intends to bring MANF to human studies. It plans to start a human proof-of-concept study in RP in 2018, and may also investigate MANF's ability to preserve neuroretinal function in other indications, including glaucoma or retinal artery occlusions, as well as its prospects for Parkinson's disease or myocardial infarcts.

Amarantus Diagnostics focused on neurology

Amarantus entered into a licence agreement in 2012 with privately held Memory Dx to obtain exclusive rights for the Lymphocyte Proliferation Test (LymPro) and its related intellectual property (IP) in Alzheimer's disease (AD) diagnosis. Amarantus acquired DioGenix in January 2015 to obtain rights to the MSPrecise platform directed at improving MS diagnostic accuracy. Also in January 2015, Amarantus entered a one-year option agreement with Georgetown University to in-license the IP related to certain blood-based biomarkers for memory loss. Georgetown published data[6] showing that 10 lipid biomarkers obtained in peripheral blood had 90% accuracy in predicting the onset of MCI or AD in patients over the age of 70. The DioGenix and Georgetown agreements bolster the breadth and marketability of the Amarantus Diagnostics division, which the firm is seeking to out-license, spin out or divest to further focus its resources on its therapeutics assets.

LymPro could provide more convenient, earlier AD detection

LymPro is based on the hypothesis from several groups[7] that AD patients have a dysfunctional cell cycle regulatory machinery, which inappropriately allows neurons in the brain to start (but not complete) the cell division (mitosis) process. LymPro is a blood test that evaluates the presence of cell surface marker CD69 on peripheral blood lymphocytes following a mitogenic (mitosis-promoting) stimulus. LymPro assumes that if the cellular division machinery is working correctly,

[6] Mapstone M, Cheema AK, Fiandaca MS, et al. Nat Med. 2014 Apr;20(4):415-8. doi: 10.1038/nm.3466. Epub 9 Mar 2014.

[7] Including the University of Leipzig, Albert Einstein College of Medicine, Oxford University and Case Western Reserve University.

CD69 would be upregulated following this stimulation on certain lymphocytes; however, if CD69 is not upregulated, cellular division dysfunction and AD are more likely.

Current AD diagnostic toolkit can be invasive or costly

AD cannot be truly confirmed without a verification of brain tissue via biopsy (impractical). Non-invasive cognitive tests (such as the mini-mental state exam, MMSE) are commonly applied but their ability to accurately measure brain function can be limited by subject bias and the need for patient co-operation. Imaging tests such as positron emission tomography (PET) can be used, but PET scans can cost over $3,000 per session per patient. PET scans are not accessible to mobile and portable sites of use, limiting their reach. Cerebrospinal fluid (CSF) extractions involving lumbar punctures are among the most effective established detection methods for early AD, but are invasive, painful and could pose complications. Sunderland et al[8] reported detection sensitivities and specificities of 70-100% and 40-90% respectively, for CSF marker AB42, and of 40-85% and 65-85% with tau biomarker. Rubino[9] reported that using a combination of CSF AB42, T-tau and P-tau provides sensitivity of 89% and specificity of 77% in predicting AD.

Early clinical data support role for LymPro in AD

Data released in 2014 from a 72-patient LP-002 study showed that CD69 expression on specific lymphocyte subpopulations was statistically significantly lower in the AD arm versus the control arm. Data were measured under two different mitogenic stimulation conditions (Version 1 and Version 2). Version 1 correctly classified AD patients and healthy controls with an accuracy of 87% (p=0.0015), with 80% sensitivity and 86% specificity.[10] Version 2 had an accuracy of 83% (p=0.0059) with 90% sensitivity and 71% specificity. The firm recruited 68 additional patients and reported data from the combined 140-subject group in January 2015, which similarly showed statistically significant separation between patients with AD from healthy controls. In July 2015, the firm presented expanded (multivariate) analyses from the LP-002 data, which confirm the previously reported results, and may support LymPro's potential utility as a blood biomarker for AD pathology.

Commercialisation initiative for IUO market, CLIA process for clinical care

LymPro was cleared in late 2014 for commercial sales in the investigator use-only (IUO) market following the completion of assay validation at Icon Central Laboratories. This process allows the assay to be offered to drug development firms for evaluation in therapeutic AD clinical trials, but not yet for use in the general clinical population. Amarantus estimates that the AD IUO market is at US$150m and is offering LymPro (with assay performed at Icon facility) for clinical trial sites in the US and EU. A longer-term objective would be applying LymPro for AD detection in the general patient population, throughout primary healthcare and neurology clinical care settings. LymPro will require Clinical Laboratory Improvement Amendments (CLIA)[11] certification as a laboratory-determined test (LDT) to proceed, which could be completed in 2016. We assume the US LymPro market opportunity at $750m (assuming $500/test and that one million US people suspected of having AD and 10% of the five million diagnosed AD patients are tested yearly). LymPro may need to compete with other blood-based AD tests in development, including NanoSomiX.

[8] JAMA. 2003;289(16):2094-2103. doi:10.1001/jama.289.16.2094.
[9] Neurology February 12, 2013; 80 (Meeting Abstracts 1): IN3-2.003.
[10] TP = True Positives; TN = True Negatives; FP = False Positives; FN = False Negatives; Accuracy = (TP + TN) / TP + FP + TN + FN); Sensitivity = TP / (TP + FN) ; Specificity = TN / (TN + FP).
[11] CLIA refers to federal regulatory standards that apply to all human clinical laboratory testing performed in the US except clinical trials and basic research. LDTs cleared through CLIA can only be used by the laboratory entity where they are developed and validated. Medical devices or tests intended to be used at multiple sites (eg laboratories, hospitals, etc) are required to go through FDA premarket approval (PMA) or 510k regulatory pathways.

Amarantus Diagnostics entered its first commercial biomarker services agreement for LymPro in February 2015 with Avanex Life Sciences (OTC: AVXL). Additional collaborators are being sought to build further data for LymPro in AD, which could influence its commercial viability.

MSPrecise to improve multiple sclerosis detection accuracy

Standard protocols for MS detection include MRI imaging and motor function tests, but can include CSF analysis using oligoclonal banding (OCB) in instances where further testing is needed. OCB testing examines for the presence of certain immunoglobulins (antibodies) in a bodily fluid, and the presence of oligoclonal bands in CSF can be an important diagnostic indicator of MS. A 2010 review study assessing the accuracy of CSF OCB banding in MS diagnosis showed sensitivities between 69% and 91%, with specificities between 59% and 94%.[12] MSPrecise is a proprietary DNA sequencing assay for the identification of patients with relapsing-remitting multiple sclerosis (RRMS).[13] MSPrecise measures codon[14] replacement frequencies and other DNA changes in the variable region of immunoglobulin (Ig) heavy chain (IGHV) genes in immune B lymphocyte cells (B-cells) isolated from CSF, and peripheral blood B-cells.

MSPrecise is based on research which showed that patterns of DNA mutations observed in rearranged IGHV genes of B-cells isolated from CSF of MS patients are different from those observed in CSF B-cells isolated from people without MS. MSPrecise uses an algorithm that interprets these mutational changes to distinguish between patients with RRMS and those with other diseases. MSPrecise uses CSF fluid and requires no additional samples beyond what would be required for conventional OCB banding testing. When combined with OCB analysis, MSPrecise can strengthen the specificity and sensitivity of MS diagnostic testing and reduce false positives.

In a 13-site validation study (commencing in 2012) of 334 subjects being evaluated for non-specific neurological symptoms, when MSPrecise results were combined with the OCB results, the combined accuracy was 92% ($p < 0.001$) with 96% sensitivity and 83% specificity. These results suggest a potentially meaningful improvement in classifying early-stage RRMS patients compared to published literature data for the current standard CSF/OCB analysis.

CLIA clearance the next step before potential commercialisation

CLIA certification is required for MSPrecise to be commercialized as a diagnostic in vitro LDT for use in clinical neurology settings. We estimate that approved laboratory selection and remaining steps (validation, performance studies) for CLIA clearance will occur once the Amarantus Diagnostics divestiture or spin-out is completed.

Estimates of MS prevalence are generally 50-95 per 100,000 in the US and Europe,[15,16] and the National MS Society estimates annual incidence in the US of 10,400 cases. Amarantus estimates that even reducing as little as three false positive MS per 100 treated patients would deliver positive ROI for payers. A 2002 Epocrates Market Research Survey on 100 US neurologists found that, on average, respondents indicated that 15.1% of patients coming to their practice with an existing RRMS diagnosis did not have the disease (ie misdiagnosed false positives).The value of the North American MSPrecise market could be c $300m (assuming a cost of $4,000-4,500 per test and peak market share of two-thirds). The targeted annual testing market would include not only newly diagnosed or suspect cases, but a larger group of patients (up to c 100,000 per year) with other conditions with neurological symptoms (eg patients with vascular disease, psychiatric diseases, migraine, patients diagnosed with RRMS suspecting misdiagnosis, etc).

[12] Schäffler N1, Köpke S, Winkler L. Acta Neurol Scand. 2011 Sep;124(3):151-64. doi: 10.1111/j.1600-0404.2010.01454.x. Epub 2010 Nov 11.
[13] MS is classified into four subtypes, with approximately 85-90% of MS patients having the RRMS form.
[14] A codon is a three-nucleotide long genetic sequence embedded within DNA or RNA, which codes for a specific amino acid or stop signal during protein synthesis.
[15] Noonan CW, Williamson DM, Henry JP, et al. Prev Chronic Dis. Jan 2010;7(1):A12.
[16] Pugliattia M, Rosatia G, Carton H, et al. European Journal of Neurology 2006, 13: 700–722.

Valuation

We value Amarantus using a risk-adjusted net present value (rNPV) model, with a 12.5% cost of capital. Our model assumes that Amarantus will complete ESS-W development and market the product internally, and that it will out-license eltoprazine at the end of Phase II studies, with the company retaining 20% net royalties. Given the early preclinical stage of development for MANF, we are not yet including it in our valuation. For Amarantus Diagnostics, we forecast peak revenue of over $250m for LymPro and more than $160m for MSPrecise (both by 2025). Given the parent firm's intention to divest or spin out this unit and our view that the firm will focus resources on the therapeutic assets until such a deal occurs, we do not include this division in our valuation.

Exhibit 5: Amarantus BioScience rNPV assumptions

Product contributions (net of R&D costs)	Indication	rNPV ($m)	rNPV/share ($)	Probability of success	Launch year	Peak WW sales (US$m)	Economics assumptions
Eltoprazine	PD LID	62.0	6.93	30.0%	2021	$683m in 2026	20% royalty rate
Eltoprazine	Adult ADHD	26.0	2.91	20.0%	2022	$540m in 2027	20% royalty rate
ESS-W	Severe burns	55.9	6.25	25.0%	2019	$241m in 2026	60% peak EBITDA margin
Corporate costs & expenses							
SG&A expenses		(48.8)	(5.46)				
Net capex, NWC & taxes		(19.4)	(2.17)				
Total rNPV		**75.7**	**8.46**				
Net cash (debt) (Q115e)		(2.54)	(0.28)				
Total equity value		**73.2**	**8.18**				
FD shares outstanding (000s)* (Q115e)		8,948					

Source: Edison Investment Research. Note: *FD shares count adjusted for outstanding convertible preferred shares.

Our $76m rNPV calculation represents upside to Amarantus's current EV of c $37m, and equates to $8.18 per share fully diluted (our FD share count of 8.95m includes the 7.23m listed shares outstanding[17] on 31 March 2015, plus the 1.72m shares that would result from the conversion of all outstanding convertible preferred shares).[18]

Sensitivities

Development and regulatory risk: to gain approval, ESS-W, eltoprazine and MANF must deliver success in randomised clinical studies without significant safety risks. CLIA-compliant laboratory and validation activities are required for LymPro and MSPrecise to reach clinical care markets.

Competition considerations: competing products are being developed for many of the markets Amarantus is targeting, and commercial success will depend on relative performance.

Financing risk: we expect Amarantus to require additional funds to develop its programmes. The firm has access to $14.5m in equity capital available under the financing facility with Lincoln Park Capital. We assume that this line of credit would be exhausted by mid-2016, which would raise the FD share count (including preferred share conversion) to 12.0m at current ($4.50/share) market pricing. We do not expect the firm to become cash flow positive until 2020, driven by ESS-W sales.

Partnership risk: Amarantus is seeking to out-license or divest its diagnostics division and therapeutics assets such as ESS-W or eltoprazine once certain clinical milestones are met. Challenges could lead to unnecessary development delays and/or unfavourable terms.

Intellectual property risk: the success of commercial products will depend on Amarantus's ability to defend the IP assets surrounding them. We assume market exclusivity through 2030 for ESS-W

[17] After the 150:1 reverse consolidation completed in July 2015.

[18] Includes effects from conversions of following Preferred share series: 750,000 of Series C, 350 of Series D, 7,721 of Series E and 1,087 of Series G.

and eltoprazine, and expect a longer IP lifetime for MANF. The eltoprazine composition of matter patents has expired. While its use patents expire after 2029, these may not provide as robust protection against generics, and could limit its market exclusivity to under six or seven years.

Financials

On 31 March 2015, Amarantus had $0.1m in cash and equivalents, $0.2m in restricted cash and $2.85m in loan payables (net debt of $2.54m). Its trailing 12-month cash burn rate through Q115 (operating cash flow minus net capex) was $18.1m and we expect this to decrease, given the non-recurring nature of costs already disbursed relating to the DioGenix and Reginicin settlements. We forecast 2015 and 2016 burn rates of $15.5m and $17.1m, respectively (not including the $4m ESS-W purchase). The firm entered a $20m share purchase agreement with Lincoln Park Capital in 2014. $14.5m in capital from the line was available at Q115, which we estimate will be depleted by mid-2016 (we assume $10m to be drawn in Q215 through Q415, and $4.5m in 2016). Amarantus raised $5m in convertible preferred shares (paying 8.25% pa) in April 2015. We assume it will raise $11m in additional funds by YE16 which, for illustrative purposes, we assign to long-term debt.

Exhibit 6: Financial summary

US$(000)	2012	2013	2014	2015e	2016e	2017e
31-December	IFRS	IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS						
Revenue	0	0	0	0	0	0
Cost of Sales	0	0	0	0	0	0
General & Administrative	(3,506)	(3,552)	(7,439)	(8,510)	(7,000)	0
Research & Development	(577)	(2,089)	(13,762)	(5,727)	(10,100)	0
EBITDA	(4,083)	(5,641)	(21,201)	(14,237)	(17,100)	(12,600)
Depreciation	(7)	0	(35)	(50)	(65)	(89)
Amortization	0	(70)	(118)	(1,698)	(2,339)	(1,905)
Operating Profit (before exceptionals)	(4,090)	(5,711)	(21,354)	(15,985)	(19,504)	(14,594)
Exceptionals	473	(6,790)	(5,110)	0	0	0
Other	0	0	0	0	0	0
Operating Profit	(3,617)	(12,501)	(26,464)	(15,985)	(19,504)	(14,594)
Net Interest	(1,518)	(2,631)	(813)	(48)	(49)	(336)
Profit Before Tax (norm)	(5,609)	(8,272)	(22,049)	(14,336)	(17,214)	(13,025)
Profit Before Tax (FRS 3)	(5,136)	(15,132)	(27,277)	(16,033)	(19,553)	(14,930)
Tax	0	0	0	0	0	0
Profit After Tax and minority interests (norm)	(5,609)	(8,310)	(22,924)	(15,164)	(17,214)	(13,025)
Profit After Tax and minority interests (FRS 3)	(5,136)	(15,170)	(28,152)	(16,861)	(19,553)	(14,930)
Average Number of Shares Outstanding (m)	0.9	3.0	5.3	8.1	10.3	10.3
EPS - normalised ($)	(5.98)	(2.76)	(4.36)	(1.87)	(1.68)	(1.27)
EPS - normalised and fully diluted ($)	(5.98)	(2.76)	(4.36)	(1.87)	(1.68)	(1.27)
EPS - (IFRS) ($)	(5.47)	(5.05)	(5.35)	(2.08)	(1.91)	(1.45)
Dividend per share (C$)	0.0	0.0	0.0	0.0	0.0	0.0
BALANCE SHEET						
Fixed Assets	532	611	1,846	13,119	10,902	9,115
Intangible Assets	532	611	1,497	12,611	10,272	8,367
Tangible Assets	0	0	145	304	427	545
Current Assets	678	1,248	412	3,685	1,848	3,705
Short-term investments	0	0	0	0	0	0
Cash	157	1,033	214	3,183	1,346	3,203
Other	521	215	198	502	502	502
Current Liabilities	(2,969)	(1,624)	(6,329)	(7,628)	(7,628)	(7,628)
Creditors	(2,969)	(1,624)	(6,329)	(4,778)	(4,778)	(4,778)
Short term borrowings	0	0	0	(2,850)	(2,850)	(2,850)
Long Term Liabilities	(1,769)	(6,915)	0	0	(11,000)	(26,000)
Long term borrowings	(740)	(932)	0	0	(11,000)	(26,000)
Other long term liabilities	(1,029)	(5,983)	0	0	0	0
Net Assets	(3,528)	(6,680)	(4,071)	9,176	(5,877)	(20,808)
CASH FLOW						
Operating Cash Flow	364	(842)	(10,518)	(15,513)	(17,100)	(12,600)
Net Interest	(1,518)	(2,631)	(813)	(48)	(49)	(336)
Tax	0	0	0	0	0	0
Capex	0	0	(181)	(171)	(188)	(207)
Acquisitions/disposals	(56)	(70)	(1,100)	(4,900)	0	0
Financing	0	0	11,599	20,751	4,500	0
Net Cash Flow	(1,210)	(3,543)	(1,013)	119	(12,837)	(13,143)
Opening net debt/(cash)	66,087	583	(101)	(418)	(537)	12,300
HP finance leases initiated	0	0	0	0	0	0
Other	66,715	4,227	1,330	0	0	(0)
Closing net debt/(cash)	583	(101)	(418)	(537)	12,300	25,443

Source: Company accounts, Edison Investment Research. Note: We assume the remaining $14.5m of the Lincoln Park equity credit facility would be exercised in 2015 ($10m to be drawn) and 2016 ($4.5m to be drawn) at an average price of $4.50/share. The 2015 financing line also includes preferred share offerings, including the $5m in Series G preferred shares raised in April 2015.

Contact details	Revenue by geography
Amarantus BioScience Holdings 655 Montgomery Street, Suite 900 San Francisco, CA 94111 US +1-(415) 688-4484 www.amarantus.com	N/A

Management team

President & CEO: Gerald Commissiong	Chief Financial Officer: Robert Farrell
Mr Commissiong co-founded Amarantus with John Commissiong in 2008 and became the CEO in October 2011. Previously, he served as the company's COO and chief business officer. In these roles, he raised financing and sought business development, in-licensing and strategic transaction opportunities and research collaborations. He received a BSc in Management Science & Engineering with a focus on financial decisions from Stanford University.	Mr Farrell joined Amarantus as CFO in April 2014. Previously, he served as CFO of Titan Pharmaceuticals (1996-2008) and as president and CEO (2008-10). He also served as CFO at Sanovas and as CFO, corporate group VP and general counsel at Fresenius USA and Fresenius Medical Care. He currently serves on the board of directors of Prime Genomics and holds a J.D. from the University of California's Hastings School of Law.
Chief Medical Officer, Therapeutics: Charlotte Keywood	**Chief Scientific Officer: John W Commissiong**
Dr Keywood joined Amarantus as CMO of the Therapeutics division in April 2014. She was previously CMO at Addex Pharma for 10 years, overseeing clinical development of the company's allosteric modulator programmes. She served as medical director for Axovan, a Swiss biotech company acquired by Actelion in 2003. She was medical director at Vernalis (1996-2001) and medical director of the European subsidiary of US biotechnology company, Gensia (1991-96). Dr Keywood is a cardiologist and completed her post-graduate training at St Thomas' Hospital, London.	Dr Commissiong has served as the CSO and a director of Amarantus since co-founding the company in 2008. Previously, he served as the CSO of Neurotrophics and Prescient Neuropharma, which he co-founded in 1999. Much of his research and activities have been focused on the discovery of novel neurotrophic factors for the treatment of neurodegenerative diseases, and he discovered MANF in 2003. He holds a PhD in Neurophysiology and an MSc from the University of Southampton and a BSc from the University of the West Indies.

Principal shareholders	(%)
Dominion Capital	3.22
John W. Commissiong (co-founder, CSO)	2.50
Gerald E. Commissiong (co-founder, CEO)	1.00

Companies named in this report

Lonza Group (0QNO-LSE), PsychoGenics, Regenicin (RGIN-Non-ASDAQ OTC), Avanex Life Sciences (AHIX-XETRA), Catalent Biologics (CTLT-NYSE), Abbvie (ABBV-NYSE), Endo Pharmaceuticals (ENDP-NASDAQ)