skye BIOSCIENCE

Unlocking the Pharmaceutical Potential of Cannabinoids

CORPORATE PRESENTATION

2021 • OTCQB: SKYE

Legal Disclaimer

This presentation contains "forward-looking statements", including statements regarding Skye Bioscience, Inc. and its subsidiaries, within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. All the statements in this presentation, whether written or oral, that refer to expected or anticipated future actions and results of Skye Bioscience are forward- looking statements. In addition, any statements that refer to expectations, projections, or other characterizations of future events or circumstances are forward-looking statements. These forward-looking statements reflect our current projections and expectations about future events as of the date of this presentation. Skye Bioscience cannot give any assurance that such forward-looking statements will prove to be correct. The reader is cautioned not to place undue reliance on these forward-looking statements.

The information provided in this presentation does not identify or include any risk or exposures, of Skye Bioscience that would materially adversely affect the performance or risk of the company. For a description of the risks and uncertainties related to the business of Skye Bioscience, see our Annual Report or Form 10-K filed with the Securities and Exchange Commission and our subsequent periodic reports filed with the Securities and Exchange Commission.

All information contained in this presentation is provided as of the date of the presentation and is subject to change without notice. Neither Skye Bioscience, nor any other person undertakes any obligation to update or revise publicly any of the forward-looking statements set out herein, whether as a result of new information, future events or otherwise, except as required by law. This presentation shall not constitute an offer to sell or the solicitation of an offer to sell or the solicitation of an offer to buy any securities of Skye Bioscience, nor shall there be any sale of securities in any jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such jurisdiction. This is presented as a source of information and not an investment recommendation.

Overview

Biopharmaceutical company developing differentiated, synthetic, proprietary cannabinoid derivatives to treat diseases with significant unmet medical needs

OTCQB:
SKYE

NOVEL TECHNOLOGY

Bioengineered, synthetic cannabinoid derivatives designed to significantly enhance therapeutic benefits

COMMERCIAL OPPORTUNITY

$6.6B+ market opportunity for lead indication, glaucoma

INTELLECTUAL PROPERTY

Broad patent protection including “composition of matter”

EXPERIENCED TEAM

Track record of rapidly advancing preclinical candidates through to human trials and securing strategic pharma partnerships

MILESTONES

Key preclinical data expected in H1-21 & first-in-human data in H1-22

Glaucoma is the leading cause of irreversible blindness

Glaucoma is a disease that leads to the progressive damage of retinal ganglion cells, which make up the optic nerve, and without intervention will gradually lead to irreversible blindness

Healthy Vision

Early Glaucoma

Advanced Glaucoma

Large & growing patient population

78M

Current Glaucoma Patients

100M

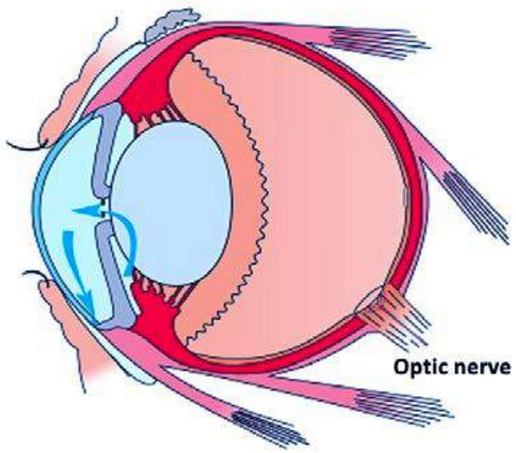
2040 Predicted Glaucoma Patients

$6.6B current global market and expected to reach $11B by 2027 with a growing aging population (CAGR 6.6%)

How does glaucoma cause blindness?

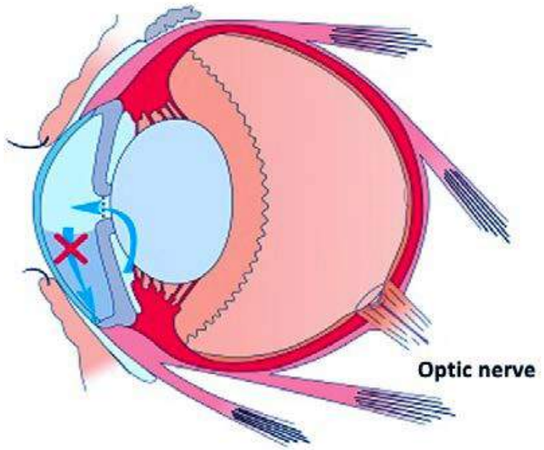
A common trait of glaucoma involves increased pressure in the eye – intraocular pressure (IOP)

HEALTHY

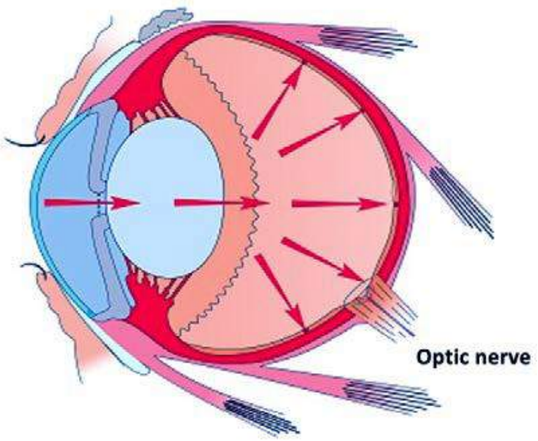


Production/drainage of aqueous humor (fluid) balanced

GLAUCOMA



Drainage canal becomes blocked, fluid builds up and leads to increased pressure



Increased pressure damages optic nerve cells, resulting in vision loss

Current therapies leave notable unmet needs

- Current drugs aim to lower IOP in order to slow disease progression
- Many patients are non–responders, have poor response, or develop tolerance
- >50% of patients require 2 or more drugs, can increase side effects and reduce compliance
- Lack of innovation, presents an opportunity and need for new classes of therapy

Class of Medication	Generic Example	IOP Reduction	MOA		Potential Side Effects
Prostaglandins	Latanoprost	30-35%	↑ Outflow		irritation, redness, blurred vision, dry eyes, light sensitivity, headaches, eyelash changes, browning of iris
β-Adrenergic Blockers	Timolol	20-25%		↓ Production	irritation, dry eyes, headache, slowed heart rate
α-Adrenergic Blockers	Brimonidine	20-25%	↑ Outflow	↓ Production	irritation, redness, blurred vision, dry eyes, light sensitivity, fatigue, headaches, nausea, insomnia
Carbonic Anhydrase Inhibitors	Dorzolamide	20-25%		↓ Production	irritation, redness, blurred vision, dry eyes, light sensitivity, fatigue, headaches
Cholinergic Agonists	Pilocarpine	20-25%	↑ Outflow		irritation, blurred vision, poor vision in dim light, headaches
Rho-kinase inhibitors	Netarsudil	16–21%	↑ Outflow	↓ Production	irritation, redness, corneal deposits, broken blood vessels
Nitric oxide-donating prostaglandin analogue	Latanoprostene bunod	32–34%	↑ Outflow		Irritation, redness, discharge, pain, eyelash changes
FC rho-kinase inhibitor/latanoprost	Netarsudil/ latanoprost	30–36%	↑ Outflow	↓ Production	irritation, redness, corneal deposits, broken blood vessels

Relevance of THC to glaucoma

- Cannabinoid receptors throughout the body play an important role in managing many vital body functions
- Eye is rich with cannabinoid receptors, specifically in tissues involved in managing fluid production and drainage as well as cells responsible for vision
- THC and the CB1 receptor, specifically, have been shown to be involved in IOP lowering activity
- First report that smoking cannabis lowers IOP appeared in early 1970s
- Multiple human studies have validated THC's ability to lower IOP

Multiple independent studies have demonstrated THC's ability to lower IOP

Table 1
Studies using cannabinoids in human subjects to lower intraocular pressure (IOP).

Subjects	Administration route	Observations	Ref.
15 Male, 18–30 years old	smoking marijuana (12 mg Δ^9-THC)	significant IOP decrease after 80 min, more frequent users showed lower or no IOP drop	[74]
10 healthy volunteers, 20–30 years old	0.022 or 0.044 mg/kg of Δ^9-THC intravenously	IOP decrease in 9 patients with low dose and all subjects with high dose	[75]
256 glaucomatous patients	smoking marijuana (1–4% Δ^9-THC) or 5–20 mg oral Δ^9-THC	most patients showed IOP reduction, additive effect was seen with conventional glaucoma drugs	[76]
A 23-year-old male (suffers of HPPD), 4 young subjects (control), 23–28 years old	smoking marijuana	HPPD in patient, no change in the controls	[77]
9 patients with end-stage open angle glaucoma, 38–77 years old	smoking marijuana or oral Δ^9-THC capsules	lower IOP, development of tolerance and significant systemic toxicity that limit the usefulness	[78]
6 patients with ocular hypertension or early primary open angle glaucoma	single sublingual preparation (5 mg Δ^9-THC or 20 and 40 mg CBD)	significant IOP decrease by Δ^9-THC, 40 mg CBD produced a transient IOP increase, no significant side effect	[79]
8 patients with glaucoma resistant to conventional treatments, 53–72 years old	topical application of WIN55212-2	IOP decreased directly through CB1	[80]
18 patients suffers of glaucoma	single oral dose of nabilone (0.5 mg)	IOP decreased by 27.9%, 2–6 h after administration, no visual side effect	[81]
32 patients suffers of glaucoma	BW29Y (5 or 10 mg) or BWI46Y (4, 8, or 12 mg)	BW29Y: ineffective, BWI46Y: IOP drop, lightheaded, dizzy, disorientation, blood pressure drop	[82]

HPPD: Hallucinogen persisting perception disorder; IOP: intraocular pressure; Δ^9-THC: Δ^9-tetrahydrocannabinol; CBD: cannabidiol; WIN55212-2, Nabilone, BW29Y, BWI46Y: synthetic cannabinoids.

Y. Panahi et al. / Biomedicine & Pharmacotherapy 86 (2017) 620–627

Challenges to THC as an effective treatment of glaucoma

Systemic Delivery

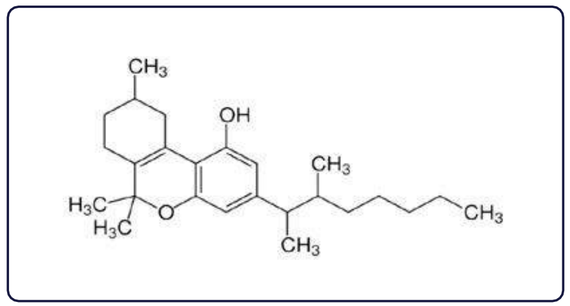
- Requires relatively high dose to achieve therapeutic effect in the eye
- Variable pharmacokinetics and pharmacodynamics
- Poor oral bioavailability when ingested (<10% due to poor absorption)
- Limited duration of effect when inhaled/ smoked (<90 min)
- Systemic side effects – psychoactive effect (high from THC); detrimental drops in blood pressure

Local Delivery

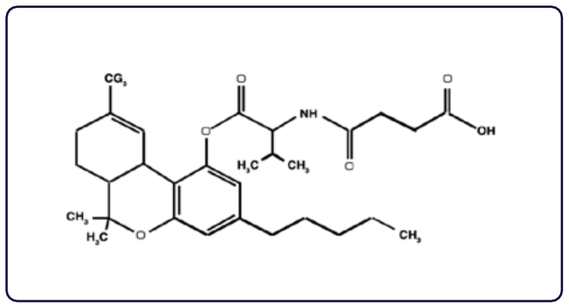
- THC is lipophilic – challenging to deliver into and penetrate aqueous tissue, like the eye
- Oil and water don't mix!

SKYE's approach unlocks therapeutic value of THC

- Rational drug design and bioengineering used to develop a synthetic prodrug of THC, called THCVHS
- **Valine-hemi-succinate** amide ester (**VHS**) addition to THC enhances aqueous solubility and polarity characteristics, enabling significantly improved local delivery into the eye and avoiding systemic effects
- Inside the eye, THCVHS is converted back into THC by enzymes that cleave VHS arm of the molecule
- THCVHS is a proprietary molecule with composition of matter patents providing intellectual property protection that is instrumental to value creation



THC

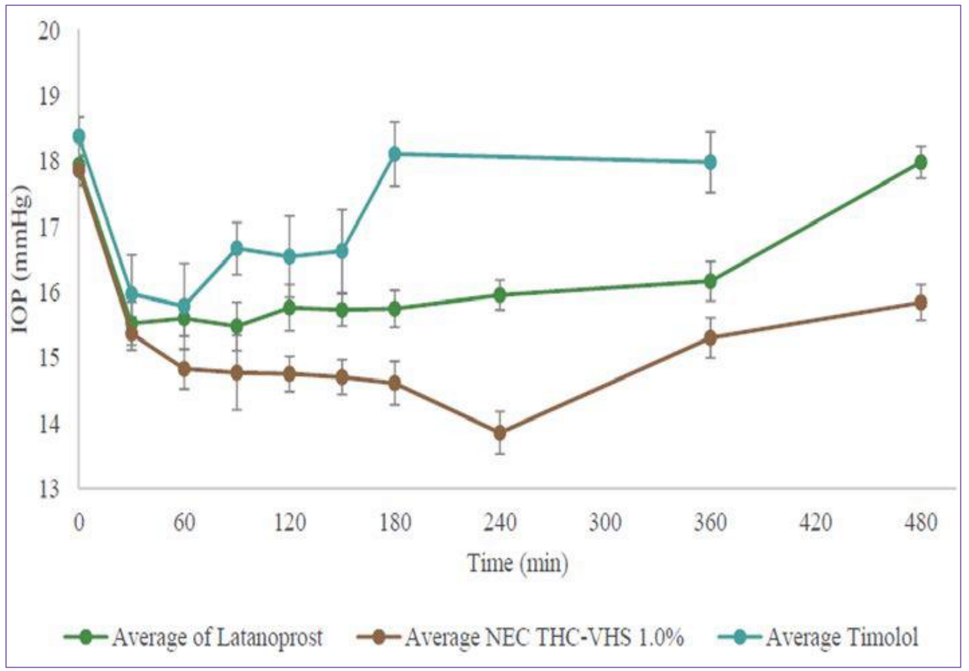


THCVHS

THCVHS lowers IOP better than both market leaders

- In a rabbit model, THCVHS achieves superior decline in IOP versus latanoprost and timolol
- Superior duration of response
- Potential for once-daily dosing
- No detectable THC or metabolites outside the eye
- Additional head-to-head studies against and in combination with Rhopressa (netardusil) and latanoprost planned for Q2-21 to further assess/validate IOP-lowering properties

Average IOP vs Time profile of Latanoprost (0.005%) vs THCVHS-NEC (1.0%) vs Timolol (0.25%)



Multi-factorial mechanism of action

- In an *ex vivo* model of human trabecular meshwork, the tissues responsible for fluid drainage
- THC significantly lowered pressure and increased drainage in both healthy and diseased tissue
- THC treatment also significantly reduced markers of fibrosis and inflammation, which are associated with glaucoma
- IOP-lowering capability of THC may be multi-factorial, including anti-inflammatory and anti-fibrotic responses
- Potentially a new class of treatment with therapeutic attributes distinct from existing IOP-lowering drugs

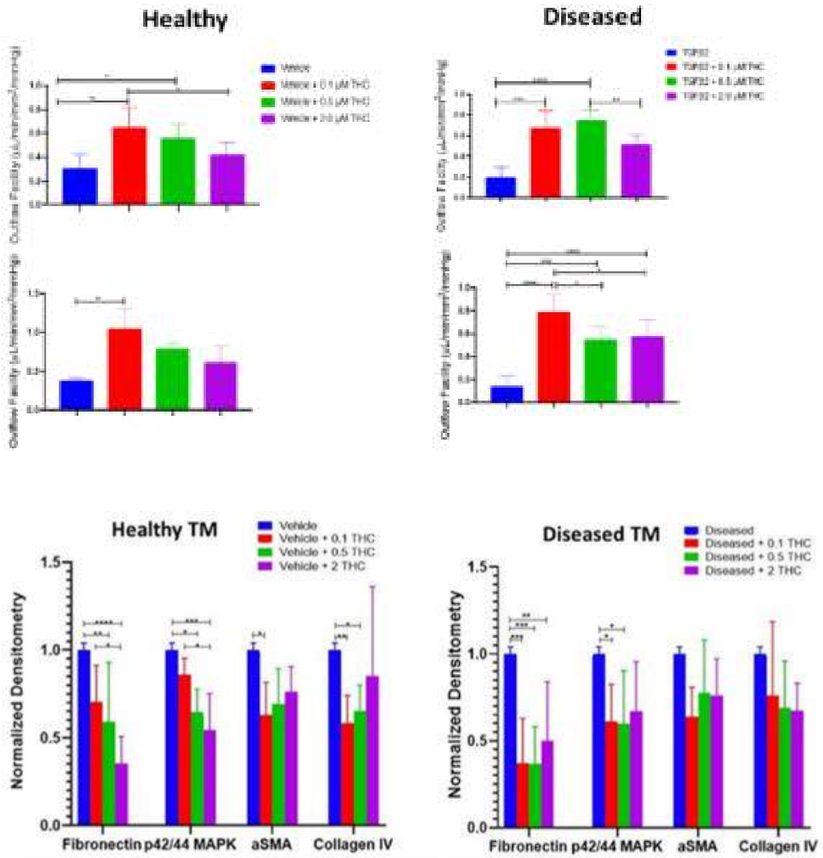
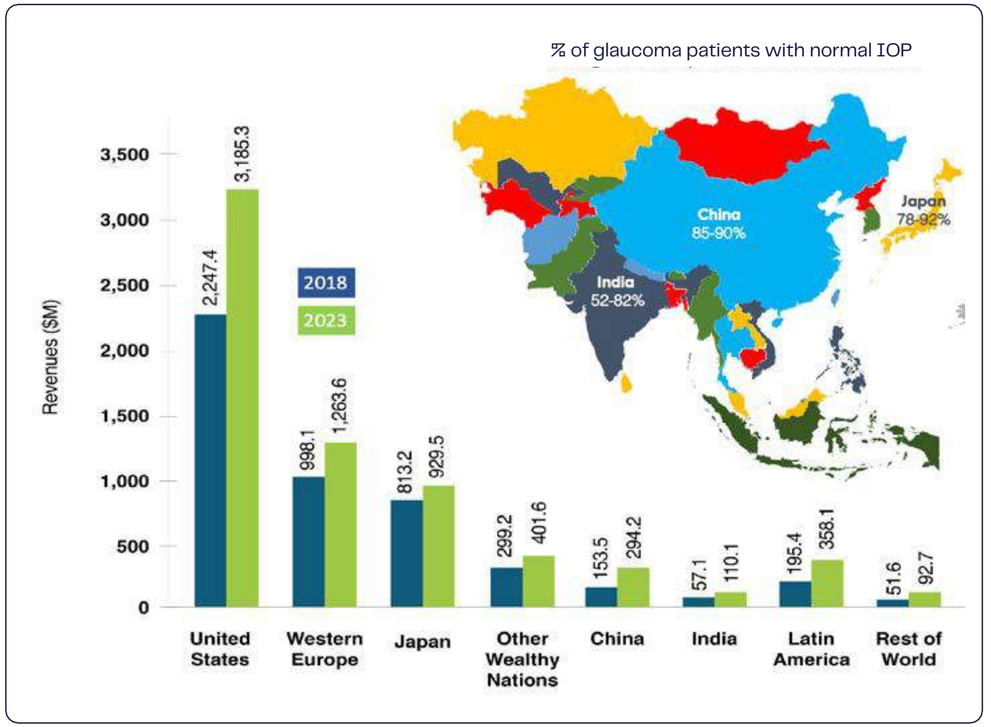


Figure 2. Protein analysis of markers linked to fibrosis at the 3D HTM after 6 days of treatment with THC. All samples of three donors were analyzed using Two-way ANOVA ****P<0.0001, ***P<0.001, **P<0.01, *P<0.05, N ≥ 4 per donor.

Not all glaucoma patients have elevated IOP

- Large proportion of glaucoma patients present with normal IOP, but still suffer progressive damage to optic nerve cells and vision loss
- Not clear what causes **neurodegeneration** of optic nerve in these patients
- A disproportionate number of patients have normal IOP levels in Asian countries
- Estimated that ≥ 1/3 of all glaucoma patients globally have normal IOP
- Significant unmet need and tremendous market opportunity for a neuroprotective drug



Cannabinoids demonstrate neuroprotection

- Multiple studies in different animal species & models of glaucoma have demonstrated ability of cannabinoids to promote health and survival of optic nerve cells
- Optic nerve injury model in rats planned in Q2–21 to validate neuroprotection properties of THCVHS

Drug	Delivery	Study	Model	Neuroprotective effect versus vehicle (treatment versus control)
THC	IP	Crandall et al., 2007 [68]	Episcleral vein cauterization	~20–40% increase (10–20% loss)
THC	IV	El-Remessy et al., 2003 [69]	Intravitreal NMDA	~9% of vehicle*
CBD	IV	El-Remessy et al., 2003 [69]	Intravitreal NMDA	~4% of vehicle*
WIN 55,212-2	Topical	Pinar-Sueiro et al., 2013 [70]	Ischemia-reperfusion (high IOP)	9.88% increase (2.45% loss)
MetAEA	IVit	Nucci et al., 2007 [44]	Ischemia-reperfusion (high IOP)	18.6% increase (9.4% loss)
URB597	IP	Nucci et al., 2007 [44]	Ischemia-reperfusion (high IOP)	15.1% increase (12.9% loss)
URB597	IP	Slusar et al., 2013 [71]	Axotomy	1 week, 19.5% increase (27.9% loss) 2 weeks, 22.7% increase (58.9% loss)
Celecoxib	IP	Sakai et al., 2009 [72]	Ischemia-reperfusion (high IOP)	25.8% increase (39.1% loss)
SC-58236	IP	Ju et al., 2003 [45]	Ischemia-reperfusion (high IOP)	Central, 28.4% increase (27.3% loss) Peripheral, 28% increase (26.8% loss)

IP, intraperitoneal; IV, intravenous; IVit, intravitreal; *study reported quantification of tunnel positive cells only.

Elizabeth A. Cairns, William H. Baldridge, Melanie E. M. Kelly, "The Endocannabinoid System as a Therapeutic Target in Glaucoma", *Neural Plasticity*, vol. 2016, Article ID 9364091, 10 pages, 2016. https://doi.org/10.1155/2016/9364091

Phase 1 human clinical trial

OBJECTIVES

- Assess safety, tolerability, pharmacokinetics of single and multiple ascending doses in healthy subjects and subjects with elevated IOP
- Assessment of intraocular pressure

STUDY DESIGN

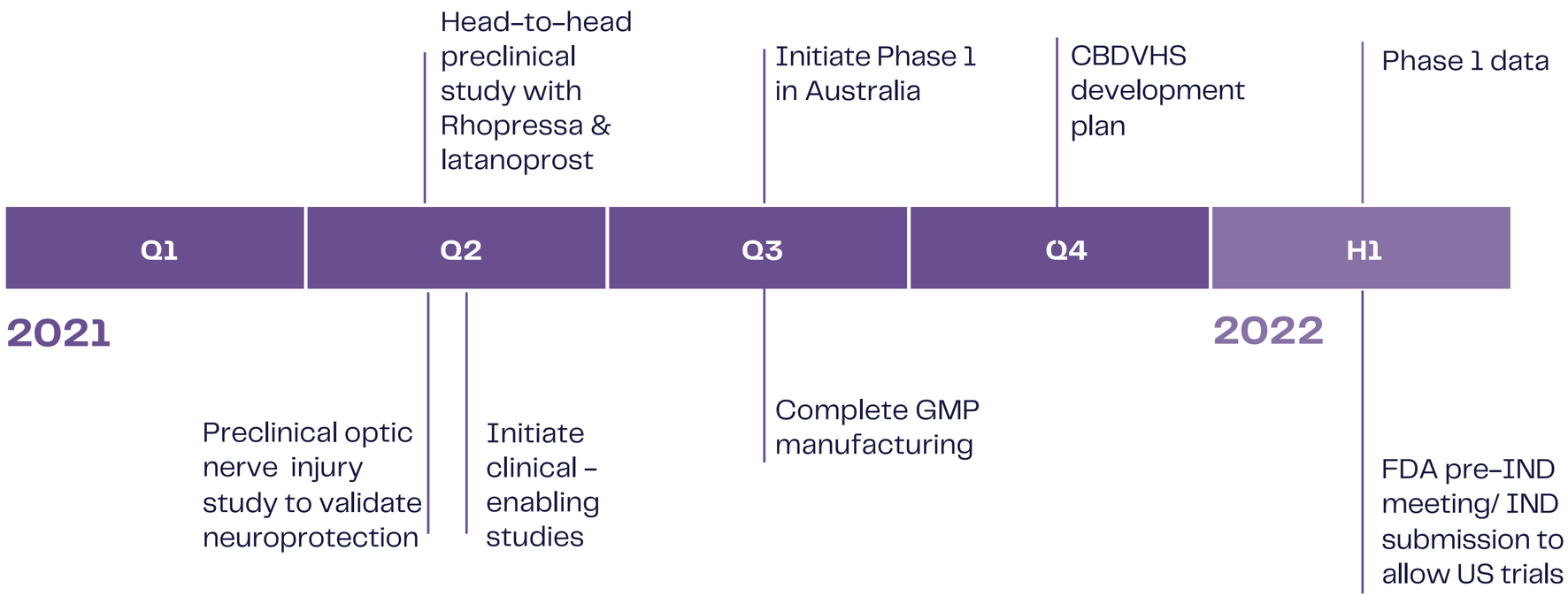
- 64 subjects, double-blinded, 3:1 randomization
- 5 SAD cohorts, n=8, healthy subjects
- 3 MAD cohorts, n=8, healthy & elevated IOP subjects

ELIGIBILTY

- Healthy cohorts: IOP ≥ 12 to ≤ 22 mmHg
- Elevated IOP cohorts: IOP ≥ 18 to ≤ 26 mmHg

Positioned for value creation

First human trial will be fast, low cost, and include assessment of intraocular pressure



Capitalization

1

350.0 M

Common Shares Outstanding

1

117.6 M

Options & Warrants

2

5.1 M

Convertible Debt Shares

(As Converted Basis)

1

472.7 M

Fully Diluted

3

$43.8 M

Market Cap

San Diego, CA

Base of Operations

1 Based on 10K filed 21/03/01

2 Based on principal balance and accrued interest outstanding as of 21/03/01 on multi-draw credit facility which is convertible at $.40 per share

3 Based on 21/03/23 OTCQB closing price of $0.125

Management: Focused on delivering near-term data outcomes

Punit Dhillon

Chief Executive Officer

- Co-founded and led OncoSec Medical, a cancer immunotherapy company, through early development and a partnership with Merck to launch Phase 2/3 multi-center trial; raised over $200M
- VP Finance and Operations, Inovio Pharmaceuticals: helped raise more than $160M

Richard Janney

Principal Accounting Officer

- 30 years of business experience and served as a Vice President to CFO on multiple companies in a wide range of industries both public and private, domestic and international
- Previously operated consulting firm scaling start-ups to mid-size companies, offering financial services across an array of industries including software and medical devices

Tu Diep, MSc

Sr Vice President, Development

- Senior leaderships positions at Element Biosciences, Emerald Health Science, OncoSec Medical and Protox Therapeutics
- Over 15 years experience in research, clinical and strategic operations, business process, CMC, regulatory affairs, and business development

Karam Takhar

VP, Corporate Development & Investor Relations

- Life sciences executive with over 15 years experience in research, project management, operations, finance, business development, sales and investor relations
- Previously held with various leadership roles at Emerald Health Science, Promega Corporation and Stemcell Technologies

Tom Kim, Esq

General Counsel & Director of IP

- Previously SVP and Corporate Secretary for Inovio Pharmaceuticals built global patent portfolio, led M&A transactions, closed license and partnering deals with large pharma
- Practiced law at large firms and Fortune 100 companies, eg. Monsanto and DuPont. 20 years experience counseling biotech companies

Board Directors & Advisors Offer Expert Guidance

Eminent experts in cannabinoid science, ophthalmology, research, and development

Board of Director

Punit Dhillon

Chair

Former co-founder, CEO, and director of OncoSec Medical. Experienced in finance, M&A, licensing, strategy implementation, and collaborations with industry and academic partners

James Heppell, Esq

Director

Former founder, CEO, director of BC Advantage Life Sciences venture fund. Director of multiple life science companies. Extensive experience in corporate finance law

Margaret Dalesandro, PhD

Director

25+ years drug development experience in pharmaceutical, biotechnology and diagnostics industries. Currently President of Brecon Pharma Consulting

Clinical Advisors

Robert Ritch, MD

Professor of Ophthalmology, Mt. Sinai

Shelley and Steven Einhorn Distinguished Professor of Ophthalmology; Surgeon Director Emeritus and Chief, Glaucoma Services, The New York Eye & Ear Infirmary; Professor of Ophthalmology, The New York Medical College

Jeffery Goldberg, MD, PhD

Professor of Ophthalmology, Stanford

Professor and Chair of Ophthalmology and Director of Spencer Center for Vision Research at Byers Eye Institute, Stanford University

Louis Pasquale, MD

Professor of Ophthalmology, Mt. Sinai

Professor Ophthalmology, Icahn School of Medicine, Chair, Department of Ophthalmology, Vice Chair of Translational Ophthalmology Research, Mount Sinai Healthcare System

Scientific Advisors

Giovanni Appendino, PhD

Professor of Organic Chemistry, U.Piedmont

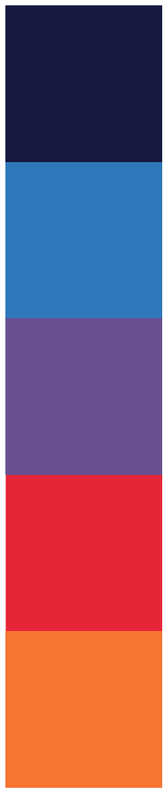
Over 40 years of research in natural products, leading to the discovery and isolation of over 200 novel compounds, including novel cannabinoids and chemistry for cannabinoid-derived molecules

Eduardo Muñoz, MD, PhD

Professor of Immunology, U.Córdoba

Over 30 years of experience in biomedical research, focused on cannabinoids, pharmacology, and inflammation, providing deep expertise in the mechanism of actions of cannabinoids and the development of novel cannabinoid-derived molecules

Unique competitive position



Demonstrated greater IOP lowering than market-leading glaucoma therapeutics

Potential neuroprotection capabilities would be a game changer

Key preclinical data (IOP/neuroprotection) in Q2-21

First clinical trial: fast; low-cost; will include assessment of intraocular pressure

Many glaucoma licensing deals have been completed in phase 2 or earlier

To learn more please contact:

Punit Dhillon
Chief Executive Officer
ir@skyebioscience.com
1 (858) 410-0266

Karam Takhar
VP, Corporate Development & Investor Relations
ir@skyebioscience.com
1 (858) 410-0266