

INVESTOR UPDATE WEBINAR

NeuroScientific Biopharmaceuticals Ltd (**ASX:NSB**) (“**NeuroScientific**” or “**the Company**”) wishes to advise shareholders and investors that the Company will be conducting a live investor update on Tuesday 31st October 2023.

A copy of the investor presentation to be delivered during the webinar is attached.

The company invites shareholders and investors to participate in this online event by registering via the link below:

https://us06web.zoom.us/webinar/register/WN_0WrxqpQjQY2flxewUCLf3w

Start time:

11am Perth Time (AWST) / 2pm Sydney Time (AEDT)

A link to the replay of the webinar will be made available on the NeuroScientific’s social media accounts as soon as it is available for those unable to attend the live session.

Authorised by the board of NeuroScientific Biopharmaceuticals Ltd.

-ENDS-

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About NeuroScientific Biopharmaceuticals Ltd

NeuroScientific Biopharmaceuticals Limited (ASX: NSB) is a company developing peptide-based pharmaceutical drugs that target a number of neurodegenerative conditions with high unmet medical demand. The company's product portfolio includes EmtinB™, a therapeutic peptide initially targeting Alzheimer's disease and glaucoma, as well as other Emtin peptides (EmtinAc, EmtinAn, and EmtinBn) which have demonstrated similar therapeutic potential as EmtinB™. For more information, please visit www.neuroscientific.com

About EmtinB™

EmtinB™ is a peptide-based compound that binds to surface-based cell receptors from the LDLR family, activating intracellular signalling pathways that stimulate neuroprotection, neuroregeneration and modulate neuroinflammation. EmtinB™ is modelled on a specific active domain of the complex human protein called Metallothionein-IIA, which is produced as part of the human body's innate immune response to cell injury.

Our preclinical research has established that EmtinB™ is highly specific and selective for its target receptor, safe and well tolerated at high concentrations.



NeuroScientific
BIOPHARMACEUTICALS

NOVEL DRUG THERAPIES FOR
NEURODEGENERATIVE CONDITIONS

CEO Review of EmtinB™ Project

31 October 2023

neuroscientific.com



DISCLAIMER



The purpose of the presentation is to provide an update of the business of NeuroScientific Biopharmaceuticals Ltd (“NeuroScientific”, or “the Company”). These slides have been prepared as a presentation aid only and the information they contain may require further explanation and/or clarification. Further information is available upon request.

The views expressed in this presentation contain information derived from publicly available sources that have not been independently verified. No representation or warranty is made as to the accuracy, completeness or reliability of the information. Any forward looking statements in this presentation have been prepared on the basis of a number of assumptions which may prove incorrect and the current intentions, plans, expectations and beliefs about future events are subject to risks, uncertainties and other factors, many of which are outside NeuroScientific’s control. Important factors that could cause actual results to differ materially from assumptions or expectations expressed or implied in this presentation include known and unknown risks. Because actual results could differ materially to assumptions made and NeuroScientific’s current intentions, plans, expectations and beliefs about the future, you are urged to view all forward looking statements contained in this presentation with caution.

This presentation should not be relied on as a recommendation or forecast by NeuroScientific. Nothing in this presentation should be construed as either an offer to sell or a solicitation of an offer to buy or sell shares in any jurisdiction.

BACKGROUND



- NeuroScientific Biopharmaceuticals Ltd (NSB) has been developing a peptide-based product EmtinB™ for the treatment of neurodegenerative conditions such as Alzheimer's disease, Multiple Sclerosis and Glaucoma.
- EmtinB™ (Figure 2) is a peptide modeled on the β -domain of the human protein metallothionein-II (MT-II) (Figure 1). MT-II is noted for demonstrating neuroprotective, neuritogenic and anti-apoptotic properties which underpin positive effects in the CNS after injury and during illness. EmtinB™ has been able to mimic the therapeutic activity of MT-II in *in vitro* and *in vivo* studies.
- EmtinB™ is manufactured as a tetrameric dendrimer, in which four monomer peptides (14aa monomers) are linked via a lysine backbone. Since monomer peptides usually demonstrate a short half-life due to rapid proteolytic breakdown, the dendrimer structure increases the stability of EmtinB™ in biological environments.

FIGURE 1: HUMAN MT-II

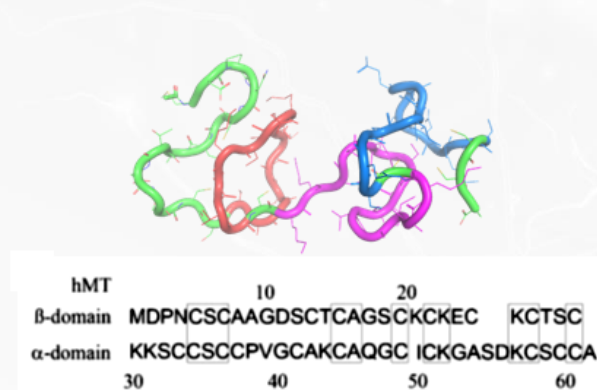
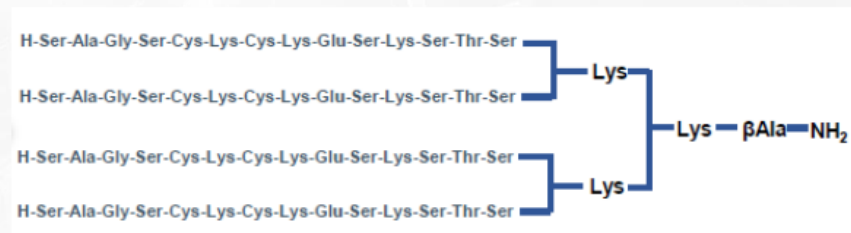


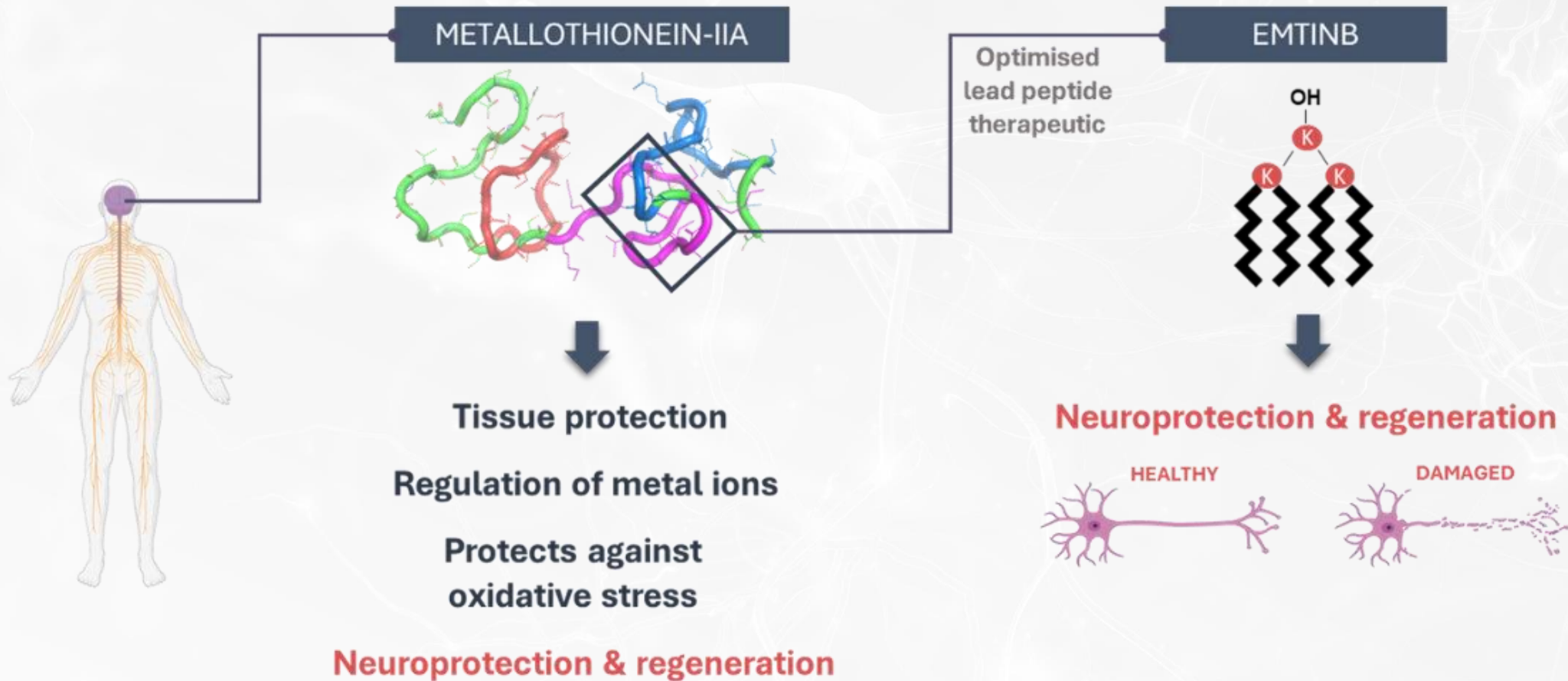
FIGURE 2: EMTINB



EMTINB™ IS A NOVEL LEAD DRUG CANDIDATE



EmtinB™ is modelled on a specific domain of human MT-IIA



Neuroprotection & regeneration

PROJECT REVIEW



- Over the past six weeks since mid-September 2023 the Company's CEO Stephen Carter has worked with the Board, executive team and key consultants, in conducting a full analysis and review of the NeuroScientific's Research and Development programs of EmtinB™ for use in the treatment of neurodegenerative diseases of the brain and spinal cord, Relapsing Remitting Multiple Sclerosis, Multiple Sclerosis, Alzheimer's Disease and Ocular disease.
- The results of this review have confirmed that it is very clear that NeuroScientific's Board, management and shareholders have very good reasons to be positive about EmtinB™'s therapeutic potential. The early non-clinical and pre-clinical studies, carried out across a wide range of animal studies confirmed that EmtinB™ is an exciting lead prospect with significant therapeutic potential and, if able to be successfully developed and shown safe to use, could be a game-changing product in the fight against neurodegenerative diseases.

PROJECT REVIEW: Highlights



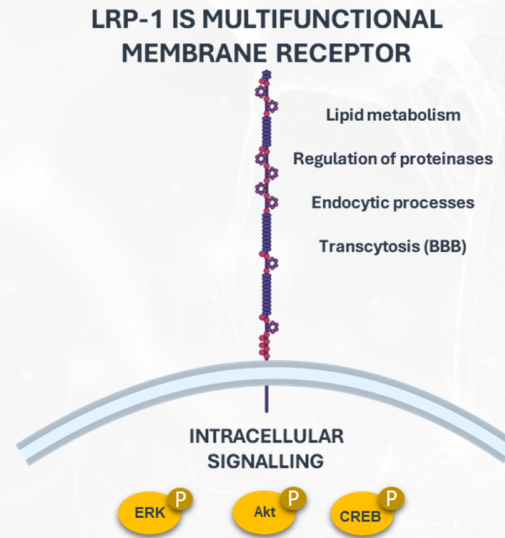
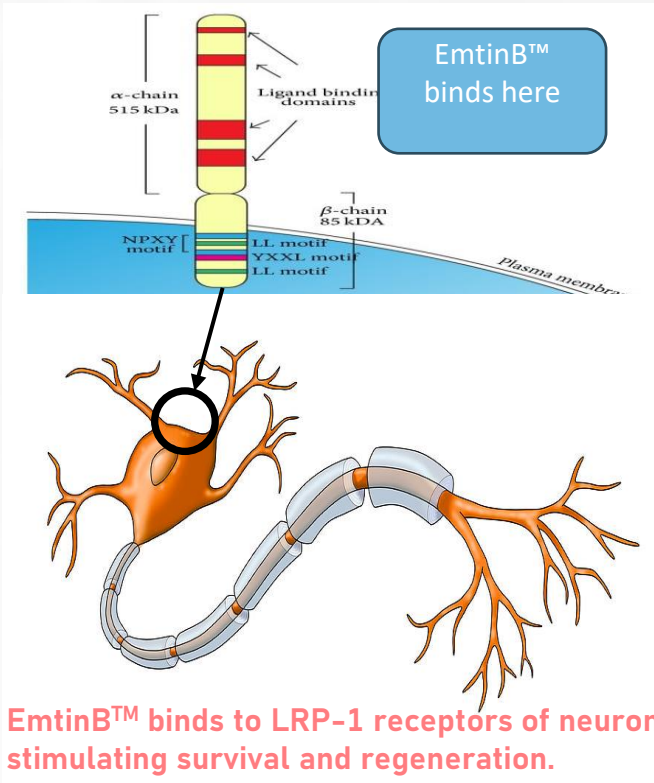
- EmtinB™ targets LRP-1.
- MoA has potential for multiple treatment indications.
- EmtinB™ preclinical data has demonstrated:
 - Neuroprotection in cell survival models >90%;
 - Significant axonal regeneration (including significant results in spinal injury rat model);
 - Proliferation of myelin forming cells (oligodendrocytes) and myelin formation in Multiple sclerosis model;
 - Slowed cognitive decline in Alzheimer's disease animal models;
 - Slowed glaucoma-induced damage to the optic nerve in animal model;
 - Showed absorption in all major optic tissues;
 - Showed a neuroprotective effect in Glaucoma rabbit and pig models;
 - Advanced safety program in animals, including non-human primates;
 - No significant safety concerns in any models at NOAEC.

EMTINB™ : NOVEL THERAPEUTIC TARGET

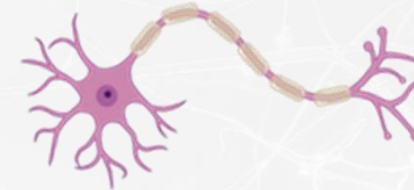


LRP-1 activates protective signalling pathways

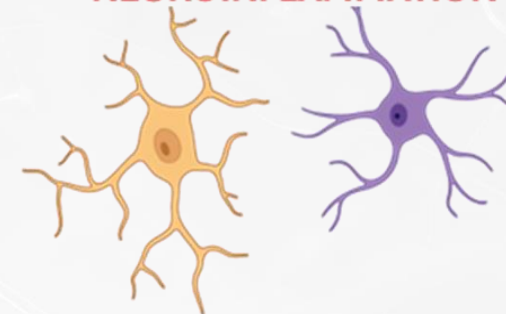
LRP-1 signaling



PROTECTS NEURONS

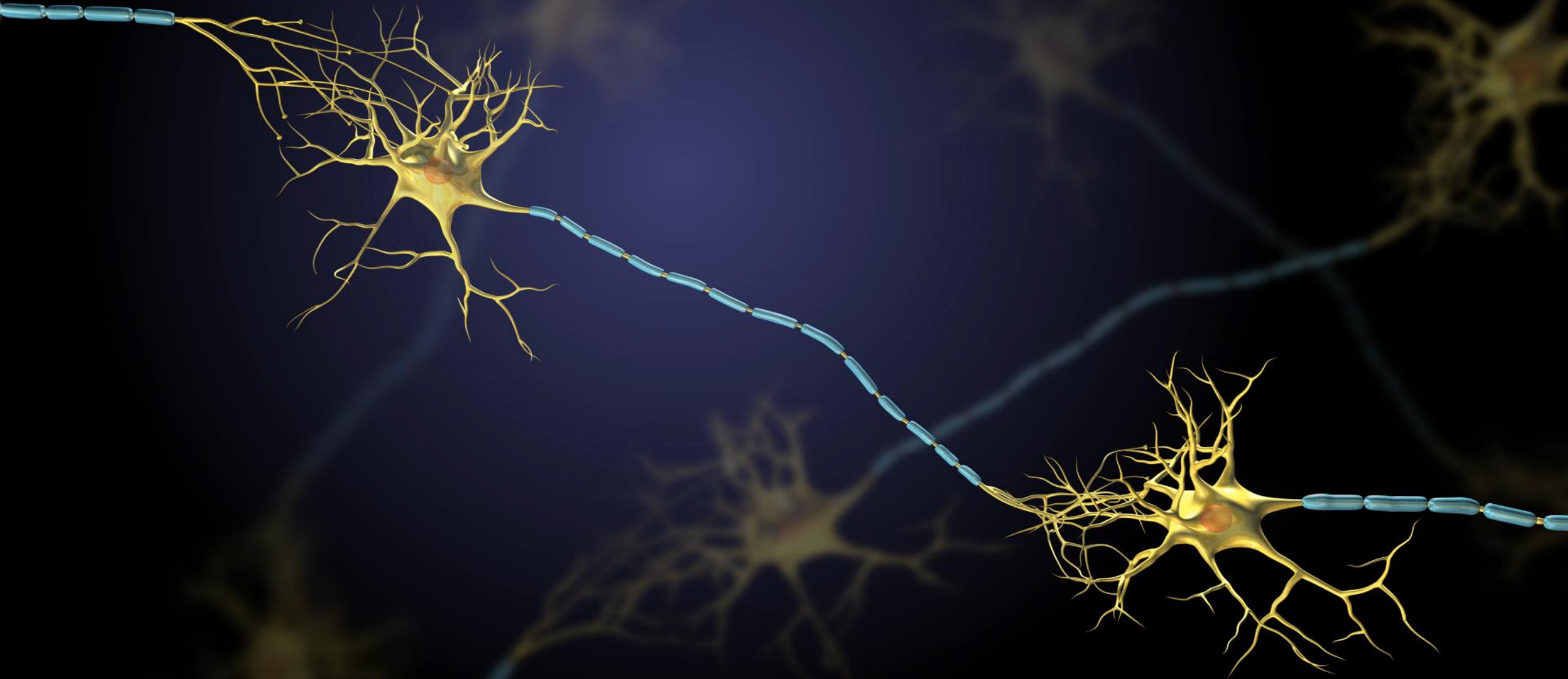


DOWN REGULATES NEUROINFLAMMATION



MODULATES DIFFERENTIATION

EMTINB MECHANISM OF ACTION:
Binding LRP-1 receptor



TARGET RECEPTOR STUDIES



FIGURE 3: SPR ANALYSIS OF EMTINB BINDING TO LRP1

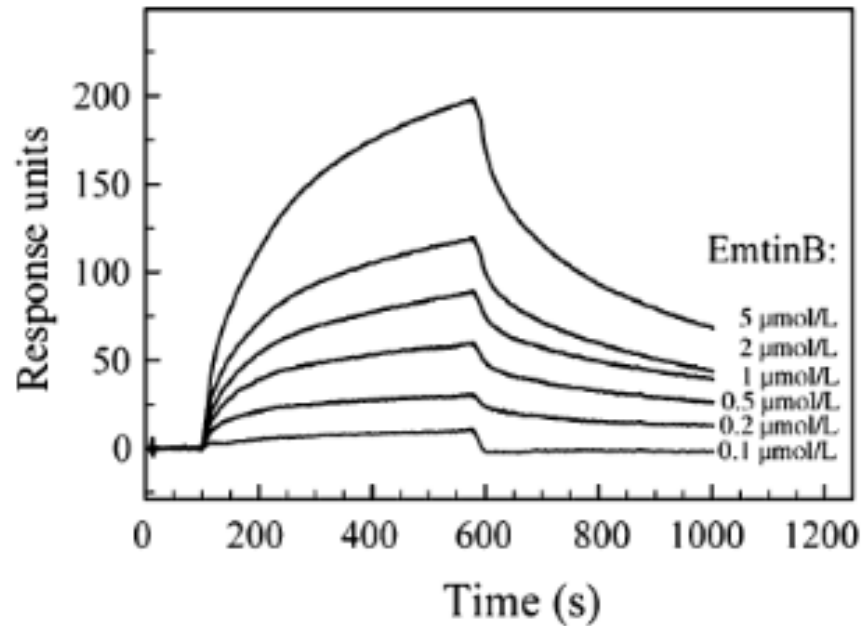
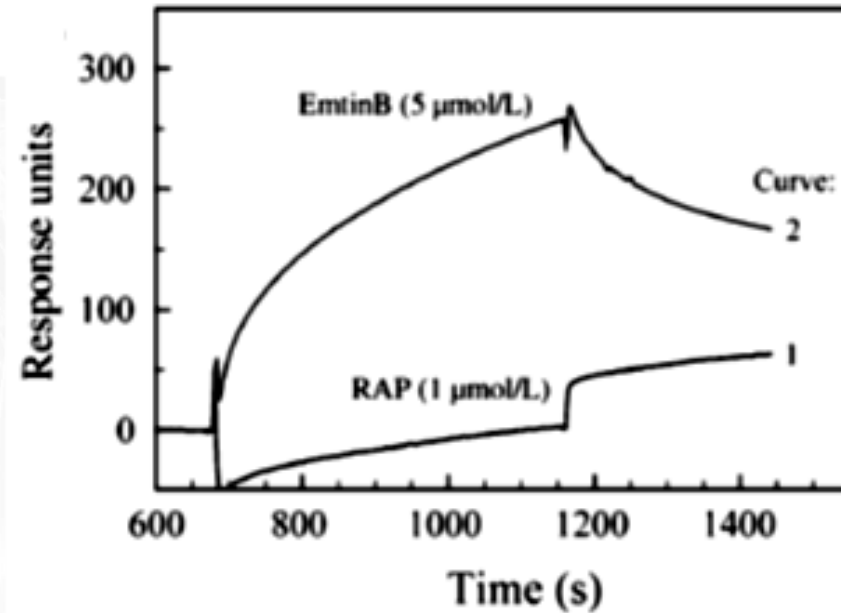


FIGURE 4: SPR ANALYSIS OF EMTINB BINDING TO LRP1 AND INHIBITION BY RAP



EmtinB™ binds LRP1 as demonstrated using surface plasmon resonance studies (Figure 3).

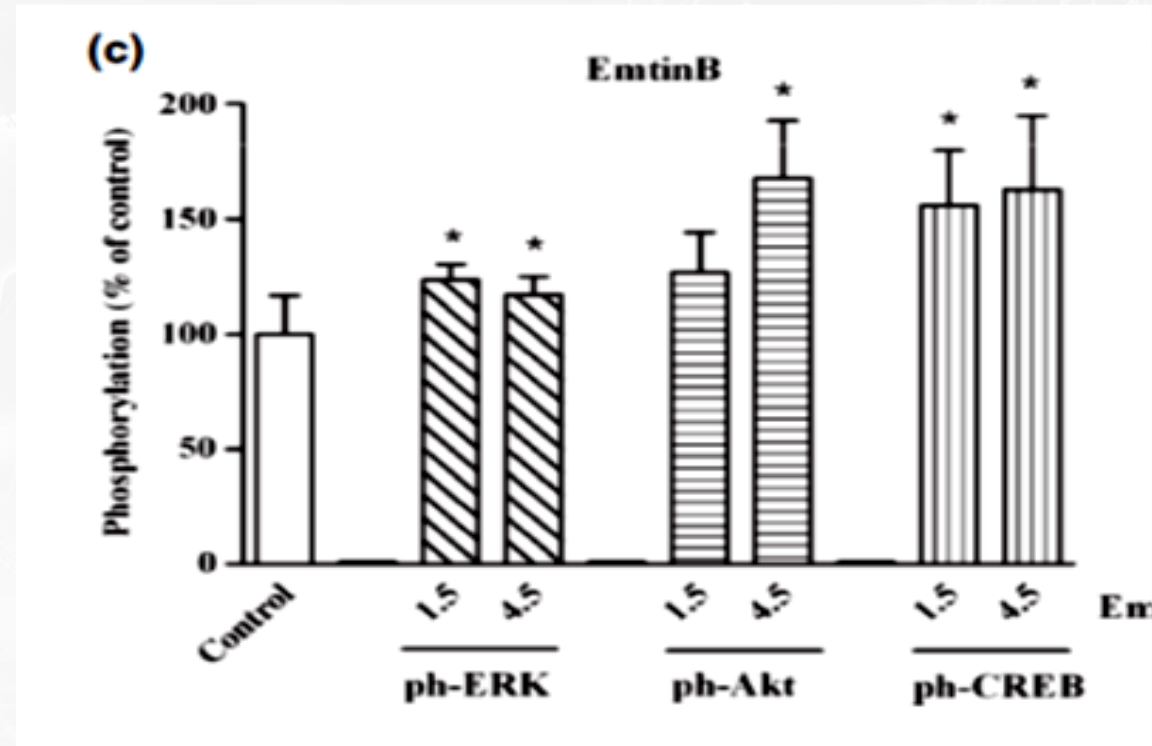
Pre-bound LRP antagonist, receptor associated protein-1 (RAP), inhibited the binding of EmtinB™ to LRP1 (Figure 4).



TARGET RECEPTOR STUDIES (continued)

- ERK, PKB/Akt and CREB are downstream signaling molecules that can be linked to either direct or indirect activation pathways as a result of LRP1 ligand binding.
- Both ERK and PKB/Akt are positively associated with pathways of neuronal survival, while CREB is associated with neuroregeneration, neuron survival and memory formation

FIGURE 5: EMTINB ACTIVATES ERK, PKB/AKT, AND CREB



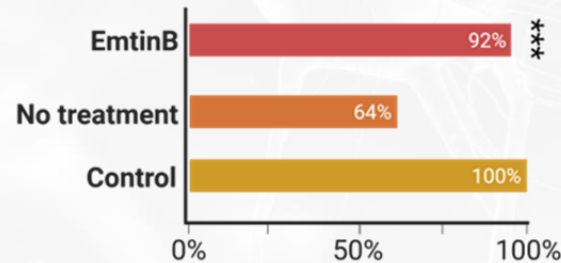


PROJECT REVIEW: General Studies

- The early work evaluated the effect of EmtinB™ on nerve regeneration and we saw a statistically significant increase in the mean neurite length, synaptic density, neural survival, oligodendrocyte proliferation and myelin formation.
- Thus, confirming the exciting potential for EmtinB™ to regenerate damaged nerves.

STIMULATES SURVIVAL OF NEURONS

>90% mean improvement of *in vitro* survival of neurons



PROMOTES REGENERATION

>200% *in vitro* regeneration of axons

CORTICAL NEURONS

Neurite length: 24-hour treatment period



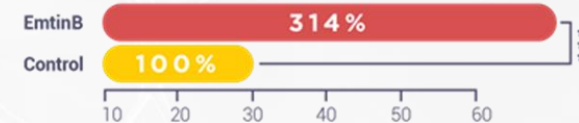
HIPPOCAMPAL NEURONS

Neurite length: 24-hour treatment period



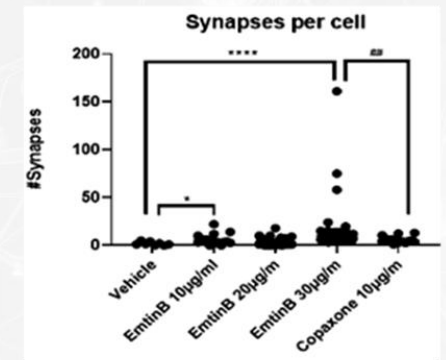
SPINAL CORD: INJURY MODEL

Neurite length: 7-day incubation period



RESTORES SYNAPTIC CONNECTIONS

10x increase in synaptic density



This information provides a strong argument for the drug's ability to specifically target the neural protective and regenerative target signaling pathways

PROJECT REVIEW: Safety



- Studies evaluating the Central Nervous System Safety Pharmacology, Cardiovascular Safety Pharmacology and Respiratory Safety Pharmacology of EmtinB™ confirmed the overall lack of any key safety concerns of EmtinB™.
- EmtinB™ was shown not to be mutagenic or genotoxic in standard Ames tests.
- A number of studies were carried out on multiple species (rats, dogs and non-human primates (NHP)), that looked at the safety of EmtinB™. **All of these studies** confirmed that there were no EmtinB-related ophthalmic observations; differences in body weight, body weight change, or food consumption changes; ECG changes; organ weights changes; or macroscopic observations. The studies confirmed that EmtinB™ is safe to use.
- There was concern as to the irritation that appeared around the injection sites and this was originally identified as a formulation issue. The drug was reformulated, and the irritation was reduced. There was a pay-off though with the new formulation not being as stable as the earlier formulation.

The data supports the safety of EmtinB™

PROJECT REVIEW: Systemic projects



- EmtinB™ has shown considerable therapeutic potential in the laboratory and pre-clinical animal models of AD and MS.
- In our preclinical mouse model of MS we saw statistically significant functional improvement in the EmtinB™ treated animals.
- We evaluated the effect of EmtinB™ in combination with Teva's Copaxone (an MS drug) in an MS cell model. A co-treatment of EmtinB™ and Copaxone, significantly promoted neurite length and cortical neurons survival as well as the myelin formation around cortical neurons. This effect appeared to be additional.

The systemic models confirmed that, if we were able to get the drug to the target sites, there was the potential to see functional improvement.

EmtinB™ action in Neurodegenerative diseases of the eye.

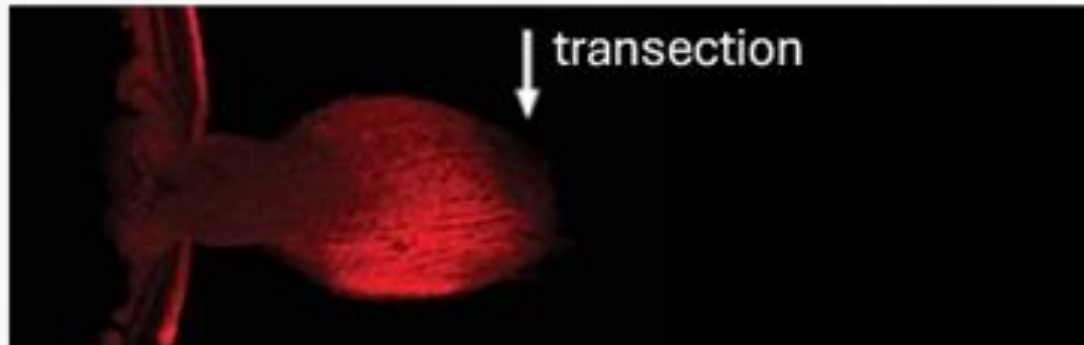


METALLOTHIONEIN II: OPTIC NERVE STUDY

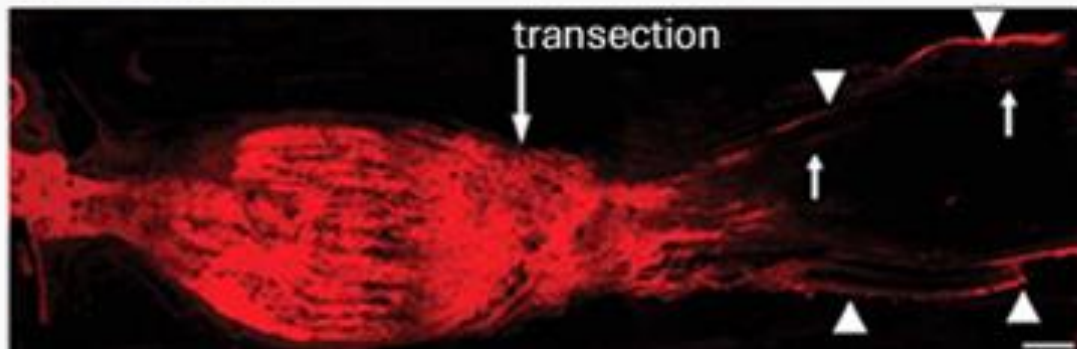


MTII INDUCED REGENERATION OF THE OPTIC NERVE IN RATS

No Treatment



Treatment



- In a study the optic nerve of a rat was severed.
- One group was treated with Metallothionein II and the other untreated.
- The treated group regrew the optic nerve.

EMTINB™ promotes survival of retinal ganglion cells and protects the optic nerve

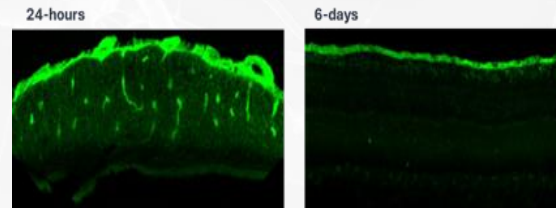


- We evaluated where EmtinB™ was distributed in the eye. The study confirmed that EmtinB™ was distributed through-out the eye and was seen in the optic nerve and nerve head. There were no signs of toxicity.
- We have carried out a number of studies looking at the neuroprotective and neuroregenerative abilities of EmtinB™. These studies looked at the ability of EmtinB™ to trigger known signalling pathways in the eye. We saw significant initiation of the main neuroprotective and regenerative pathways.

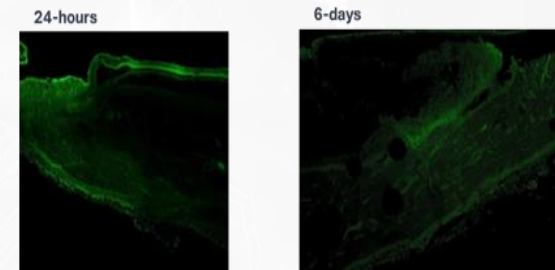
EMTINB™ TREATMENT OF GLAUCOMA

ESTABLISHED OCULAR PK & TISSUE PENETRATION

RETINAL TISSUE



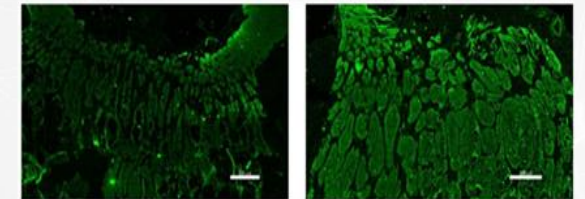
OPTIC NERVE TISSUE



SIGNIFICANT NEUROPROTECTION IN SEVERE ACUTE GLAUCOMA ANIMAL MODEL

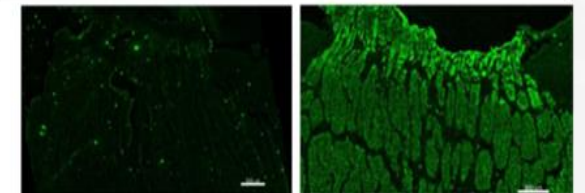
NFHp Non-treatment

NFHp EmtinB



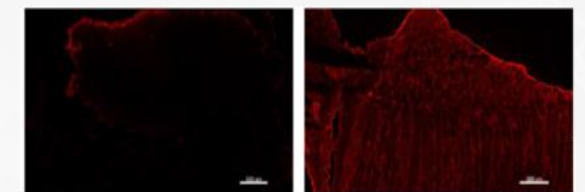
MAP Non-treatment

MAP EmtinB



MAP Non-treatment

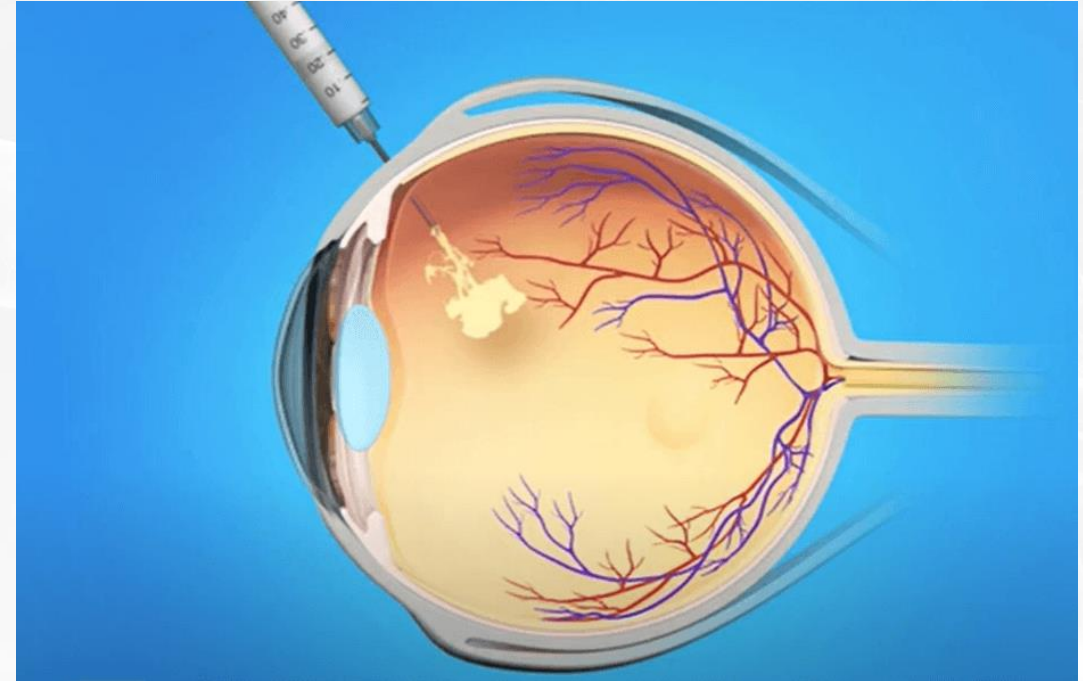
MAP EmtinB



PROJECT REVIEW: Ophthalmology Projects



- In the ophthalmology studies EmtinB™ is presented as an injection (IVT) into the vitreous humour of the eye. Whilst this sounds unfavourable, it is a normal way of treating ocular disease.
- We have evaluated the distribution of EmtinB™ in the eye for up to 14 days after an IVT injection. EmtinB™ was found to distribute to both the aqueous and vitreous humor of the eye and was still present after 14 days. (Note; in the systemic program the EmtinB™ was cleared from the body after approx. 30 hours.)



PROJECT REVIEW: Ophthalmology Projects



- A 13-week study in NHP's looked at multiple (4) injections into the eye with a 4-week washout. From this study we noted the presence of EmtinB™ in the eye at all concentrations and determined a safe injection concentration (NOAEC) of 1500micrograms. This provides data for determining the dose in the first in human clinical studies.
- This study will be followed up with a GLP Rabbit study to confirm the activity and provide further data for the Phase I clinical trial.

PROJECT REVIEW: Ophthalmology Projects



- The proposed route of Administration and therapeutic focus opens opportunities to increase Intellectual Property.
- There are other neurological ocular diseases (e.g. ischaemic optic neuropathy (ION)) that provide an opportunity to apply for orphan drug designation giving the product substantial market protection.
- Orphan drug market protection refers to the market exclusivity granted to a drug that has been designated as an orphan drug. The FDA grants a seven-year market exclusivity to a drug that has been approved as an orphan drug, which applies specifically to the designated orphan use. In Europe, pharma companies that bring orphan drugs to market are awarded 10 years of market exclusivity.

GLAUCOMA OPPORTUNITY



- Glaucoma is the leading cause of irreversible blindness in Australia and is rapidly increasing in prevalence due to an aging population. Other risk factors associated with glaucoma, such as high myopia, are also projected to increase exponentially in the coming decades, creating a potential public health dilemma.
- The global prevalence of glaucoma reached 80 million in 2020 with six million of these patients bilaterally blind because of end-stage disease. The prevalence of glaucoma in Australia is estimated to be 3.7%, which increases to 10% in patients over the age of 80. This prevalence is projected to increase by 80% by 2025.
- Being a relatively asymptomatic disease, especially in the early stages, a significant proportion of individuals with glaucoma remain undiagnosed. It is estimated that approximately 50% of Australians with glaucoma do not know they have the disease. This is even greater in minority and/or socioeconomically disadvantaged groups, which have up to 4.4 times greater odds of undiagnosed and/or untreated glaucoma. New AI scanning technology has the potential to increase the early diagnosis of ocular diseases.
- In addition to association with worse patient outcomes and increased burden on the health system, delayed diagnosis and treatment also has significant economic implications as the cost of glaucoma increases exponentially with progressive disease.

EARLY TREATMENT IS THE KEY

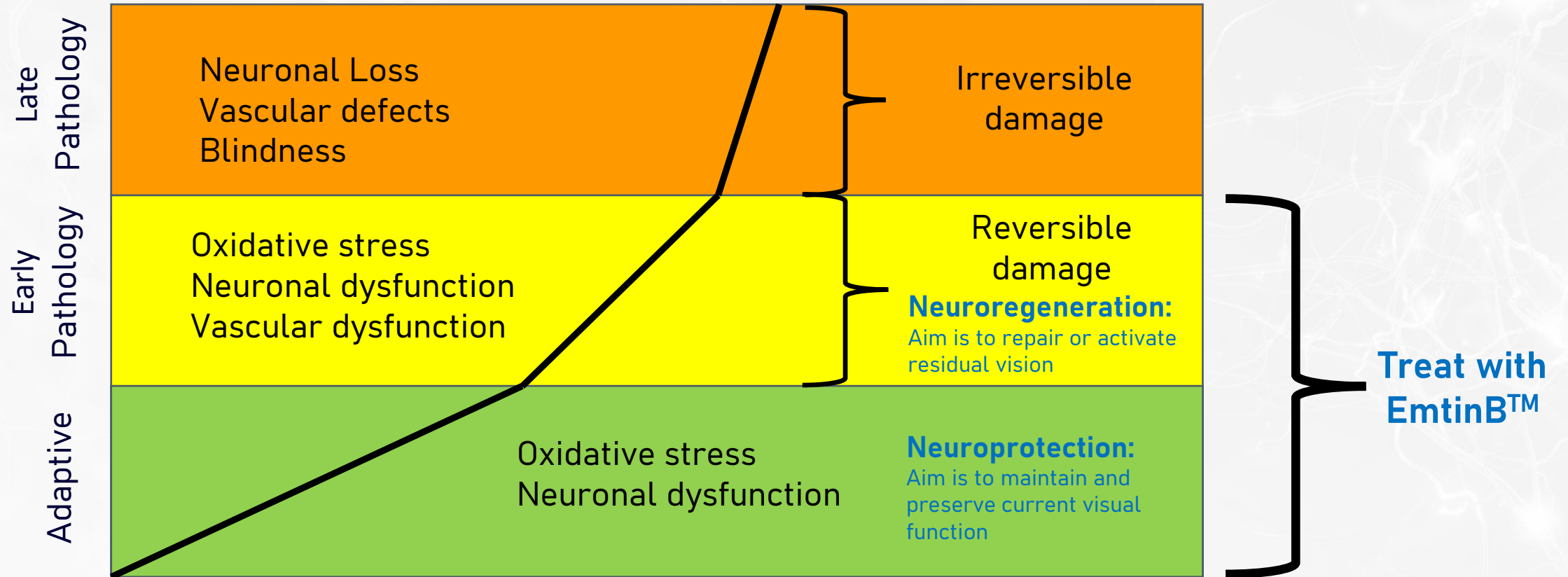


Figure.

Stages of retinal disease that reflect when neuroprotective strategies should be started to provide the most benefit. The black line shows the hypothetical progression of retinal disease through adaptive, early and late pathology. During early pathology, retinal disease is detectable and potentially reversible while irreversible damage occurs in late-stage pathology. Starting neuroprotective treatments at the first signs of retinal disease would provide the most benefit in preserving vision

PROJECT REVIEW: Ophthalmology Projects Summary



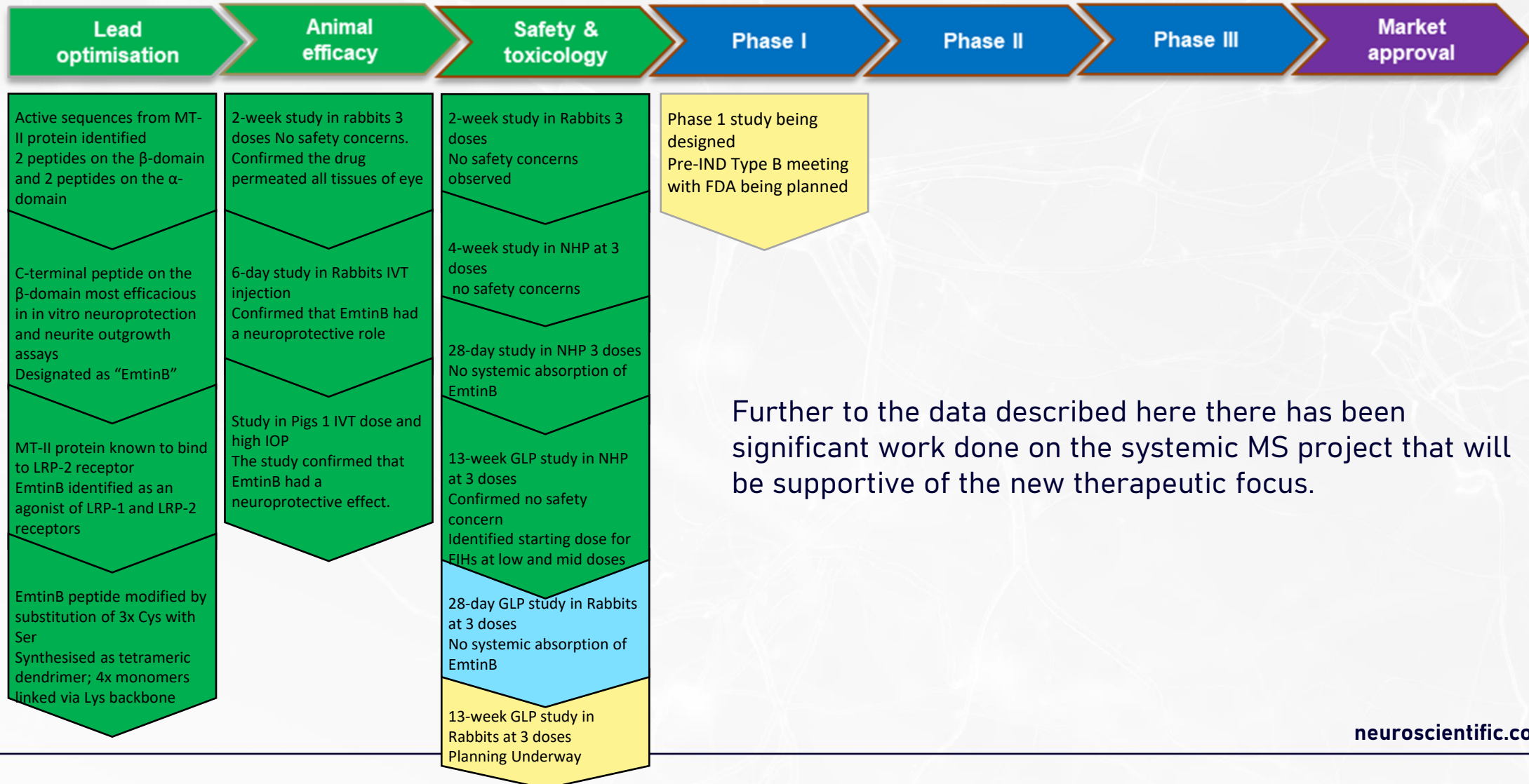
- The proposed treatment of Glaucoma or one of the other potential neurodegenerative diseases of the eye is not done at home; it is carried out in a medical facility. This changes the product dynamics.
- The current drug formulation is satisfactory for the proposed treatment protocol which is a once-monthly injection of a small amount of the drug into the eye.
- The stability of a few hours is acceptable in a medical environment.
- The lower dose and the once monthly injection protocol coupled with the size of the market provides a very strong health economic evaluation with a potentially significant margin for the product owner.
- The preclinical data confirms that there is a strong argument for developing EmtinB™ for ocular disease.



DEVELOPMENT OF EMTINB™ FOR OPHTHALMOLOGICAL USE

Preclinical Development

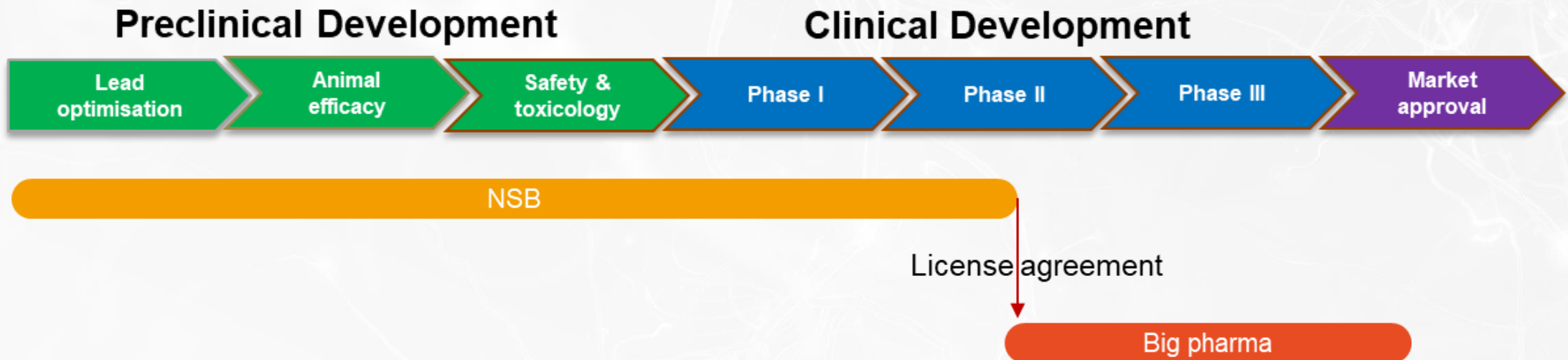
Clinical Development



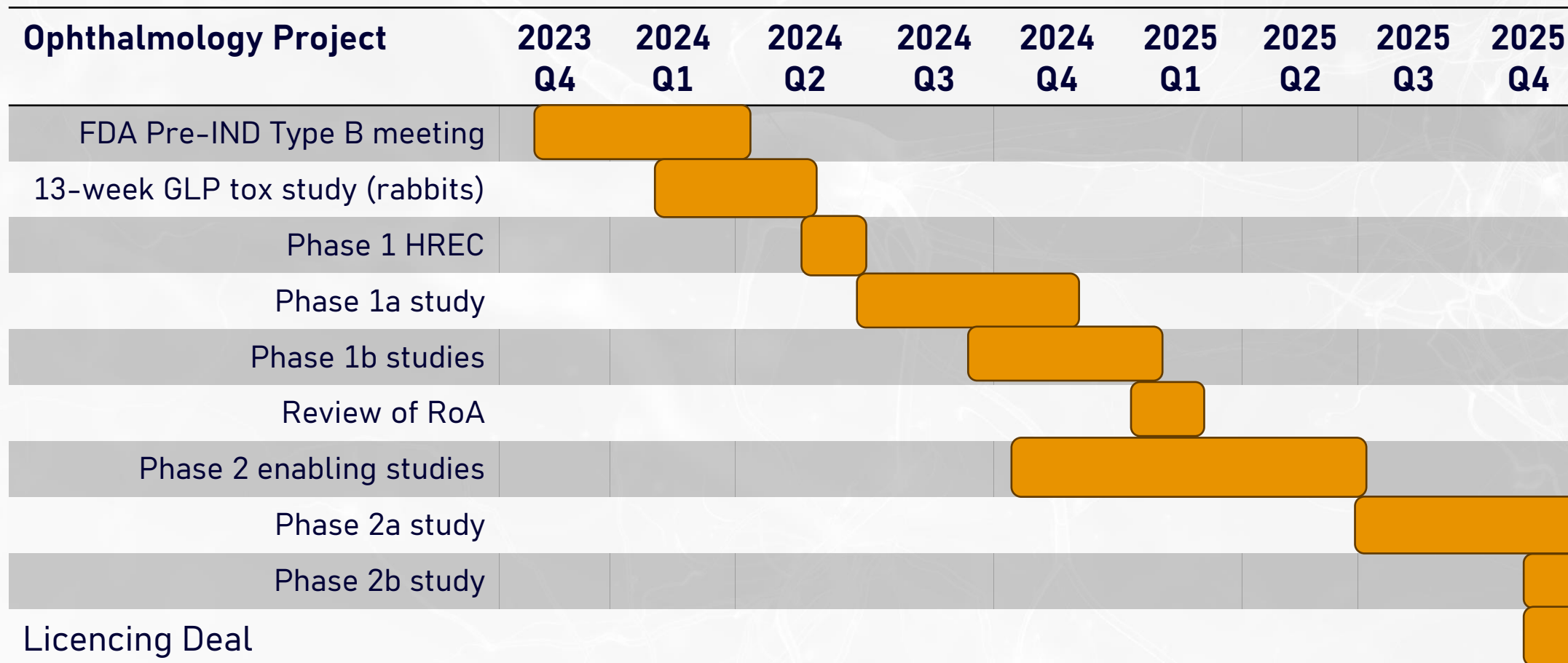
COMMERCIALISATION STRATEGY



The Company's commercialisation strategy involves developing its drug candidates through to successful completion of Phase II clinical studies and then license them to a pharmaceutical or biotechnology company for further clinical development / market approval.



R&D STRATEGY AND INDICATIVE SCHEDULE



Milestone target dates are subject to change due to reliance on independent contract research organisations to undertake and successfully complete each stage.

BOARD AND LEADERSHIP



**Dr Anton Uvarov, PhD,
MBA**
NON-EXECUTIVE
DIRECTOR

Founding director of Actinogen Medical (ASX:ACW). Former Equities Analyst with Citigroup, US and former director at Dimerix (ASX:DXB) and Imugene (ASX:IMU).



**Stephen Quantrill,
MBA**
NON-EXECUTIVE
DIRECTOR

20 years' executive corporate advisory and company directorship, Executive Chairman of McRae Investments



**Paul Rennie MBM,
MSTC**
NON-EXECUTIVE
CHAIR

Founding and current CEO of Paradigm Biopharmaceuticals (ASX:PAR). Former COO and Executive VP New Product Development at Mesoblast Ltd



Dr Linda Friedland
NON-EXECUTIVE
DIRECTOR

A physician with over 25 years clinical experience. International advisor to many Fortune and Forbes global companies. Asia-Pacific partner for Camelot BioCapital



**Abby Macnish
Niven, CFA**
COMPANY
SECRETARY & CFO

Investment professional with over 15 years' experience. Board member of Muscular Dystrophy WA and Chair of Investment Committee at TWD.



Stephen Carter
CHIEF EXECUTIVE
OFFICER

Experienced pharmaceutical executive with 30 years in senior roles in drug development and commercialization. Extensive clinical and regulatory experience

FINANCIAL METRICS AND MILESTONES



FINANCIALS

- ~\$4M cash on hand
- Sufficient cash to develop lead project to clinical trials.

TARGET MILESTONES*

- Q1 2024 – Lodge Pre-IND meeting request with FDA
- Q2 2024 – Completion of 13-week GLP tox study in rabbits
- Q4 2024 – Completion of ocular IND-enabling safety studies
- Q3 2024 – Phase I Ocular clinical study
- Q2 2025 – Phase 2 Ocular clinical study
- Q4 2025 – License out EmtinB™ Ocular project

CAPITAL STRUCTURE

ASX code	NSB
Shares on issue	143M
Price	\$0.06
Market cap	\$8.6M
McRae Investments Pty Ltd	18%
BNP Paribas Noms Pty Ltd	13%
Top Twenty	53%

* Milestones target dates are subject to change due to reliance on independent contract research organisations to undertake our R&D programs.

SUMMARY



- The Company has conducted an EmtinB™ project review & confirms EmtinB™ as highly prospective as NSB's lead project.
- EmtinB™ for the treatment of neurodegenerative diseases of the eye has shown great promise.
- >5% of the global population suffer vision loss due to damaged optic nerve representing huge addressable market opportunity.
- Ocular disease has outstanding health economic profile.
- EmtinB™ development for ocular diseases is commercially viable.
- NSB will focus on developing EmtinB™ for the treatment of Glaucoma and other neurodegenerative diseases of the eye.
- NSB has the management and leadership expertise to develop and commercialise EmtinB™.



NeuroScientific
BIOPHARMACEUTICALS

neuroscientific.com

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Chief Executive Officer

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