NEMUS BIOSCIENCE

LD MICRO
June 4, 2018 | OTCQB:NMUS

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Improving health through cannabinoid-based therapies

BRIAN MURPHY, MD, MPH, MBA
Chief Executive Officer

NEMUS and Emerald Health Sciences

Partnership Highlights

- Built on the value of Nemus' intellectual capital and exclusive agreement with UM for novel cannabinoid technologies
- EHS BOD Committee provides access to key clinical and development expertise
- Ability to leverage EHS financial and life science network to advance development programs

A global cannabis investment company focused on the medicinal potential of cannabis and cannabinoids

emerald™ HEALTH SCIENCES

NEMUS BIOSCIENCE

A leading biopharmaceutical company focused on the development of cannabinoid-based therapeutics

OLE' MISS:
Leading Cannabis Research in the US for Over 50 Years

THE UNIVERSITY OF MISSISSIPPI
National Center for Natural Products Research

The only entity in the US authorized to cultivate cannabis on behalf of the federal government for 50 years

NEMUS has exclusive, perpetual, worldwide exclusivity for all compounds from UM

Global patent estate

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NB1111

For the Treatment of Glaucoma

Glaucoma: A Global Cause of Blindness

- Glaucoma is a **leading cause of blindness** globally with more than **70 million patients** affected worldwide.[2]
- Damage to the **retinal ganglion cells (RGCs) is irreversible** so therapy is designed to slow disease progression by **lowering IOP** and thereby preserving remaining vision. [3]
- **Current therapies work by lowering IOP** thus enhancing drainage of fluid from the eye via canals in the anterior chamber or by decreasing fluid production. [1]
- African Americans are at highest risk of developing glaucoma in the US. [4]

1.WeinrebR, et al; JAMA, 2014; 311(18): 1901-1911
2.Quigley HA, et al; Br J Ophthalmol, 2006; 90(3): 262-267
3.NickellsRW, et al; Ann Rev NeuroSci, 2012; 35:153-179
4.Kwon YH, et al; NEJM, 2009; 360(11): 1113-1124

Current Therapies Reduce IOP but Lack Direct Neuroprotection

Class of Medication	Example	IOP Response Rates*	Local Adverse Effects	Systemic Adverse Effects
Prostaglandins	Latanoprost	6-8 mm Hg	macular edema, conjunctival hyperemia, discoloration of iris	headaches
Prostaglandin Analog	Latanoprostene bunod	7-9 mm Hg	iris and local tissue pigmentation, eyelash stimulation, conjunctival hyperemia, eye irritation, eye pain, and instillation site pain	---
β-Andrenergic Blockers	Timolol	5-6 mm Hg	ocular irritation and dry eyes	contraindicated in asthma, COPD and bradycardia
α-Adrenergic Blockers	Brimonidine	4-6 mm Hg	ocular irritation, dry eyes and allergic reactions	central nervous effects and respiratory arrest in young children; renal/hepatic failure
Carbonic Anhydrase Inhibitors	Dorzolamide	3-5 mm Hg	ocular irritation, dry eyes, burning sensation	paresthesia, nausea, diarrhea, loss of appetite, renal stones
Cholinergic Agonists	Pilocarpine	3-7 mm Hg	ocular irritation, induced myopia and decreased vision due to ciliary spasm	ciliary spasm leading to headaches
Rho kinase inhibitor	Netarsudil	Up to 5 mm Hg	conjunctival hyperemia, corneal verticillata, instillation site pain, and conjunctival hemorrhage	---

Despite improvements in IOP management, no currently approved drugs demonstrate direct neuroprotection of retinal ganglion cells (RGCs), which leads to eventual blindness in patients

Adapted from Weinrb RM et al, JAMA. 2014; 311(18): 1901-1911
*IOP response rates taken from Product Inserts for listed medicinals

Cannabinoids and Glaucoma

- The **cannabis plant** contains over 100 cannabinoid-class chemical entities that have been used over centuries in **managing multiple medical problems**.[1]
- The main constitutive molecule, **delta-9-tetrahydrocannabinol (Δ^9-THC)**, was isolated and structure determined in the early 1960's.[2]
- The first report assessing effect of cannabis on IOP appeared in 1971.
- Further human studies using routes of administration that included inhalational, oral, and IV access **showed IOP reductions** in both normal controls and as high as **a 65% decline in patients with glaucoma**. [3-6]

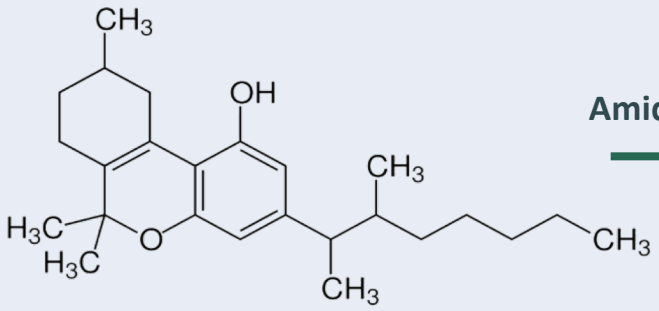
1. Tomida I, et al., Br J Opthalmol, 2004; 88: 708-713
2. Elsohly MA; Cannabis and Cannibinoids; New York: Haworth press, 2002; pgs 75-86
3. Hepler RS, Frank IR; JAMA, 1971; 217:1392
4. Cooler p et al; Southern Med J, 1977; 78:951
5. Green K et al; Proc Soc Exp Biol and Med, 1977; 154:228
6. Goldberg I et al; Australian J opthalmol, 1979; 7(2):151-157

Proprietary NEMUS Technology

NEMUS is developing an optimized cannabinoid technology that enhances bioavailability and offers more predictable pharmacokinetics

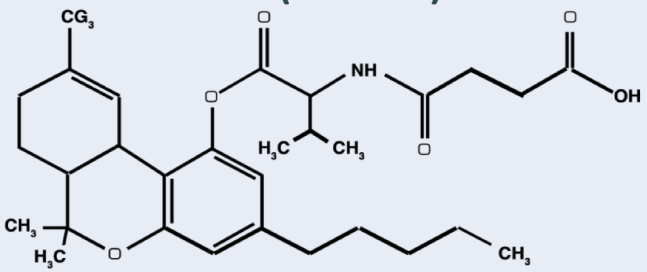
Biochemically Engineered Technology

THC



Amide-Ester

THC-Val-HS (NB1111)



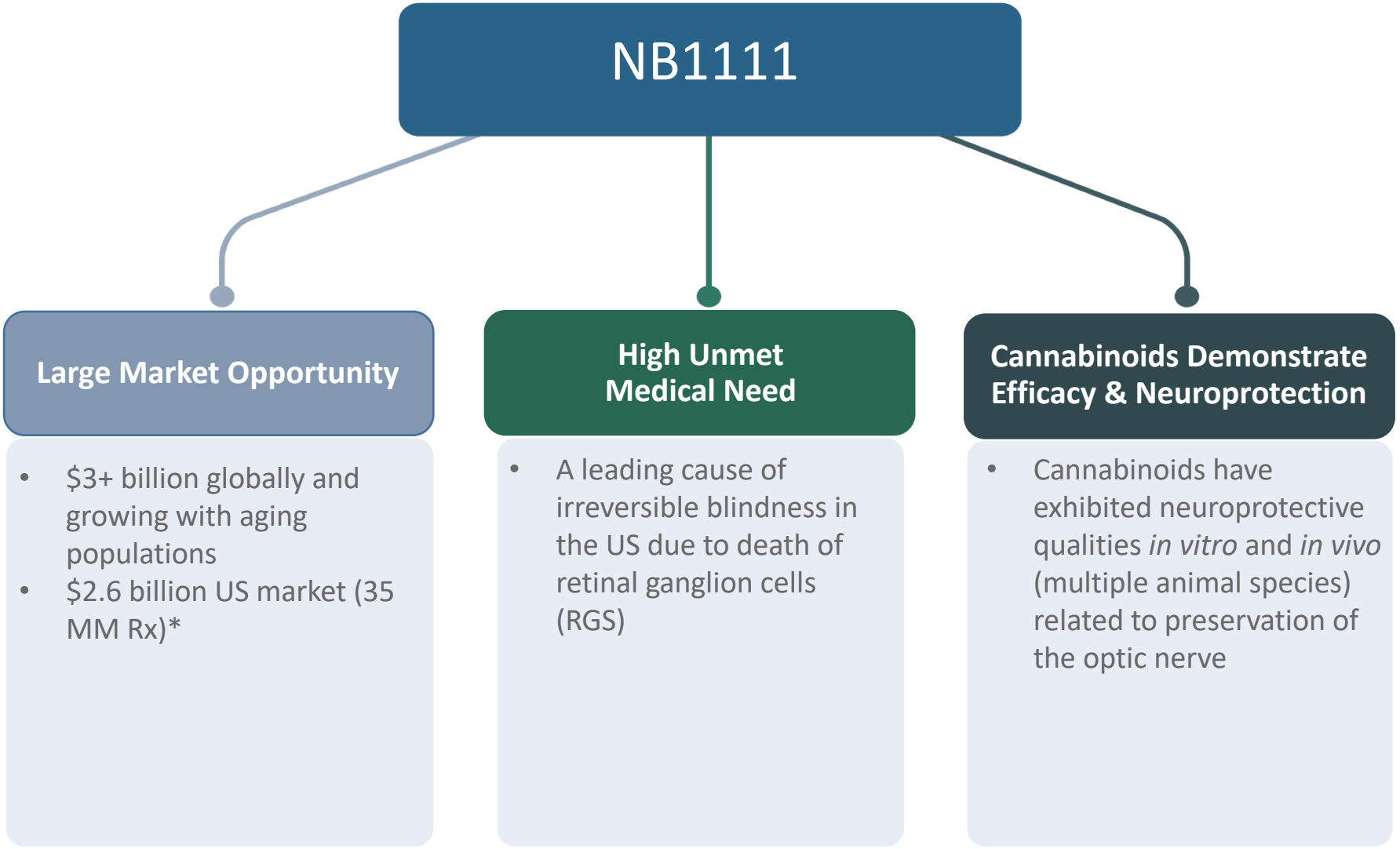
THCVHS BROAD PATENT ESTATE

NEMUS GLOBAL RIGHTS

PROPRIETARY CANNABINOID-BASED THERAPEUTICS

*Development of delta-9 THC amino acid-dicarboxylate prodrug with improved ocular bioavailability. Invest Ophthalmol Vis Sci 2017; 58:2167-217

Glaucoma Represents a Significant Global Unmet Medical Need



* IMS; 2016

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Mechanism of Action

Cannabinoid receptors are located in the key ocular tissues that regulate IOP

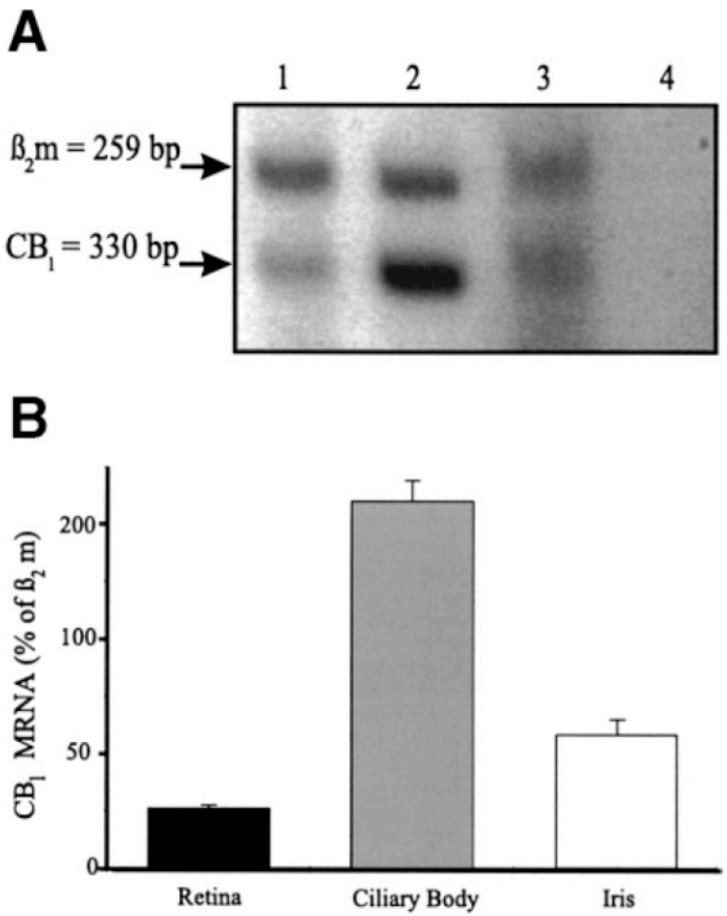


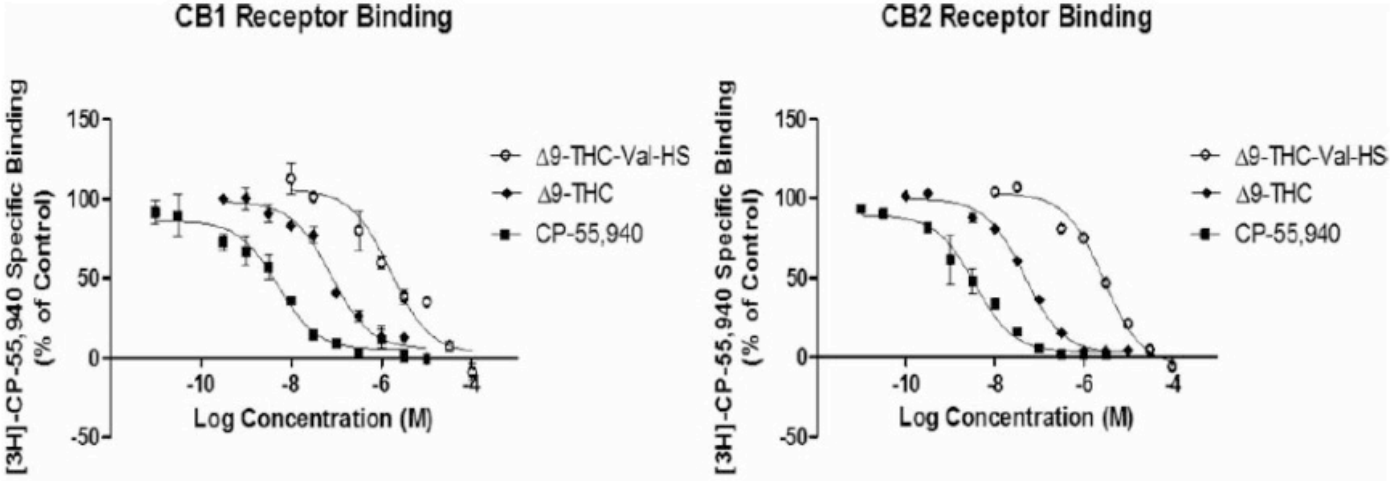
FIG. 1. (A) RT-PCR of CB1 and β_2m from human eye: retina (lane 1); ciliary body (lane 2); iris (lane 3); negative control (lane 4); run on a non-denaturing 5% polyacrylamide gel. (B) Relative differences of CB1 transcripts in the human eye. The level of mRNA in the retina (25.8 ± 2.46%), ciliary body (210 ± 11.55%) and iris (62.7 ± 5.94%) were compared by RT-PCR. CB1 mRNA content was normalized with that of β_2m and expressed relative to the β_2m mRNA level ($n = 5$; bars are SEM).

- Modulation of cannabinoid receptor tone already exists by virtue of the **endocannabinoid system located in the eye** and other organs
- **CB1 receptors display a higher density in the anterior compartment than the posterior** (1)
- CB1 receptors have been localized to ciliary epithelium, ciliary muscle, trabecular meshwork, canal of Schlemm, iris; organs that help regulate intra-ocular pressure (IOP) (2)
- **CB2 receptors are more prevalent in the posterior compartment of the eye** (1)

1. Porcella A et al; Eur J Neuroscience, 2000; 12:1123-1127
2. Chien FY, et al. Arch Ophthal, 2003; 121:87-90
3. Wei Y, et al. Molecular Vision, 2009; 15: 1243-1251

NB1111 (THCVHS) vs THC: CB receptor dynamics support NB1111 as a prodrug

- Experiments have shown that NB1111 does not substantively bind CB receptors
- The physiological effect comes from THC derived from the prodrug
- Pivotal for patent to show proof of prodrug

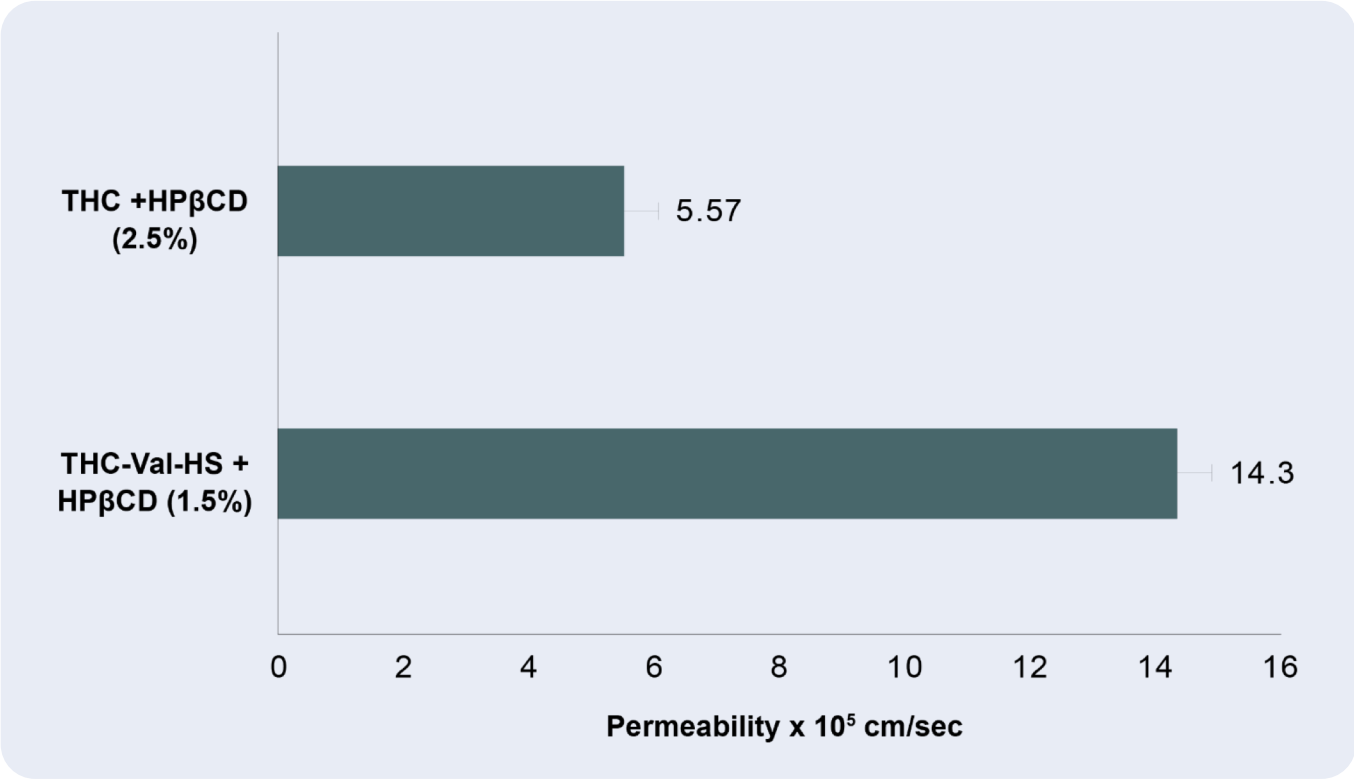


Compound	CB1		CB2	
	IC-50 (μM)	Ki (μM)	IC-50 (μM)	Ki (μM)
Δ^9-THC-VAL-HS	1.593 ± 0.289	0.960 ± 0.174	2.430 ± 0.164	1.215 ± 0.082
Δ^9-THC	0.077 ± 0.008	0.044 ± 0.005	0.047 ± 0.002	0.032 ± 0.001
CP-55,940	0.005 ± 0.001	0.003 ± 0.000	0.004 ± 0.000	0.002 ± 0.000

FIGURE 6. Cannabinoid receptor (CB1 and CB2) binding studies with THC-Val-HS, THC, and CP-55,940.

*Goutham R, et al. IVOS, 2017; 58(4): 2167-2179

NB1111 (TCHVHS) Achieves Improved Permeability into the Eye vs. THC in Ocular Surfactant* Model

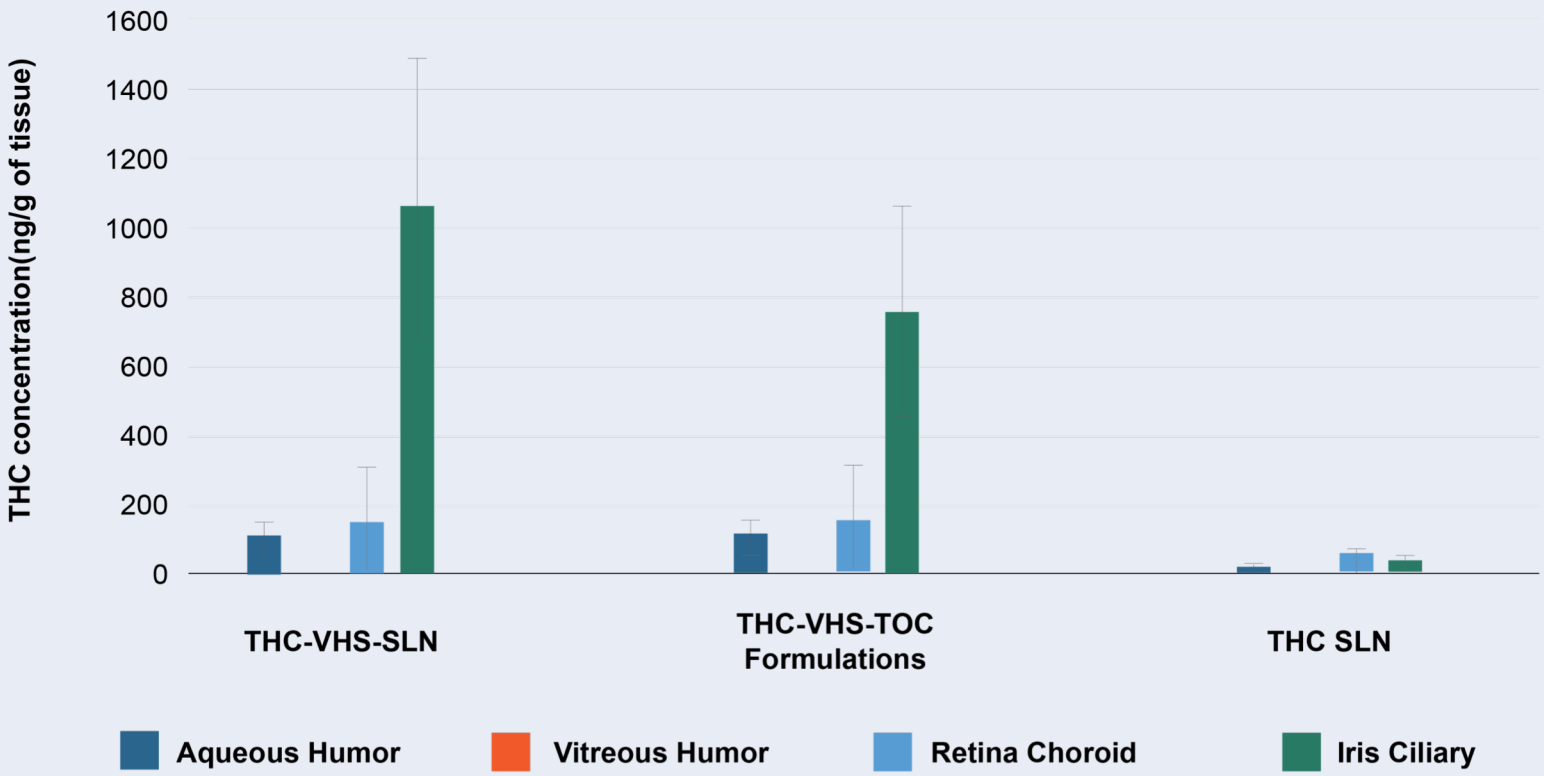


NB1111 exhibited greater permeability into the eye vs. THC

*HPβCD = 2-hydroxy propyl-beta-cyclodextrin

*Development of delta-9 THC amino acid-dicarboxylate prodrug with improved ocular bioavailability. Invest Ophthalmol Vis Sci 2017; 58:2167-217

NB1111 (THCVHS) Achieves Tissue Penetration in Organs Regulating IOP in Glaucoma Model



No THC or 11-OH-THC was detected in the plasma of study animals even after 5 days of dosing (ng sensitivity level of detection)

NB1111 (THCVHS) vs pilocarpine and timolol achieves 45% reduction in IOP*

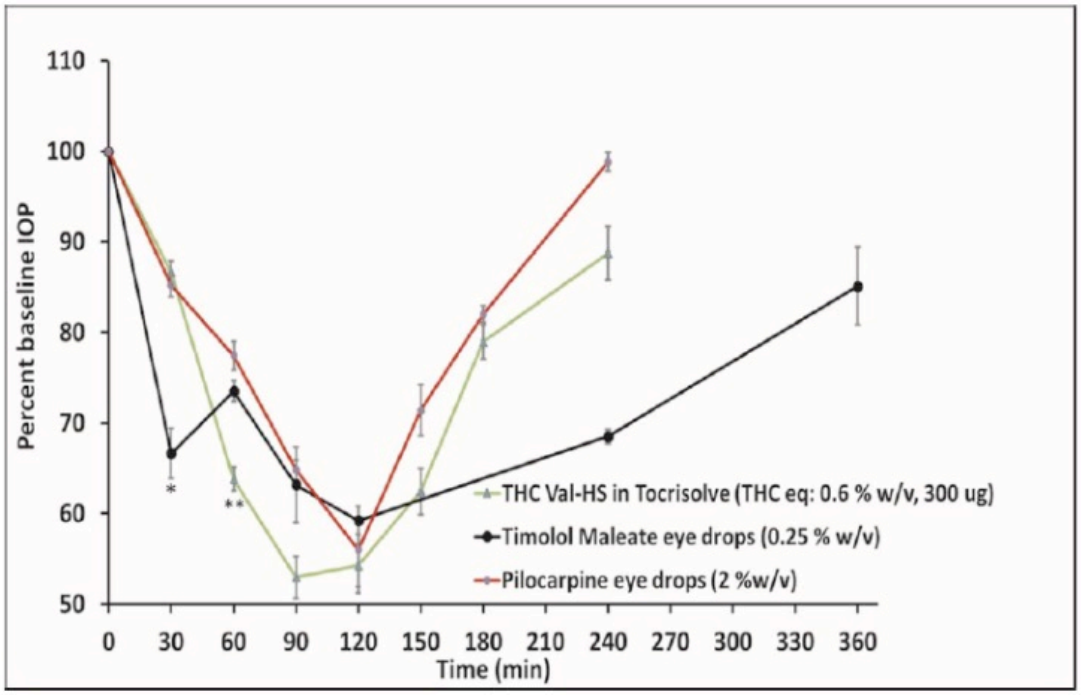
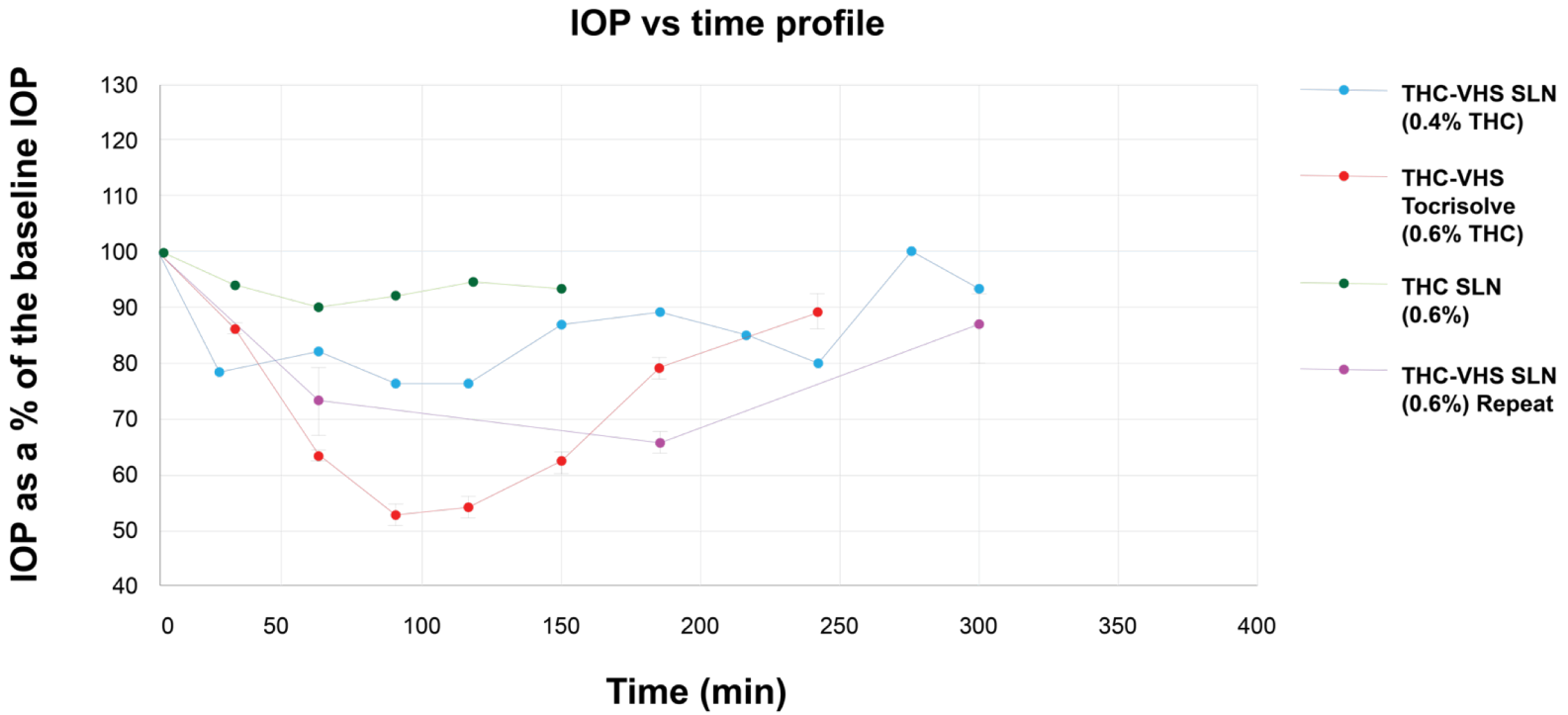


FIGURE 5. IOP–Time profiles obtained with THC-Val-HS, timolol maleate, and pilocarpine eye drops (marketed) in rabbit glaucoma model. Numbers in brackets represent concentration (%w/v) and dose equivalent to THC (μg). Actual baseline values (mean ± SEM in mm Hg) for IOP in the following different formulations: THC-Val-HS in Tocrisolve (26.8 ± 0.4), timolol maleate eye drops (24.0 ± 1.9), and pilocarpine eye drops (27.1 ± 0.3). *IOP drop from timolol maleate is significantly different form THC-Val-HS and pilocarpine ($P < 0.05$). **IOP drop from THC-Val-HS is significantly different from timolol maleate and pilocarpine ($P < 0.05$).

*Goutham R, et al. IVOS, 2017; 58(4): 2167-2179

NB1111 (THCVHS) achieves significant decline in IOP using SLN (solid lipid nanoparticle) technology



Data reveals the following:

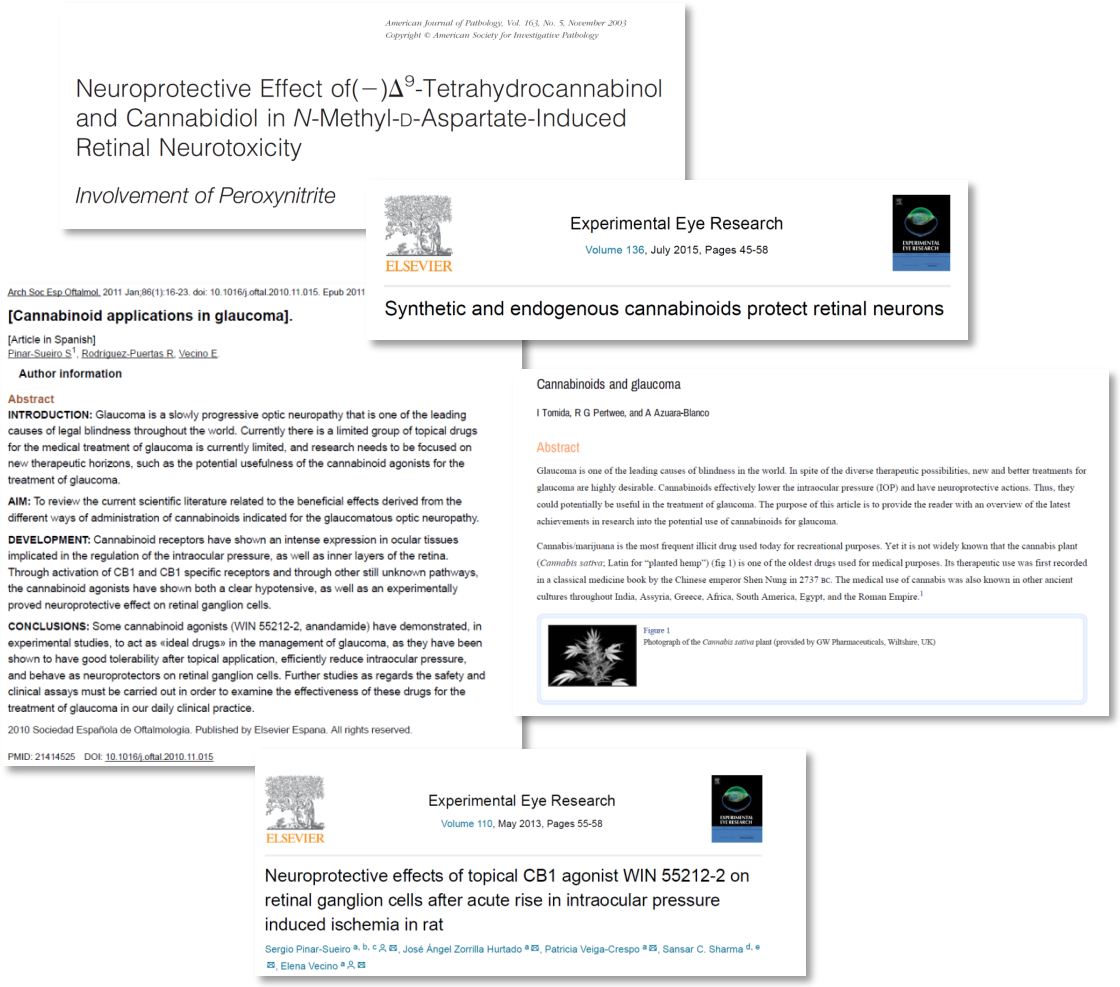
- THCVHS in Tocrisolve exhibits IOP maximum decline of 47%
- THCVHS in SLN exhibits IOP maximum decline of 35%
- THC in SLN exhibited roughly 8-10% decline in IOP
- Encapsulating THCVHS in an SLN enhanced the half-life by almost doubling the time of physiologic effect

NB1111 Fluid Dynamics Has Competitive Advantage Over Currently Available Therapies

	Mechanism of Action: Fluid Dynamics			
Drug Class	Increased flow Trabecular mesh	Increased uveoscleral outflow	Decreased fluid production	**Direct Neuroprotection**
Prostaglandins				
Prostaglandin Analog				
β- adrenergic blockers				
α- adrenergic agonists				
Carbonic anhydrase inhibitors				
Cholinergic agonists				
Rho kinase inhibitor				
NB1111 (THCVHS)				

NB1111 targets multiple mechanisms to reduce IOP. Associated NEUROPROTECTIVE qualities of THC may also PROTECT against BLINDNESS in glaucoma

Cannabinoids Shown to Be Neuroprotective in Multiple Animal Models



American Journal of Pathology, Vol. 163, No. 5, November 2003
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Neuroprotective Effect of(−)Δ^9-Tetrahydrocannabinol and Cannabidiol in *N*-Methyl-D-Aspartate-Induced Retinal Neurotoxicity

Involvement of Peroxynitrite

ELSEVIER

Experimental Eye Research
Volume 136, July 2015, Pages 45-58

Synthetic and endogenous cannabinoids protect retinal neurons

Arch Soc Esp Oftalmol. 2011 Jan;86(1):16-23. doi: 10.1016/j.oftal.2010.11.015. Epub 2011

[Cannabinoid applications in glaucoma].

[Article in Spanish]
Pinar-Sueiro S[1], Rodriguez-Puertas R, Vecino E

Author information

Abstract

INTRODUCTION: Glaucoma is a slowly progressive optic neuropathy that is one of the leading causes of legal blindness throughout the world. Currently there is a limited group of topical drugs for the medical treatment of glaucoma is currently limited, and research needs to be focused on new therapeutic horizons, such as the potential usefulness of the cannabinoid agonists for the treatment of glaucoma.

AIM: To review the current scientific literature related to the beneficial effects derived from the different ways of administration of cannabinoids indicated for the glaucomatous optic neuropathy.

DEVELOPMENT: Cannabinoid receptors have shown an intense expression in ocular tissues implicated in the regulation of the intraocular pressure, as well as inner layers of the retina. Through activation of CB1 and CB1 specific receptors and through other still unknown pathways, the cannabinoid agonists have shown both a clear hypotensive, as well as an experimentally proved neuroprotective effect on retinal ganglion cells.

CONCLUSIONS: Some cannabinoid agonists (WIN 55212-2, anandamide) have demonstrated, in experimental studies, to act as «ideal drugs» in the management of glaucoma, as they have been shown to have good tolerability after topical application, efficiently reduce intraocular pressure, and behave as neuroprotectors on retinal ganglion cells. Further studies as regards the safety and clinical assays must be carried out in order to examine the effectiveness of these drugs for the treatment of glaucoma in our daily clinical practice.

PMID: 21414525 DOI: 10.1016/j.oftal.2010.11.015

Cannabinoids and glaucoma

I Tomida, R G Pertwee, and A Azuara-Blanco

Abstract

Glaucoma is one of the leading causes of blindness in the world. In spite of the diverse therapeutic possibilities, new and better treatments for glaucoma are highly desirable. Cannabinoids effectively lower the intraocular pressure (IOP) and have neuroprotective actions. Thus, they could potentially be useful in the treatment of glaucoma. The purpose of this article is to provide the reader with an overview of the latest achievements in research into the potential use of cannabinoids for glaucoma.

Cannabis/marijuana is the most frequent illicit drug used today for recreational purposes. Yet it is not widely known that the cannabis plant (*Cannabis sativa*; Latin for "planted hemp") (fig 1) is one of the oldest drugs used for medical purposes. Its therapeutic use was first recorded in a classical medicine book by the Chinese emperor Shen Nung in 2737 BC. The medical use of cannabis was also known in other ancient cultures throughout India, Assyria, Greece, Africa, South America, Egypt, and the Roman Empire.[1]

Figure 1
Photograph of the *Cannabis sativa* plant (provided by GW Pharmaceuticals, Wiltshire, UK)

ELSEVIER

Experimental Eye Research
Volume 110, May 2013, Pages 55-58

Neuroprotective effects of topical CB1 agonist WIN 55212-2 on retinal ganglion cells after acute rise in intraocular pressure induced ischemia in rat

Sergio Pinar-Sueiro [a, b, c], José Ángel Zorrilla Hurtado [a], Patricia Veiga-Crespo [a], Sansar C. Sharma [d, e], Elena Vecino [a]

- Cannabinoid agonists have shown both a clear **hypotensive and neuroprotective effect on retinal ganglion cells**
- **CB1 receptors** to a greater extent than CB2 receptors, have been implicated in **mediating cannabinoid-induced neuroprotection**
- Experimentally, in multiple animal species, synthetic and endogenous cannabinoids have displayed a protective effect on neurons

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Development Plan

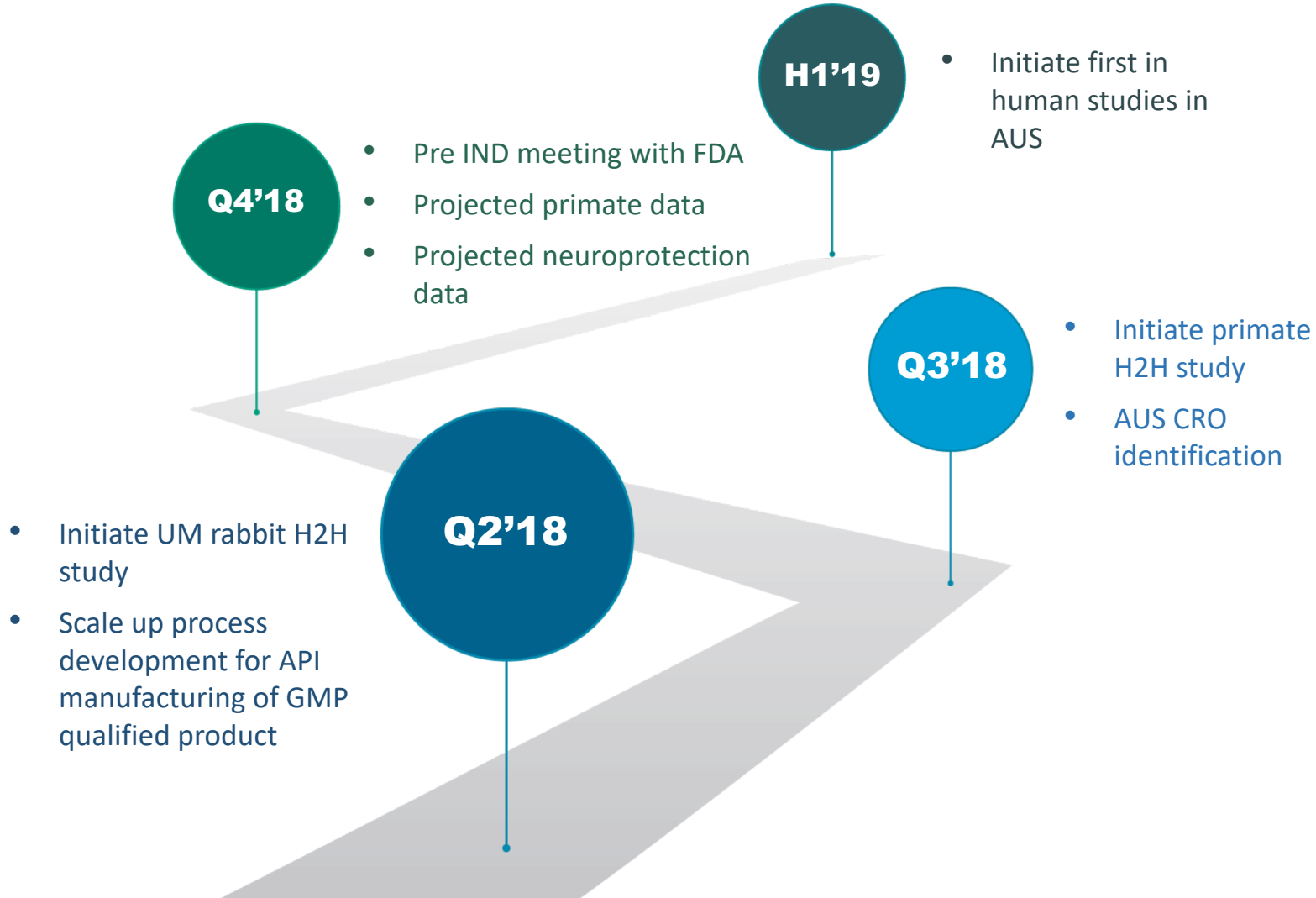
Advancing to Clinical Studies: NB1111

Objective	NB1111 Clinical Study	
Perform Phase 1b/2a clinical studies in patients utilizing sites in Australia to generate safety, efficacy, and pharmacokinetic data	**Therapy:**	NB1111
	Patients:	Patients with Glaucoma
	Timeline:	Initiating in near term
	Dosing:	Anticipated dosing design will permit patients to act as their own controls (contra-lateral eye dosing)
	Study Design:	Traditional single-ascending dose (SAD) and multiple-ascending dose (MAD) designs consistent with validated regulatory pathways

- **Australia offers centers of excellence with a pool of qualifying patients as well as economic incentives that when leveraged, could possibly lead to expedited enrollments and quality data**
- **Nemus has identified an API synthesis partner in AMRI which has expertise in cannabinoid manufacturing, scale-up capability, and a global footprint**

Key Development Milestones

Near-Term Value Creating Milestones for NB1111



Pipeline

			Research	Preclinical	Phase 1
Ocular Indications					
THCVHS	**NB1111**	**Glaucoma**			
CBDVHS	NB2222	Dry Eye			
		Macular Degeneration			
		Diabetic Retinopathy			
Other Indications					
THCVHS	NB1222	CINV			
CBDVHS	NB2111	CIPN			
Cannabinoid Platform	NB3111	MRSA			

NEMUS Value Proposition:
Disrupting the cannabinoid therapeutic space

Developing *Biosynthetic* Cannabinoids	• Currently, the only cannabinoid company with potential cost-effective and enhanced life-cycle scale-up production related to biosynthetic manufacturing of cannabinoids • The only cannabinoid company with a re-engineered cannabinoid prodrug designed for multiple routes of administration
Targeting Unmet Needs in Multi-Billion Dollar Global Markets	• Developing cannabinoids for the treatment and/or management of acute and chronic diseases
Primary Development & Commercialization Partner with UM	• NEMUS is the primary development and commercialization partner of the University of Mississippi, drawing on 50 years of intellectual capital in cannabinoid chemistry and physiology from the only entity with a Federal license to directly study cannabinoids
Proprietary Molecule with Global Patent Footprint	• The proprietary prodrug of THC has a global patent footprint including the world's largest pharma markets of USA, Japan and the EU

Capitalization

OTCQB	All Shareholders	Largest Shareholder: Emerald Health Sciences
Common Shares Outstanding	133.2 M[1]	73.1 M (54%) [2]
Options & Warrants	53.4 M[1]	40.8 M (76%) [2]
Fully Diluted	186.6 M	113.9 M (61%)
Market Cap	$37.2M[3]	
Base of Operations	Long Beach, California & Oxford, Mississippi	

[1] 18/05/25 (proforma, including pending equity grant to management) [2] 18/05/25 [3] Based on 18/06/01 OTCQB per share prices of $.28

Management

BRIAN MURPHY, MD, MPH, MBA – Chief Executive Officer; Chief Medical Officer, Director

Dr. Murphy has almost two decades of experience in drug development and evaluation, both from the academic and industry perspective. He most recently served as the CMO of Eiger Biosciences. Previously, Dr. Murphy was CMO at Valeant Pharmaceuticals International (VRX) where his responsibilities also included oversight of Global Medical Affairs, Clinical Development, Biostatistics, and Pharmacovigilance. Dr. Murphy also served as Medical Director, then VP of Marketing and Commercial Strategy of Hepatology for InterMune, Inc. (ITMN). Prior to InterMune, Dr. Murphy was Medical Director of North America for Antivirals/Interferons at Hoffmann-LaRoche. Murphy is board-certified in internal medicine and completed his residency at Tufts-New England Medical Center. He served as Chief Medical Resident in the Boston University Internal Medicine program. He went on to complete parallel fellowship tracts at Harvard Medical School (HMS) and the Massachusetts General Hospital in medicine and clinical epidemiology. He also completed a fellowship in Medical Ethics at HMS-Brigham and Women's Hospital. Dr. Murphy earned his MD, MPH (general public health), and MS (pharmacology) degrees from New York Medical College and is a graduate of the Harvard School of Public Health (MPH in Health Policy and Management). He earned his MBA at the Columbia University Graduate School of Business.

DOUG CESARIO, MBA – Chief Financial Officer

Mr. Cesario brings over 15 years of financial and operational experience across many industries. Prior to joining Nemus, Mr. Cesario served as Chief Financial Officer of Kaiser Permanente Foundation Hospitals and Health Plan in the Orange County, California marketplace, where he managed the financial performance of the health system with an operating budget of over $1 billion per year. Previously Mr. Cesario held various financial leadership positions, including founder of Community Capital Advisory Group, a real estate advisory and investment company; director of Skye Automotive, a private equity fund; and corporate finance associate at both full service and boutique investment banking firms. Mr. Cesario earned a Master's in Business Administration from the UCLA Anderson School of Management.

WENDY CUNNING – Vice President of Operations

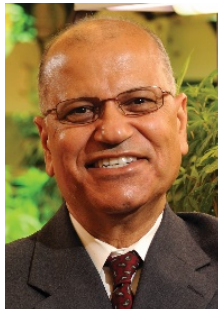
Ms. Cunning brings over 20 years of extensive expertise in U.S. sales, marketing, global new product development, commercialization, and lifecycle management in the biopharmaceutical industry. Prior to joining Nemus, Ms. Cunning served as Director, New Products, U.S. Eye Care at Allergan, where she led the creation of the business unit strategy for the U.S. ocular franchise. She was the Associate Director of Marketing at Amylin Pharmaceuticals, leading the global life-cycle management for Byetta®. Additionally, she held leadership positions at Valeant Pharmaceuticals, a multi-billion dollar pharmaceutical company, as the global marketing and commercial development lead for both the viral hepatitis and HIV franchises. Prior to joining Valeant, Ms. Cunning worked in Hepsera® marketing at Gilead Sciences and sales in HIV and respiratory medicine at GlaxoSmithKline. Ms. Cunning earned a bachelor's degree in biology from West Virginia University.

Board of Directors and Strategic Advisors

Avtar Dhillon, MD
Executive Chairman of Emerald and Strategic Advisor to Nemus
Dr. Dhillon is currently the Executive Chairman for Emerald Life Sciences and the former President and CEO of Inovio Pharmaceutics Inc. He is a life sciences entrepreneur with more than 20 years' experience building public companies.

Punit Dhillon, BA
Board of Directors
Mr. Dhillon is the Co-founder and Director of OnoSec Medical, Inc. and the former Vice President of Finance and Operations at Inovio Pharmaceuticals, Inc. He has extensive management experience spanning corporate finance, M&A and strategy implementation.

Jim Heppell, Esq
Board of Directors
Mr. Heppell is the former founder, CEO and director of BC Advantage Life Sciences I fund and is currently a director at a number of public and private life science companies. Mr. Heppell has extensive experience in corporate finance law.



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World's foremost expert on the science of cannabinoids. 300+ scientific publications . Research professor at The University of Mississippi.

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Scientific Advisor
Chief, Hematology/Oncology at UCSF
Cancer and Integrative Medicine specialist with research interests in the development of anti-cancer therapeutics and palliative care medicines.

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