Amarantus Bioscience

# New Treatments for CNS and Regenerative Medicine

www.amarantus.com

**Ticker OTCPK: AMBS**

December 2017

# Forward-Looking Statements

This presentation contains "forward-looking statements" within the meaning of the "safe-harbor" provisions of the Private Securities Litigation Reform Act of 1995. Such statements involve known and unknown risks, uncertainties and other factors that could cause the actual results of the Company to differ materially from the results expressed or implied by such statements, including changes from anticipated levels of sales, future international, national or regional economic and competitive conditions, changes in relationships with customers, access to capital, difficulties in developing and marketing new products and services, marketing existing products and services, customer acceptance of existing and new products and services and other factors. Accordingly, although the Company believes that the expectations reflected in such forward-looking statements are reasonable, there can be no assurance that such expectations will prove to be correct. The Company has no obligation to update the forward-looking information contained in this presentation.

# Executive Team

**Gerald E. Commissiong: Co-Founder, President & CEO, Director**

Co-Founder & Led acquisition of AMBS portfolio via over $40M in capital raised
Stanford University, Management Science & Engineering

**Elise Brownell, PhD: Sr. Vice President of Project Management and Operations**

Head of New Deal Flow Management, The Angels' Forum
Head of Project Management at Bayer Biotechnology; Head of Project Management, Aerovance, Inc.
Yale University, PhD in Biology

**Curt Scribner, MD MBA: Sr. Vice President of Regulatory Affairs**

Sr. VP of Regulatory Affairs at RRD International
Chief Regulatory Officer at Intarcia Therapeutics
Chief Regulatory Consultant at Quintiles

# Elto Pharma

**Amarantus**

Amarantus Diagnostics merged into

**Avant Diagnostics**

Theralink (Cancer)

MS Precise (Multiple Sclerosis)

LymPro (AD)

OvaDx (Cancer)

**Elto Pharma**

Eltoprazine

(Parkinson's)

**Cutanogen**

ESS

(Severe Burns)

**MANF Therapeutics**

MANF

(Ophthalmology)


★ = Orphan Drug Designation

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# Elto Pharma, Inc. - Eltoprazine: Pipeline in a Pill

## Oral small molecule drug candidate targeting 5HT1a/1b receptors


1. **Parkinson's Disease** – Levodopa Induced Dyskinesia **(PD-LID, Orphan Drug Designation)**
   - Addresses primary side effect of standard of care therapy (Levodopa, or L-Dopa)

2. **Alzheimer's Agitation:**
   - Clinical data package produced by Solvay (Abbvie) in 1990s studies in dementia-related agitation

3. **Adult ADHD:**
   - Non-stimulant, non-scheduled. Acts on attention & hyperactivity/impulsivity scales

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# Eltoprazine Lead Indication: Parkinson's disease Levodopa Induced Dyskenesia (PD-LID)

- **L-Dopa = most effective treatment for motor symptoms of PD**
  - With disease progression, L-Dopa is taken up by serotonergic (5-HT) pathways in the brain
  - 5HT pathways lack feedback mechanisms to control levels of dopamine
  - Excessive dopamine buildup causes uncontrolled movements
  - PD-LID's uncontrolled movements are a disabling, unwanted consequence
- **PD-LID severely impairs quality of life**
- **Only available treatment = Gycovri® (amantadine HCl) approved in 2017**
  - Moderately effective at reducing PD-LID
  - Suboptimal response rates due to mechanism of action

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# Eltoprazine Phase 2a PD-LID Trial Data Published in 2015


**Eltoprazine counteracts L-DOPA-induced dyskinesias in Parkinson's disease: a dose-finding study**

Per Svenningsson,[1] Carl Rosenblad,[2] Karolina af Edholm Arvidsson,[1] Klas Wictorin,[2] Charlotte Keywood,[3] Bavani Shankar,[4] David A Lowe,[4] Anders Björklund[5] and Håkan Widner[2]

## Phase 2a trial achieved primary endpoint

- Karolinska Institute and Univ. of Lund
- 22 patients (3 dosing arms → middle dose effective)
  - Statistically significant CDRS reduction **(p=0.003)**
- 8-week study
  - (baseline, 6 weeks, final visit)
- 0 SAEs
  - 30% Treatment-Emergent AEs (fatigue, dizziness fatigue)

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# Proposed Phase 2b or 2/3 Clinical Trial Design

- Objective: confirmation of trend in dyskinesia UDysRS score
  - Used as PD-LID approval endpoint by Adamas Pharma for Gycovri
- Double-blind, placebo-controlled, multiple dose study
  - 60-80 subjects
  - Parallel design
  - 2-3 dosing groups, 1 placebo group
  - 8 week treatment

1H-15 2H-15 1H-16 2H-16 1H-17

Phase 2/3 adaptive design may lead to an accelerated Phase 3 timeline, and may serve as the basis for FDA discussions on whether two Phase 3s are needed due to Orphan Drug Designation status



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# PD-LID Market Opportunity

- **Overall** Parkinson's Disease patient population = 1M in US
- **Growing** 3.5% annually, approximately 60,000 newly diagnosed patients/year
- **2014 → 188,000** patients with LID
  - 75% diagnosed Parkinson's patients are prescribed levodopa
    - 10% risk of LID over first 5 years
    - 35% risk of LID over 6-9 years
    - 90% risk of LID over 10 years and beyond
- Competing drug Gycovri priced at $28,000/year implying **$2B+ market opportunity**

PD LID → One of largest Orphan Indications

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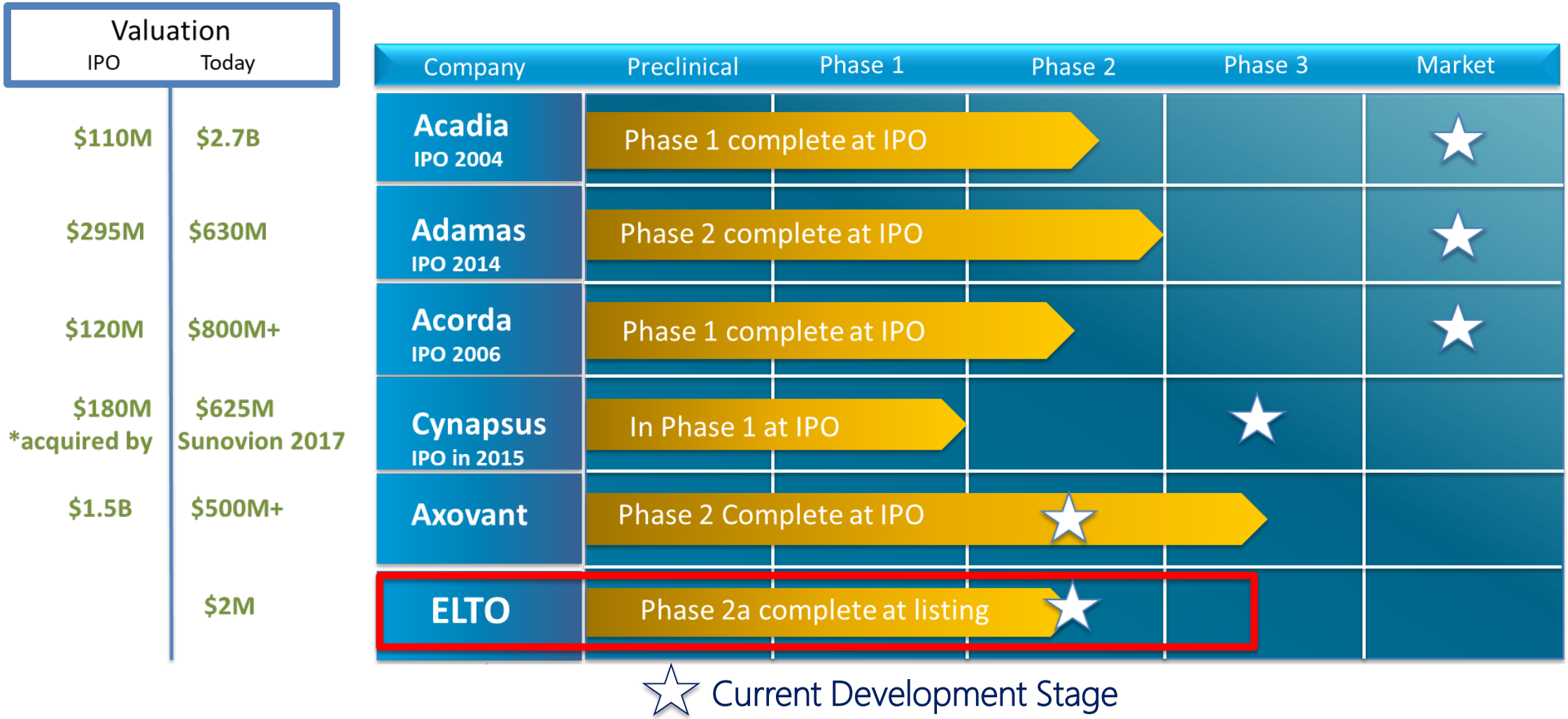
# Benchmarking Elto Pharma Valuation:

## Historic Public Valuations of CNS Companies by Stage of Lead

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# Elto Pharma, Inc. Investment Thesis

- **Phase 2 small compound program in PD-LID**
  - Open IND for Phase 2 multiple dose study (IND 124,224, eCTD format)
  - Orphan Drug Designation in PD-LID
  - Mechanism of action directly relevant to disease state
    - ✓Distinct from MoA of Gycovri
  - $2B+ market opportunity for Eltoprazine in PD alone
  - ~$6M to Phase 2b data
- **Strong safety profile demonstrated in previous studies in over 680 subjects**
- **Potential utility in additional large indications**
  - Agitation in Alzheimer's disease($3B+ market opportunity)
  - ADHD (Adult and Pediatric)
- **Demonstrated market/medical/regulatory receptivity to new approaches in this Orphan indication**
  - Adamas: GYCOVRI® (amantadine XR)

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# Cutanogen Corporation

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### Elto Pharma

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(Parkinson's)

### Cutanogen

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(Severe Burns)

### MANF Therapeutics

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(Ophthalmology)


★ = Orphan Drug Designation

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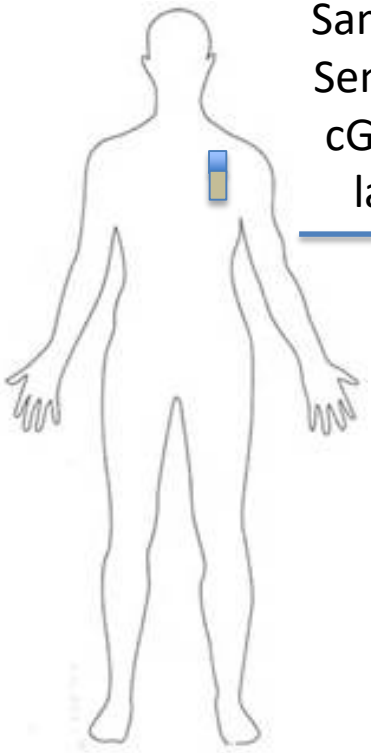
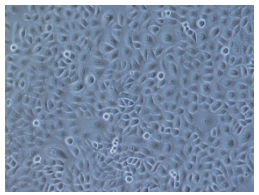
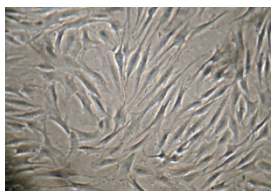
# What is ESS and How Is It Made?



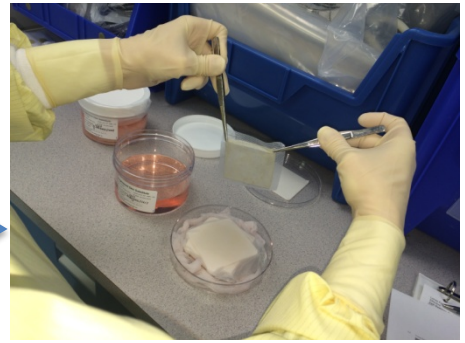
Skin Sample Sent to cGMP lab





Epidermal and Dermal Cells Isolated and Grown Separately

Cells Seeded onto Absorbable Matrix and Grown in Culture



Full Thickness Skin grafts are Packaged, then Couriered to the Burn Center



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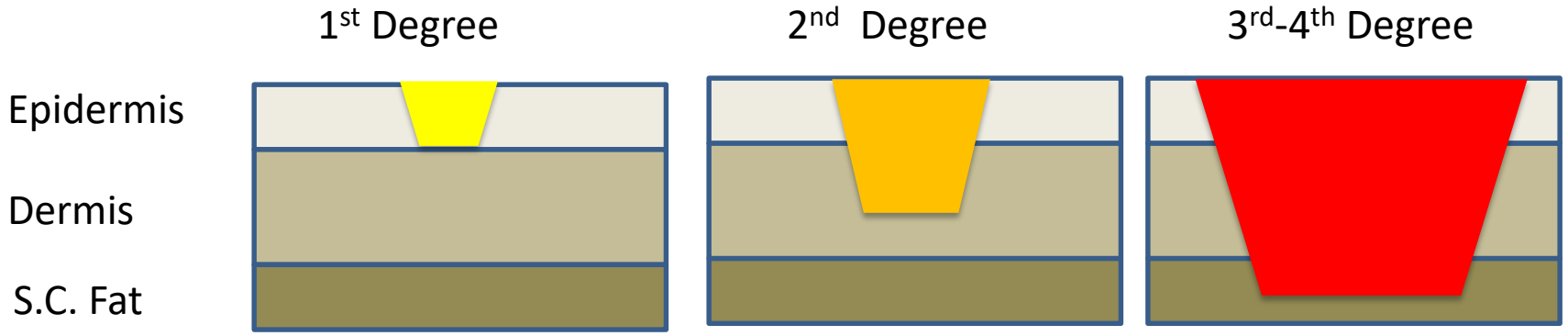
# Severe Burns: Intractable Issues Faced by Patients and Surgeons




3rd- 4th° burns over ≥ 30% of the Total Body Surface Area (TBSA)are life-threatening because of high infection rates and length of time to adequate wound closure

- Minimizing time to full wound closure is paramount to limit infection risk
- Minimizing donor skin for grafting is critical to limit surgeries/pain
- Using Patient's own skin dramatically reduces rejection risk (graft vs. host)
- Grafts that grow with patients are especially critical in pediatric patients to reduce grueling annual/semi-annual reconstruction surgeries



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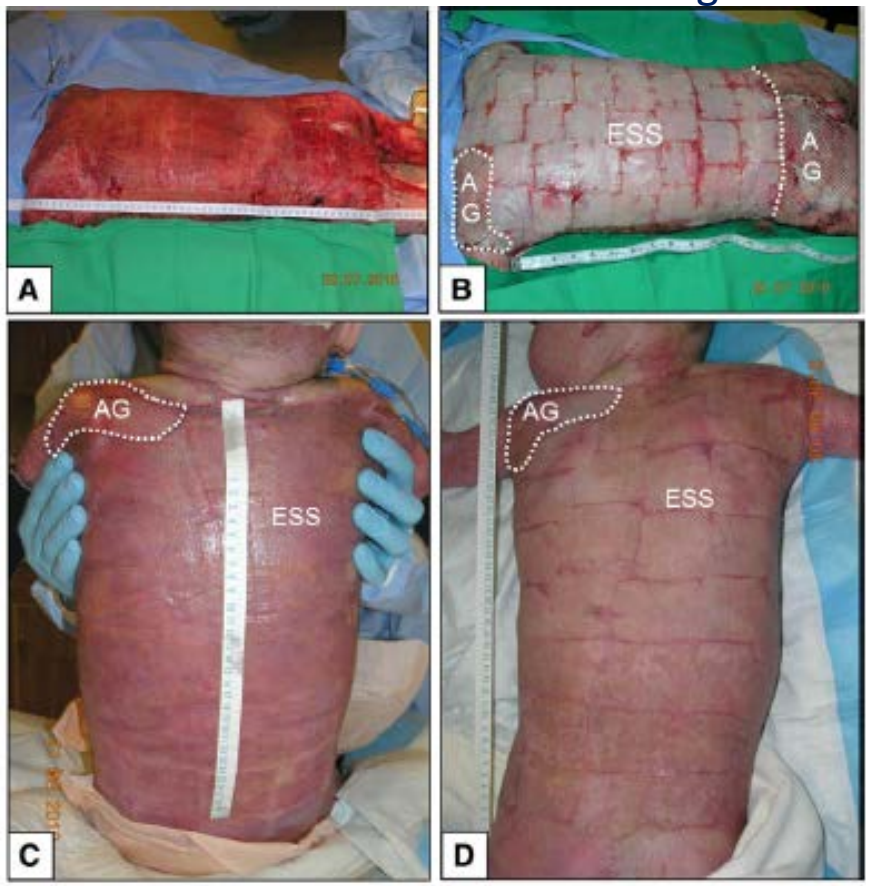
# Patient Presentation and Product Application

A. Pre-operative Wound bed

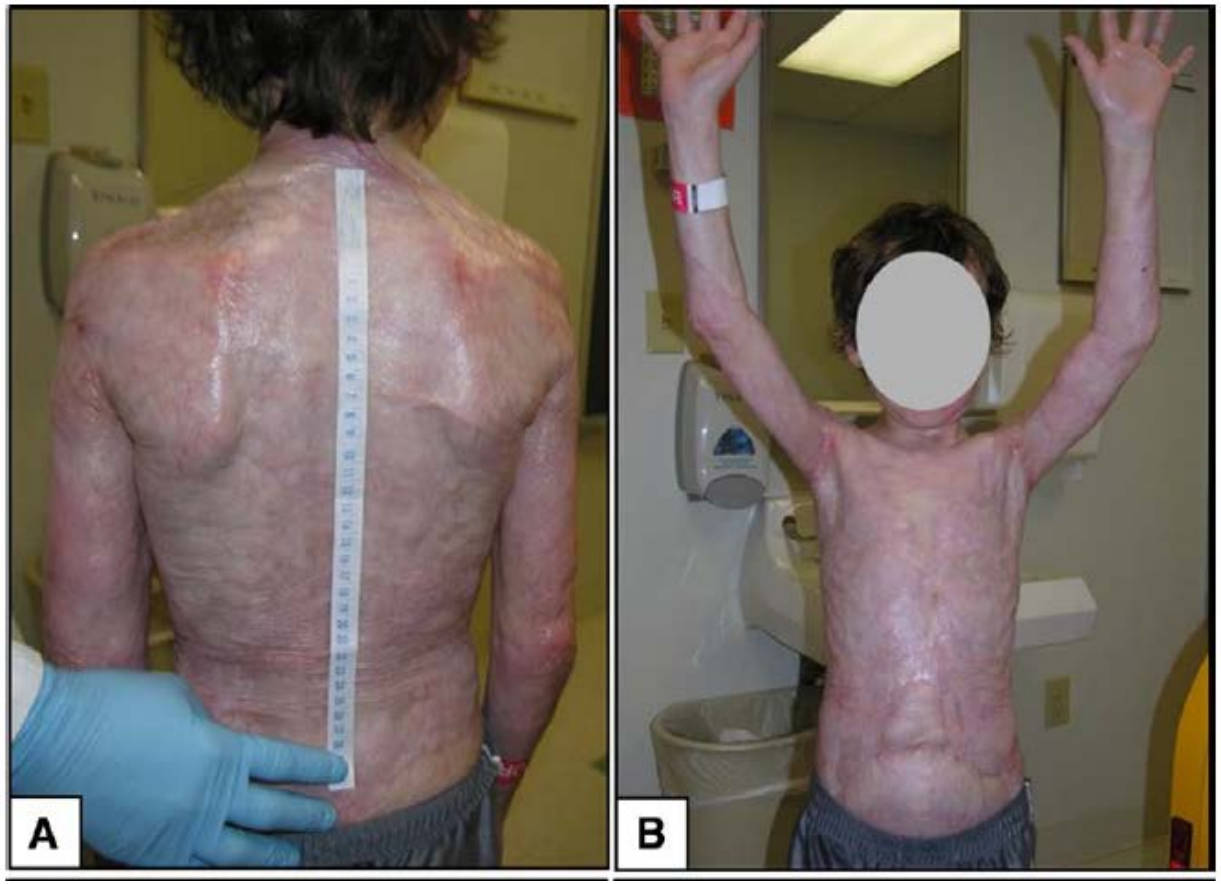
B. Application of ESS and Autograft




C. 28 Day Post Operation

D. 62 Day Post Operation

1-year post- operative evaluation




Boyce et al, "Randomized, Paired-Site Comparison of Autologous Engineered Skin Substitutes and Split-Thickness Skin Graft for Closure of Extensive, Full-Thickness Burns", JBRR (2017).



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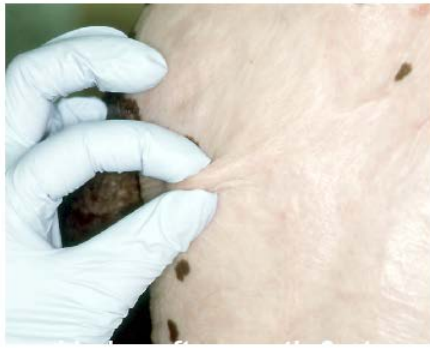
# ESS Provides Massive Improvement vs. Standard of Care in Pediatric Severs Burns

- 16 subject pediatric clinical trial
  - Data published in April 2017 in Journal of Burn Care & Research
- Key Findings:
  - ESS reduces mortality (death) by 75% + vs. historical control
  - ESS covered 27x greater body surface/harvest vs. standard of care
  - ESS yielded pliable, flexible skin that grew as patients matured (less reconstruction)



Boyce et al, JBCR 20:453, 1999.

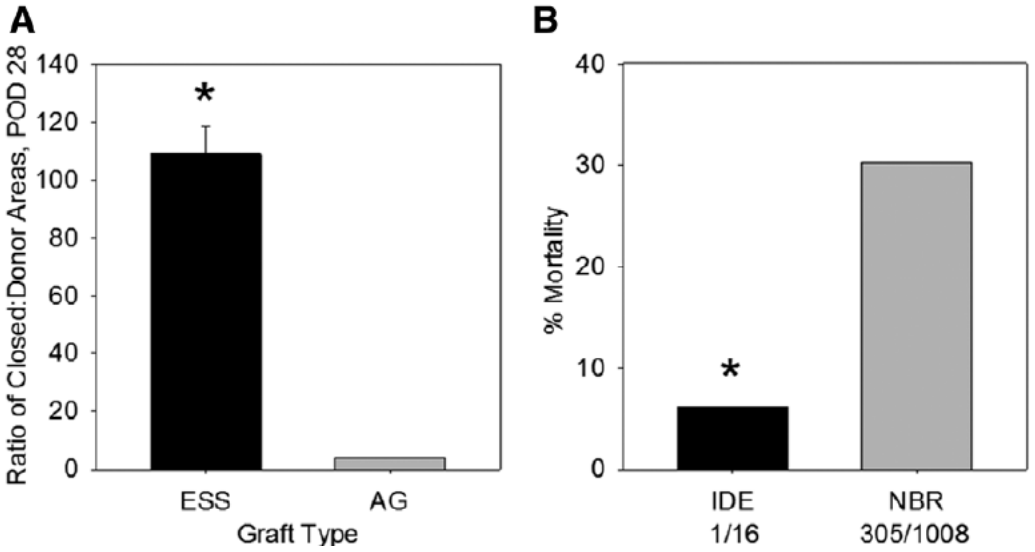



**Figure 4.** Plots of ratio of areas of closed wounds to donor biopsies, percentage mortality, percentage engraftment, and percentage TBSA at POD 28. **A. Ratios of closed-to-donor areas at POD 28 were 108.8 ± 9.7 for ESSs and 4.0 ± 0.0 for AG**. B. Percentages **mortality were 6.25% (1/16) for subjects enrolled and treated under the IDE protocol, which was significantly lower than 30.3%** (305/1008) as reported in the 2012 National Burn Repository.

Boyce et al, "Randomized, Paired-Site Comparison of Autologous Engineered Skin Substitutes and Split-Thickness Skin Graft for Closure of Extensive, Full-Thickness Burns", JBRR (2017).

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# Unconditional Support from Former Presidents of the American Burn Association

"The fact that this product is not on (the) market is the biggest disappointment of my career".

**Dr. David H. Ahrenholz**
*Former President, American Burn Association*

"ESS offers hope to care providers, who treat severely wounded individuals, that a reliable skin substitute will be available for the horrible situation when wound coverage is not possible. I have long wanted to see ESS developed so that we can offer this life-saving technology to our patients."

**Dr. Nicole Gibran,**
*Former President, American Burn Association*



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# ESS: Direct Hospital Costs for 30%+ TBSA 3rd/4th Degree Pediatric Severe Burns

| | Standard of Care | ESS |
|---|---|---|
| Days in ICU (to wound closure) | 75-120 | 35-45 |
| Avg Cost in ICU ($10,000/day) | $750,000 - $1,200,000 | $350,000 - $450,000 |
| Days in hospital post ICU | 90-120 | 45-75 |
| Avg Cost in Hospital ($3,000/day) | $270,000 - $360,000 | $135,000 - $165,000 |
| Reconstruction/revision surgeries | $100,000 - $10,000,000 | $50,000 - $500,000 |
| TOTAL HOSPITAL COSTS | $1,120,000 - $11,560,000 | $535,000 - $1,115,000 |
| ESTIMATED SAVING/PATIENT | | $585,000 - $10,410,000 |

## ESS Reduces Key Primary Cost Drivers:

- Length of Stay in ICU/Hospital
- Rehabilitation: physical (significantly less with ESS), mental and emotional
- Revision surgeries: mandatory in pediatric patients (significantly less with ESS)

# Additional Value Proposition:
# Rare Pediatric Disease Designations (RPDD)

- RPDD approval gives sponsor a Priority Review Voucher (PRV) that can be used for another treatment in development
  - Vouchers are highly sought, and can be sold to third parties
    1. Sarepta ⟶ Sanofi for $245M , 5/2015
    2. United Therapeutics ⟶ Abbvie for $350M, 8/2015
    3. Sarepta ⟶ Gilead for $125M, 9/2016

- ESS likely qualifies for RPDD in Pediatric Burns & other orphan pediatric diseases

# Cutanogen Corporation: Investment Thesis

- Differentiated autologous skin replacement fulfilling critical unmet need
- Platform technology serving as basis for organ regeneration company
- Phase 3-ready  w/Orphan Drug Designation assigned in Severe Burns
- Likely rapid adoption in pediatric severe burns due to:
  - Speed to wound closure to < 45 days from 90-180 days:
  - Cost savings. $10k-  15k/day, $0.5M –$10M per patient
  - Strong, public support from leading KOLs in US
- Non-dilutive funding opportunities
- Proprietary technology with issued patent estate
- Follow-on improvements/indications possible
- Strong KOL support

$500+ million initial market opportunity

# MANF Therapeutics, Inc.

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Eltoprazine

(Parkinson's)

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(Severe Burns)

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(Ophthalmology)


★ = Orphan Drug Designation

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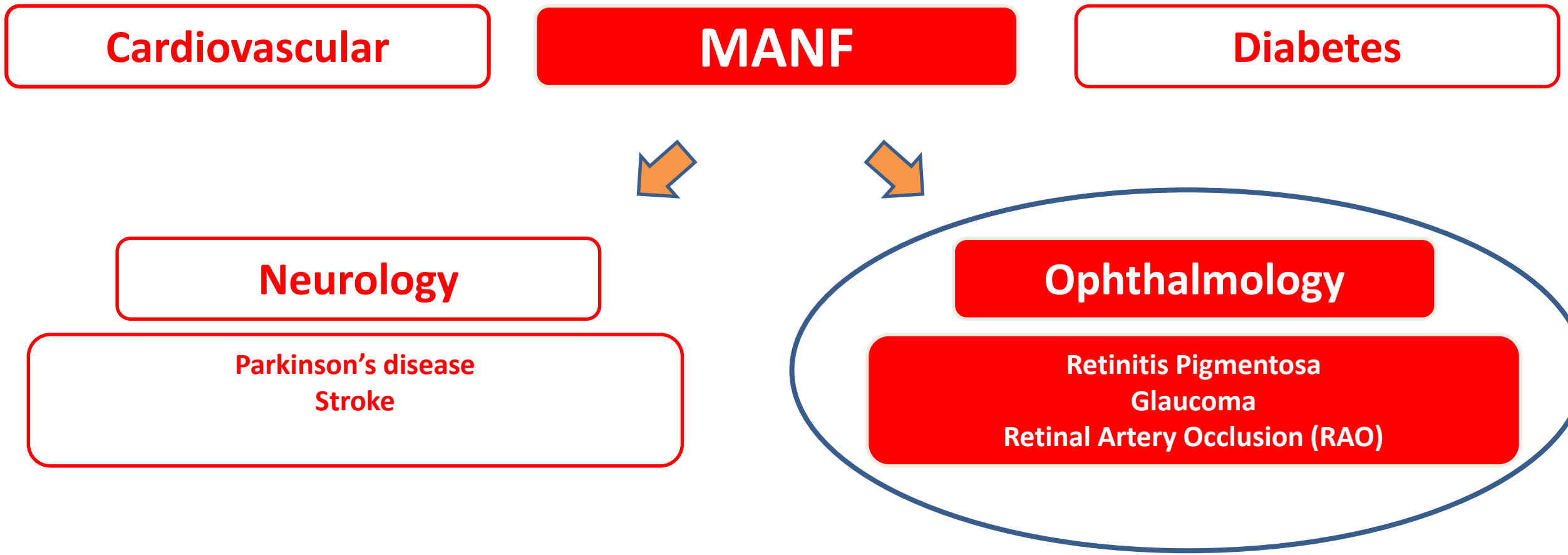
# MANF: Protective/Restorative Across Several Therapeutic Areas



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# Pipeline in a Protein: Anti-Apoptosis Across Indications

- Indications
  - Retinitis Pigmentosa, Glaucoma, Retinal Artery Occlusion (rods, cones, retinal ganglion cells)
  - Parkinson's (neuronal protection)
  - Diabetes (protection of pancreatic beta cells)
  - Myocardial infarction (protection against ischemic damage)
  - Hearing loss (preservation of hair cells)
  - Wolfram's (blindness, neurological, hearing loss and diabetes aspects)
- Potential paradigm shift in cell protection and restoration
  - Collaborations w/ Buck Institute, Wash U and UMass
  - 75+ peer-reviewed publications (Science , Nature Medicine, etc.)
  - 20+ issued patents, 20+ pending patent applications
    - Composition of Matter issued covering Protein, Gene and cell therapy
    - Method of Use in Neurology, Ophthalmology, Endocrinology, Otology, Immunology



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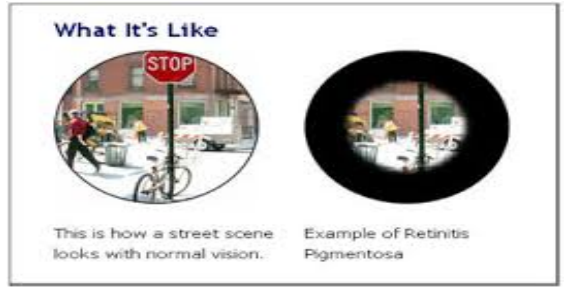
# Retinitis Pigmentosa is Lead Indication

- 100,000 patients/yr in USA
  - MANF initially targeting 50,000 sub-population
- Genetic disease of the retina
  - Orphan indication
  - No treatment currently approved
- Progressive vision loss
  - Rod photoreceptors followed by cone degeneration
  - Night vision loss followed by loss of peripheral vision
- Mutations in the rhodopsin gene
  - Mutated rhodopsins misfold and aggregate



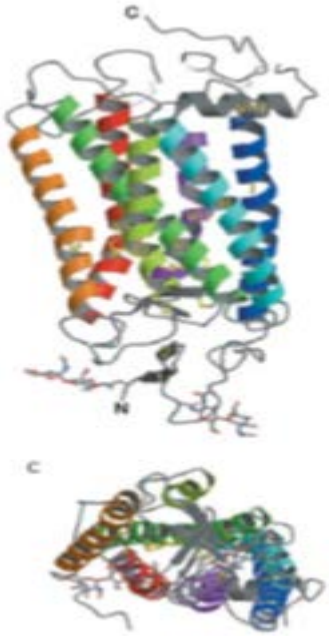



**Figure from Palczewski et al., 2000**



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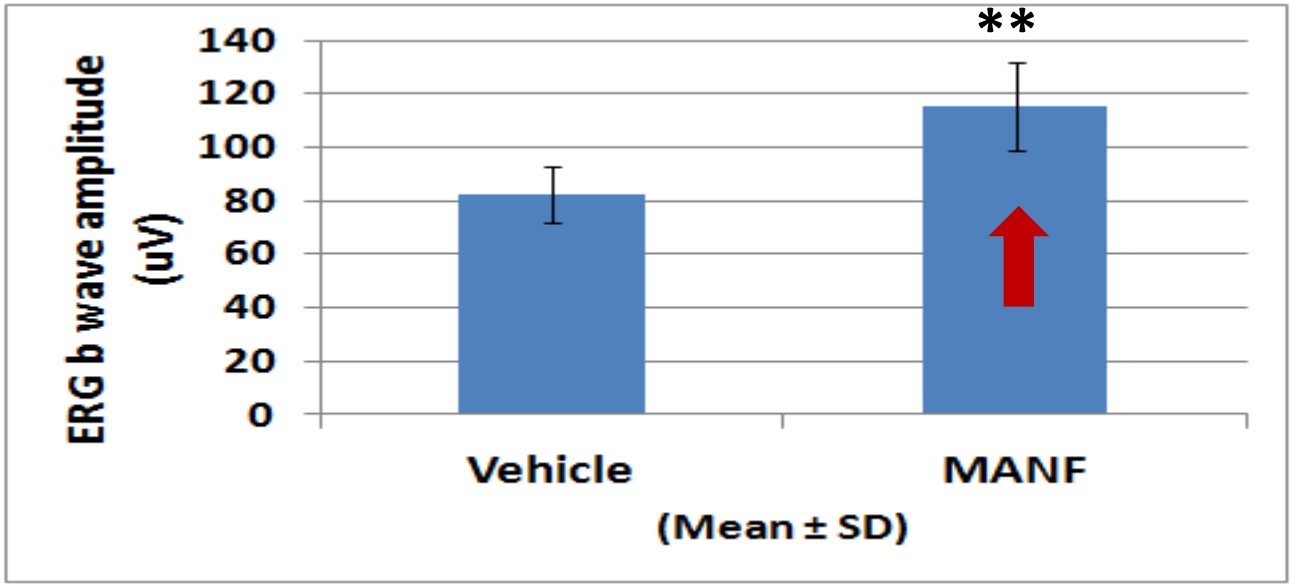
# MANF Protects Retinal Function / Retina in rd10/rd10 Rodent Model

- Abstract published at ARVO 2015
  - Bascom Palmor Institute University of Miami (Prof. Rong Wen)
- Single ivt admin of MANF (2 ug) on Day 18
- Effect on scotopic ERG b wave amplitude on Day 28




MANF protects inner retinal function in rd10/rd10 model



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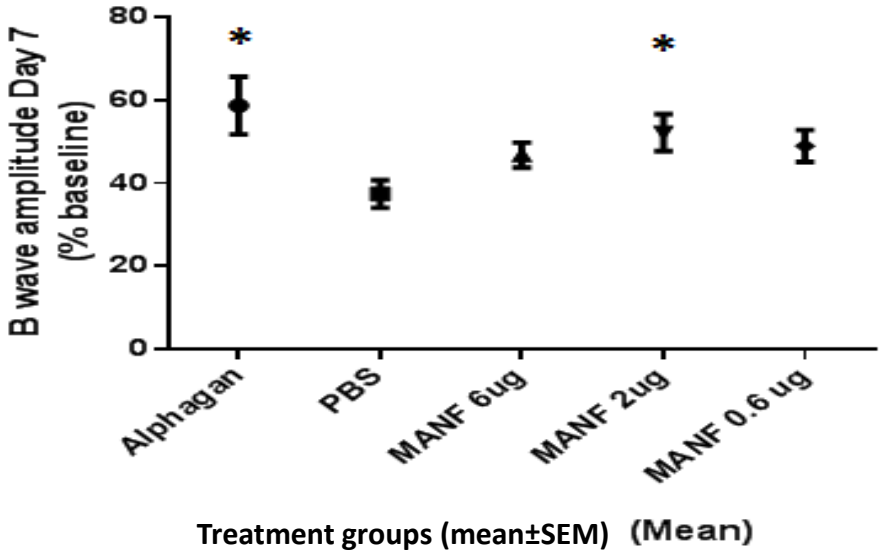
# MANF Protects Vision Function in Glaucoma / RAO Optic Nerve Ischemia Rodent Model

- Occlusion / reperfusion model
  - Retinal artery occlusion – orphan indication
  - Glaucoma
- Single intravitreal
  - MANF administration immediately after occlusion / reperfusion
- Electroretinography, b-wave amplitude on Day 7

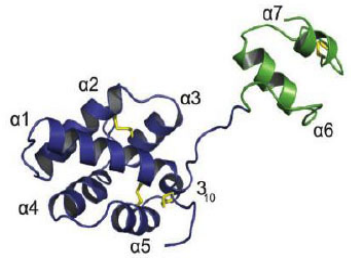



1. Functional protective effect against retinal ischemia
2. Dose-effect relationship mirrors effects in Parkinson's disease model
3. Most effective dose has a safety margin compared to the ocular tolerance study dose
4. MANF effect similar to Alphagan despite completely different MOA


AMBS sponsored data. CRO: Iris Pharma. * P<0.05, 1-way ANOVA, Dunn's post test against PBS control

# MANF : Clinical Development Strategy

- Local Delivery of Recombinant Protein Initial Development Strategy at AMBS
  - Potential for systemic administration upon safety study confirmation
  - Potential for Gene Therapy
  - Potential for Cell Therapy
- Ophthalmology→ Initial Lead indications
  - **Retinitis Pigmentosa (Orphan Drug Designation)**
  - Retinal Arterial Occlusion (Orphan Drug Designation)
  - Wolfram's syndrome
  - IND submission targeted for 2019
- Additional indications with animal proof of concept:
  - Parkinson's
  - Diabetes
  - Myocardial Infarction




*Lindholm and Saarma, DevNeurobiol (2010)*



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# AMBS Trading Snapshot

**Highlights**

- Trading Symbol: AMBS
- All-time high PPS: $30/share
- All-time high market cap: $160M
- Market Cap: $2 Million (as of 11/28/2017)
- Closing Stock Price: $0.02 per share (as of 11/28/2017)
- Shares Outstanding: ~120 Million Shares (as of 11/28/2017)
- Convertible Securities: $22M (as of 11/28/2017)
  - $21M out of $22M halted all conversions until 1/10/18
    - $1M 1st lien Sr. Debt able to trade out of position
  - If AMBS raises $1.5M by 1/10/18 conversions halted until 10/10/18
    - $21M exchanged at discount into non-convertible securities
  - If AMBS uplists to national exchange by 7/10/18 conversions halted until 2/10/19 (severe leakout for 9 months quarterly fixed price conversion)

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# AMBS Investment Highlights

- **Holding company structure designed to capture subsidiary value**
- **Elto Pharma: Eltoprazine** is a Phase 2b clinical asset for PD-LID
  - Launched Phase 2b study in PD LID in June 2015
    - Orphan designation obtained
  - Opportunities to expand into Adult ADHD, Alzheimer's Aggression
- **Cutanogen Corporation: ESS** is a Phase 3 clinical asset for pediatric severe burns
  - Orphan designation obtained
    - Intent to request Rare Pediatric Disease Designation (RPDD) to be eligible for Priority Review Voucher (PRV)
- **MANF** Therapeutics: MANF is a paradigm-shifting preclinical asset
  - Orphan Drug Designation in Retinitis Pigmentosa and Retinal Artery Occlusion
  - Multiple indications currently advancing towards first-in-human studies



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# Contact Information

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