



FOCAL POINT

Cannabinoids and the Eye

June 2022

FORWARD LOOKING STATEMENTS

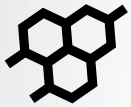
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INVESTMENT SUMMARY

Bold innovation in ophthalmology to unlock the potential of proprietary cannabinoid derivatives



Advancing lead CBR1 agonist program into Phase 1 in Q2-22 and IND in Q4-22



Transformative new class of therapeutics may play a role in multiple ocular indications



Solid clinical and preclinical foundation for glaucoma with upcoming meaningful clinical inflection points



Engaging in academic collaborations to expand pipeline of novel cannabinoid derivatives



Pursuing partnership opportunities for programs

SKYE
Ticker

\$6.0 million
cash
March 31, 2022

496M common
shares OS
(674M FD)

TRANSFORMATIVE TRANSACTION

Acquisition to fund operations into late 2023 and through Phase 2 glaucoma study

- Licensed producer under Health Canada's Cannabis Act & Cannabis Regulations
- Emerald in Q4-21 announced intent to pivot out of cannabis market to cannabinoid pharmaceutical focus
- Transaction value based on cash & non-cash assets calculated at FMV
 - 88,000 sqft facility in QC
 - 3,700 sqft licensed R&D facility in BC

skye
BIOSCIENCE

+


emerald
THERAPEUTICS

Summary of proposed transaction

- Skye to acquire all outstanding shares of Emerald
- Emerald shareholders to receive equivalent of 1.95 Skye shares for each Emerald share held
- Plan of Arrangement is process by court approval by BC Supreme Court
- Seeking shareholder approval by both Emerald and Skye shareholders
- Transaction expected to complete in Q3-22

FOCUSED ON DELIVERING VALUE FOR SHAREHOLDERS

Complete asset acquisition and wind down of discontinued operations in an efficient manner

Strengthened balance sheet to support investment in growth and value creation

Clinical development to be funded through meaningful inflection points

Exclusive focus on cannabinoid derivatives and maximizing scientific development to create optimized product candidate portfolio

Ophthalmology pipeline-driven growth to more disease-product opportunities by 2023

Advance distinct new class of therapeutics to positively impact health of patients with ocular and other diseases

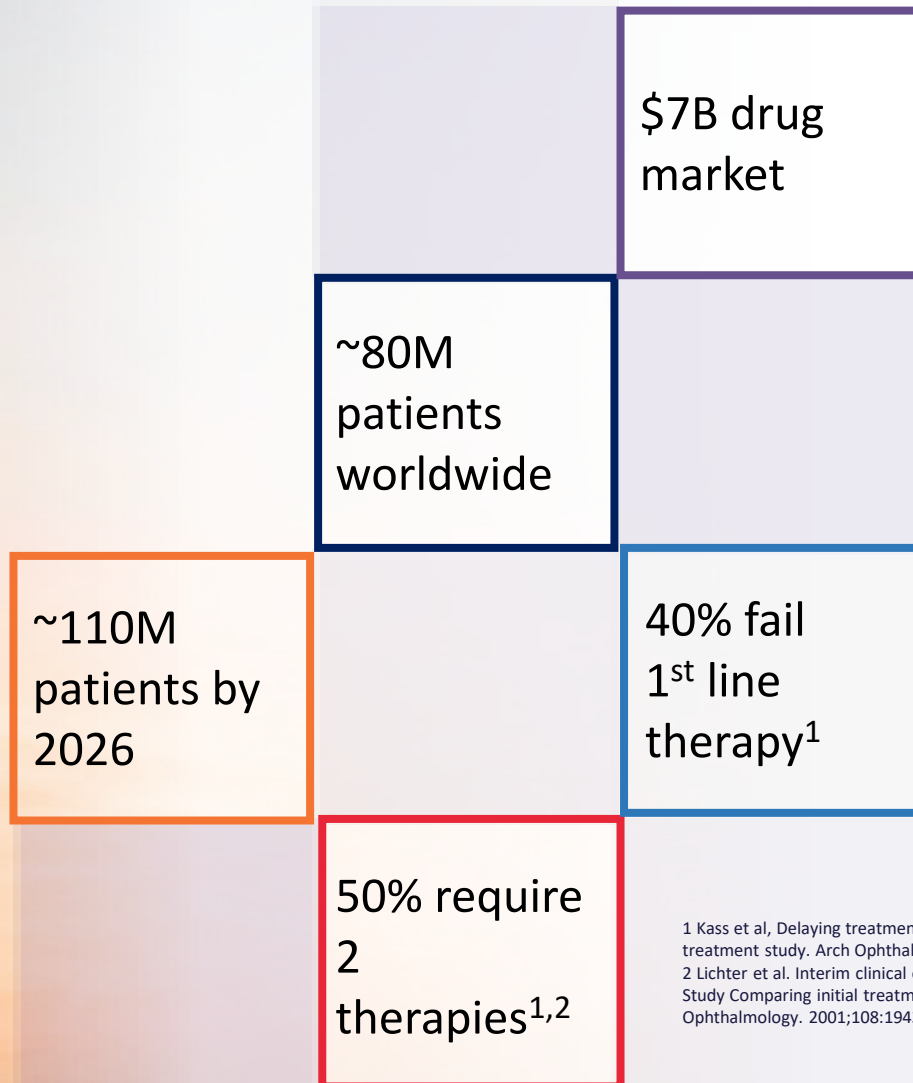
Operate sustainably to positively impact the health of patients

Clinical plan designed for relevant outcomes with optimized time and cost

Planned strategic transaction will provide sufficient capital to fund operations through Q4 2023

GLAUCOMA: SIGNIFICANT UNMET NEED

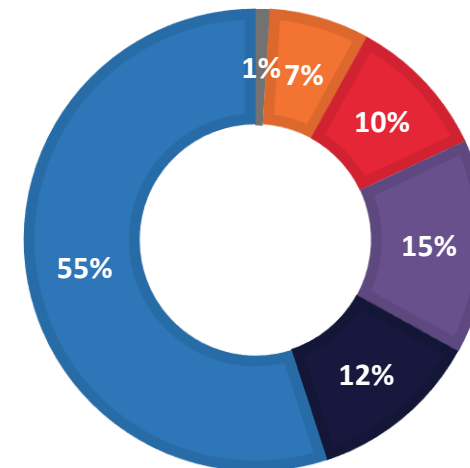
World's leading cause of irreversible blindness



¹ Kass et al, Delaying treatment of ocular hypertension: the ocular hypertension treatment study. Arch Ophthalmology, 2010; 128:276-287
² Lichter et al. Interim clinical outcomes in The Collaborative Initial Glaucoma Treatment Study Comparing initial treatment randomized to medications or surgery. Ophthalmology. 2001;108:1943-1953

MARKET PREDOMINANTLY LEGACY CLASSES OF DRUGS AND GENERIC COMPOUNDS

- ROCK Inhibitor
- Alpha Agonist
- Beta Blockers
- Carbonic Anhydrase Inhibitor
- Fixed Combo
- Prostaglandin Analogs



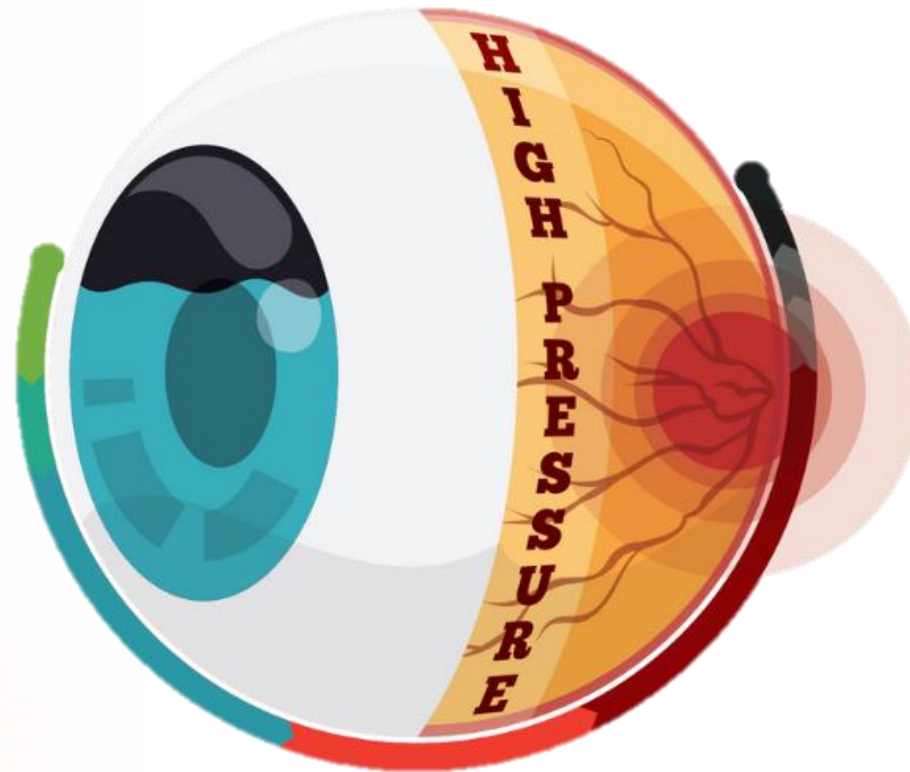
PATHOPHYSIOLOGY OF GLAUCOMA

Intraocular pressure (IOP) is currently the main addressable risk factor

Normally, aqueous humor circulates in the eye

but..

When drainage canal is blocked, more aqueous humor stays in the eye...



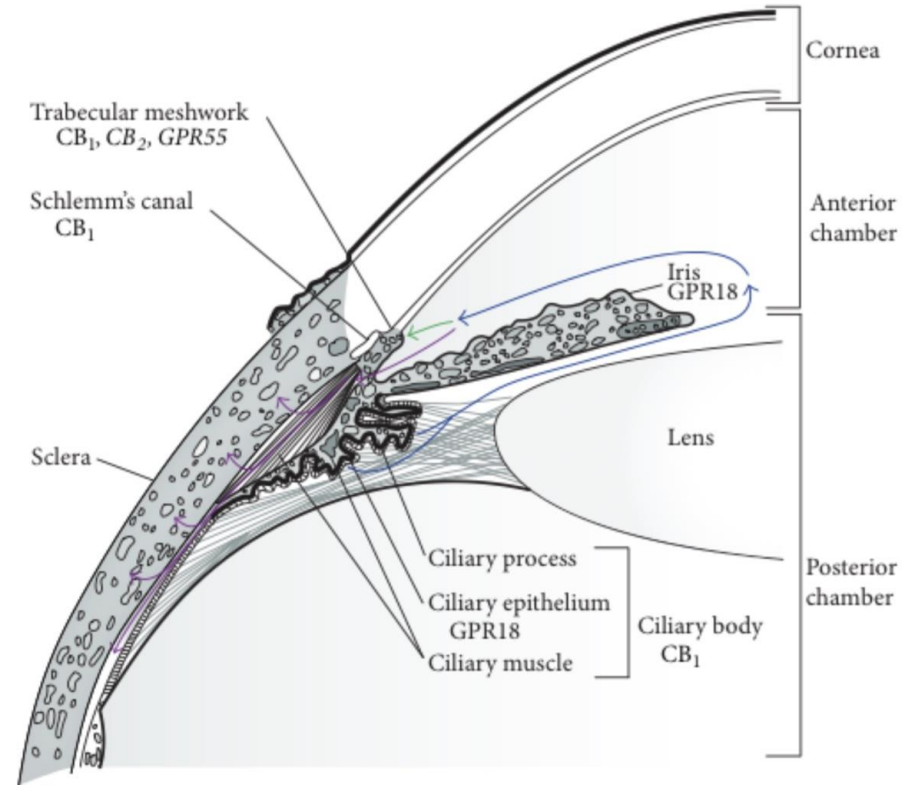
Generating progressive vision loss and blindness if not treated

Damaging blood vessels and optic nerve...

Increasing pressure inside the eye...

WHY CANNABINOIDS FOR GLAUCOMA?

- CB1 receptors are in the tissues responsible for fluid production (ciliary body) and drainage (trabecular meshwork, Schlemm's canal)
- Activation of CB1 receptors by an agonist such as THC has been shown to be involved in IOP-lowering activity
- Multiple human studies dating to early 1970s demonstrated THC's ability to lower IOP
- Multiple preclinical studies demonstrated THC's ability to be neuroprotective to cells of the optic nerve
- However, systemic administration of THC poses PK/PD challenges and potential adverse effects



Circulating aqueous humor (blue), flowing from the ciliary body in the posterior chamber to the anterior chamber, is filtered out of the eye through two different outflow pathways: the trabecular meshwork pathway (green) and the uveoscleral pathway (purple).

1 Cairns et al, The Endocannabinoid System as a Therapeutic Target in Glaucoma. *Neural Plasticity*, 2016; Article ID 9364091

CLINICAL STUDIES HAVE DEMONSTRATED CANNABINOIDS LOWER IOP

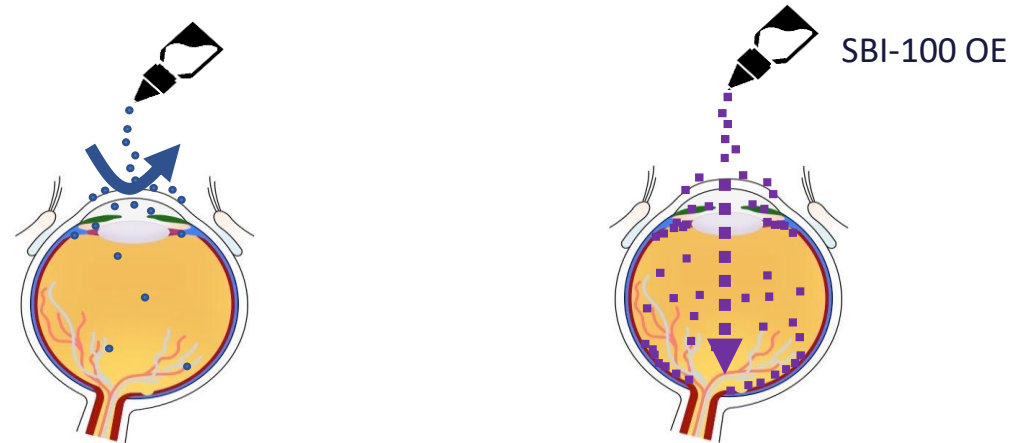
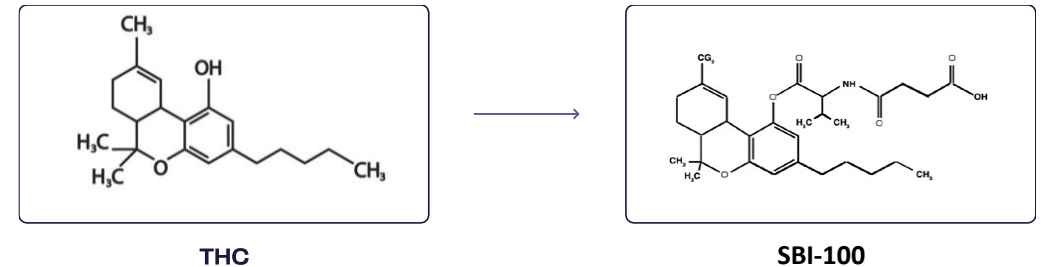
Subjects	Administration route	Observations
15 Male, 18-30 years old	Smoking marijuana (12 mg Δ^9 THC)	Significant IOP decrease after 80 min, more frequent users showered lower or no IOP drop
10 healthy volunteers, 20-30 years old	0.022 or 0.044 mg/kg of Δ^9 THC intravenously	IOP decrease in 9 patients with low dose and all subjects with high dose
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
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
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
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
8 patients with glaucoma resistant to conventional treatments, 53-72 years old	Topical application of WIN55212-2	IOP decreased directly through CB1
18 patients suffers of glaucoma	Single oral dose of nabilone (0.5 mg)	IOP decreased by 27.9%, 2-6h after administration, no visual side effect
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

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

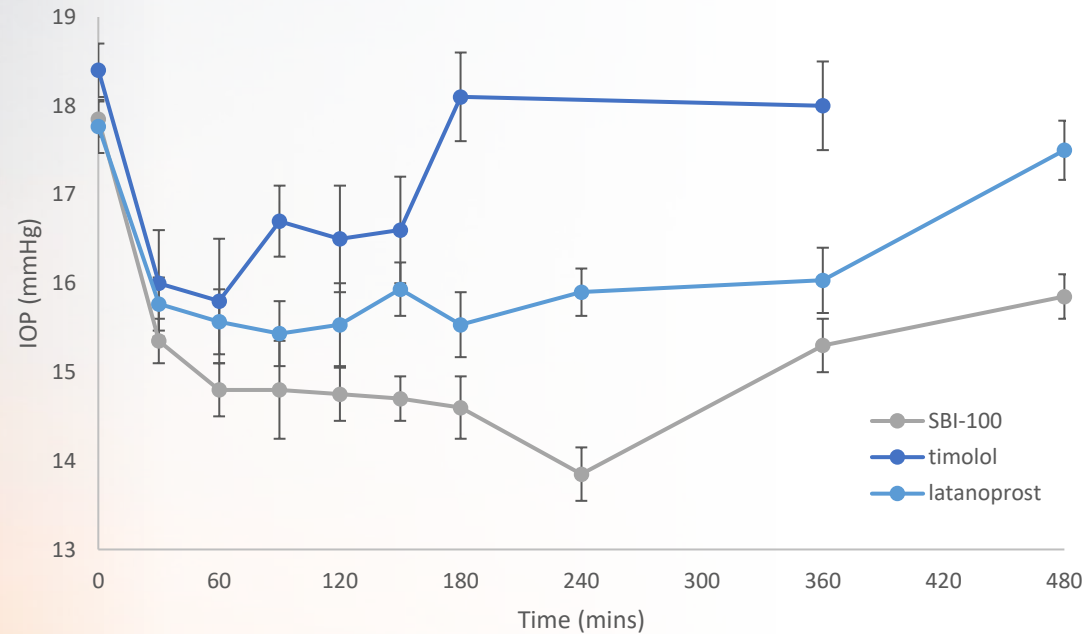
DESIGNING AN EFFECTIVE THERAPY

A cannabinoid prodrug allows local delivery into the eye, with increased efficacy and limiting systemic exposure

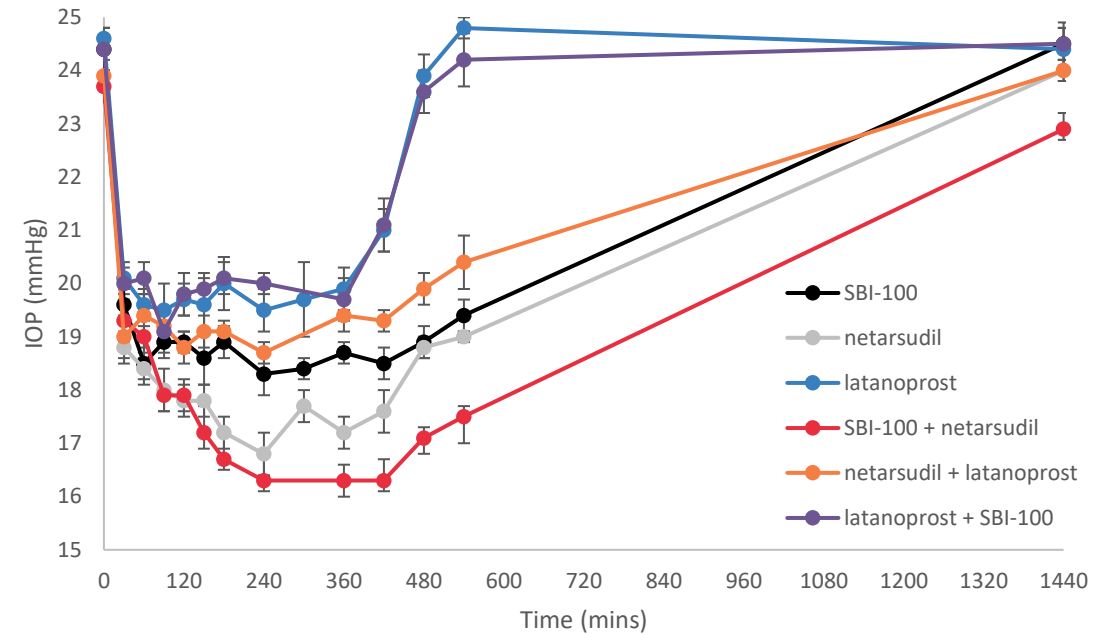
- THC is lipophilic and not easily delivered into the eye topically
- SBI-100 is a prodrug of THC that increases solubility and polarity of THC, allowing it to better penetrate ocular tissue
- Inside the eye, SBI-100 is converted back into THC
- SBI-100 OE proprietary nanoemulsion formulation containing SBI-100 that further enhances delivery of THC to ocular tissue, resulting in greater IOP-lowering effect and duration



SBI-100 HAS DEMONSTRATED SUPERIOR IOP LOWERING COMPARED TO STANDARD OF CARE



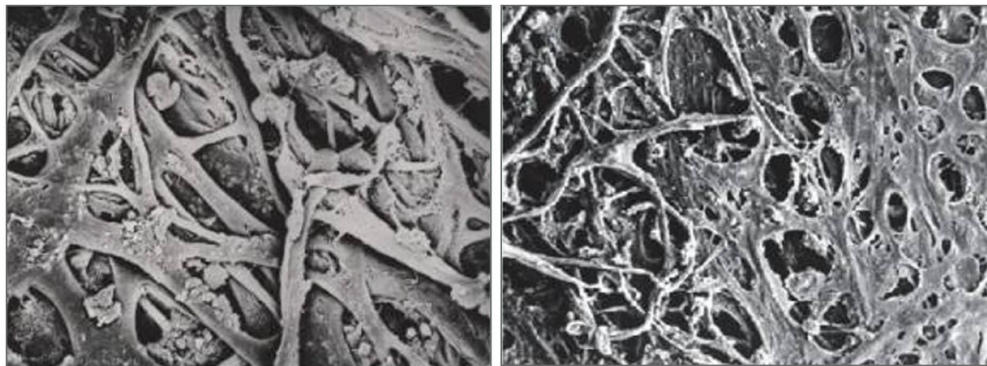
In multiple preclinical studies, SBI-100 demonstrated superior IOP lowering compared to leading therapies as a single agent



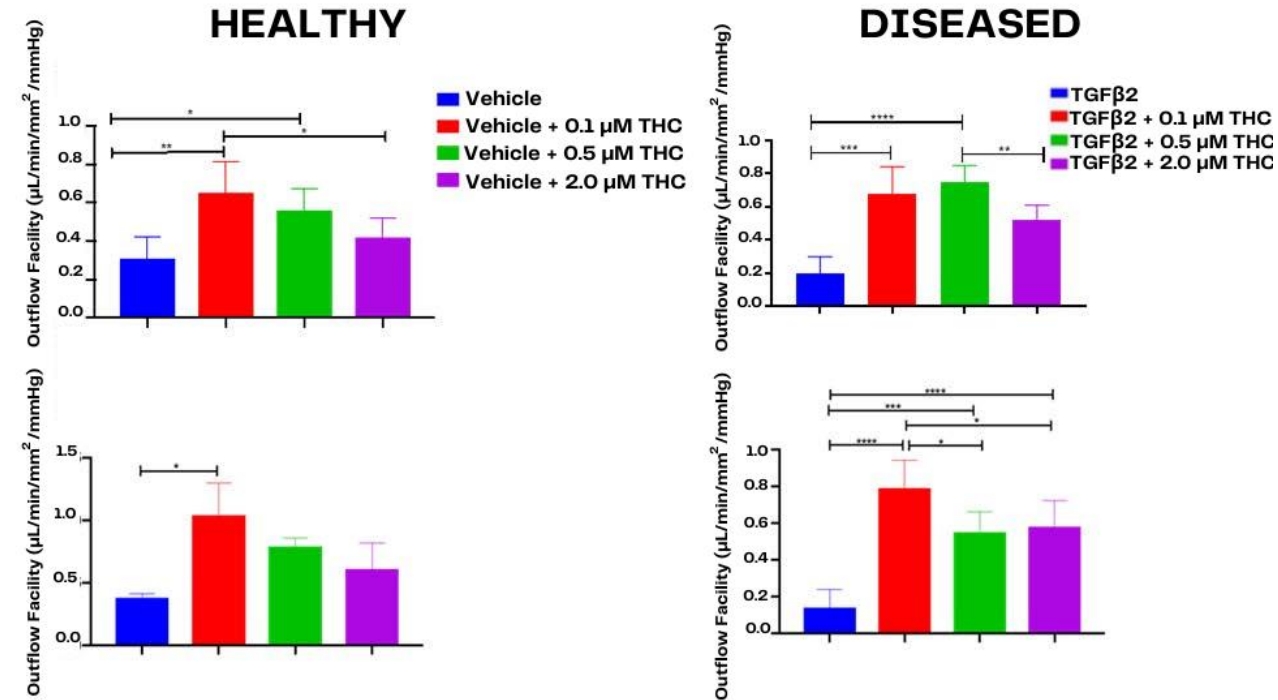
In preclinical studies, SBI-100 demonstrated enhanced efficacy when combined with other approved therapies

INCREASED OUTFLOW VIA TRABECULAR MESHWORK

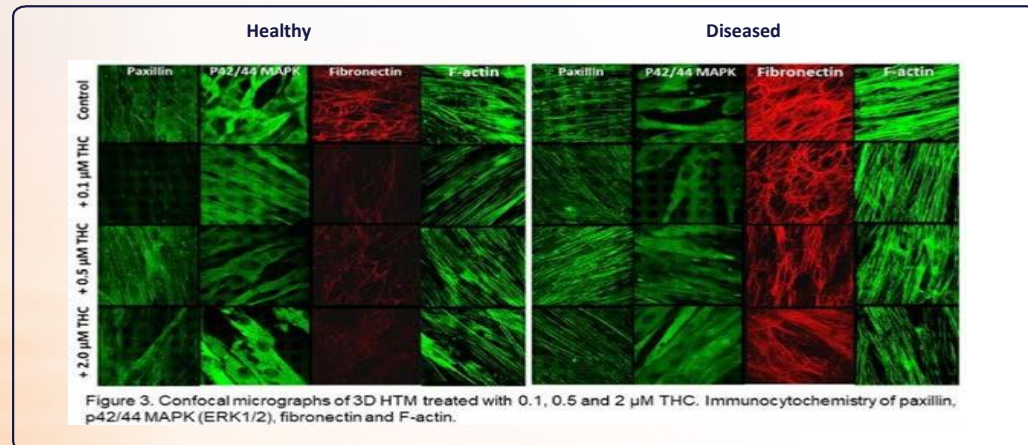
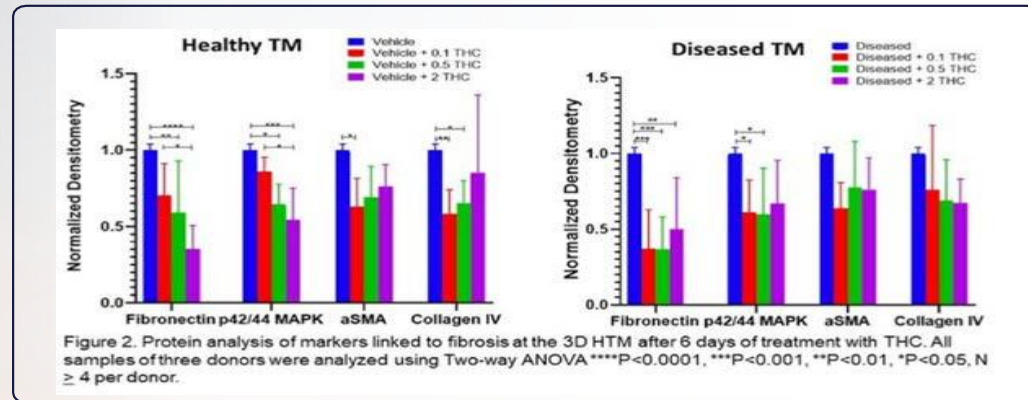
- The trabecular meshwork (TM) accounts for 90% of aqueous humor outflow (drainage)
- Restricted outflow through TM and fibrosis in tissue may be key to underlying pathophysiology of glaucoma
- The TM is avascular and depends on outflow for nutrients and health; restricted outflow leads to further structural deterioration
- In a 3D model of human TM cells, SBI-100's active pharmaceutical ingredient significantly increased outflow in both healthy and disease-simulated tissue



Normal TM (left), Primary open-angle glaucoma (POAG) TM (right)



REDUCED MARKERS OF INFLAMMATION & FIBROSIS



- THC treatment significantly reduced markers associated with fibrosis and inflammation, which are associated with glaucoma
- Potentially disease-modifying through extracellular matrix remodeling of the trabecular meshwork
- Multi-factorial mechanism of action, including anti-inflammatory and anti-fibrotic responses
- Potentially a new class of treatment with therapeutic attributes distinct from existing IOP-lowering drugs

SBI-100 OE: ADDRESSES MULTIPLE ISSUES WITH CURRENT TREATMENT OPTIONS

✓ **Targets area of disease**

- Most drugs do not target the main site of disease-causing increased IOP -- the trabecular meshwork (TM)
- THC directly targets the TM and increases flow through the eye as well as uveoscleral pathways
- THC decreases fibrosis in the TM, the main cause of blockage to flow

✓ **Potential combination and add-on to current therapies**

- Other drugs cause local and systemic side effects
- Most drugs do not combine well with each other

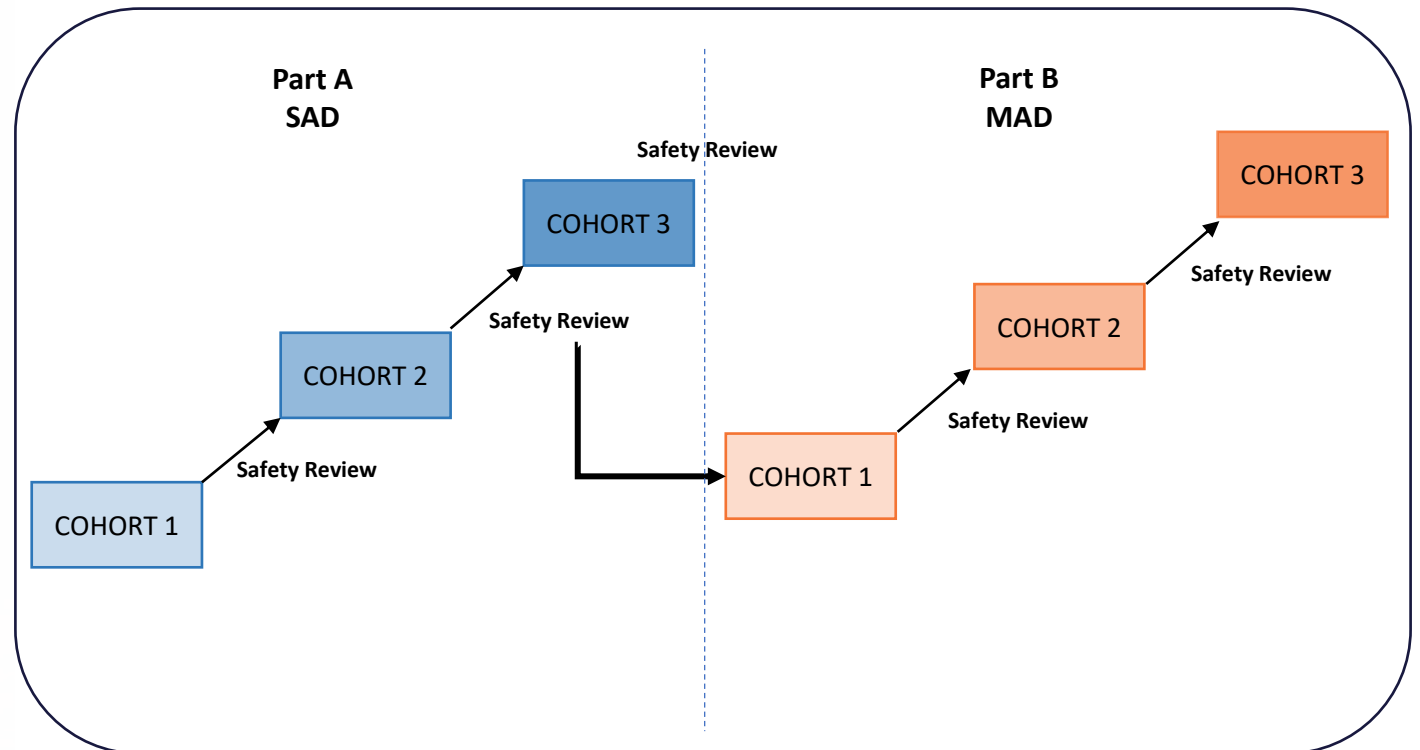
✓ **Neuroprotective capabilities**

- Cannabinoids and THC, specifically, have shown potential benefits to promote health and survival of optic nerve cells - sparing of retinal ganglion cells (RGCs) - in glaucoma models

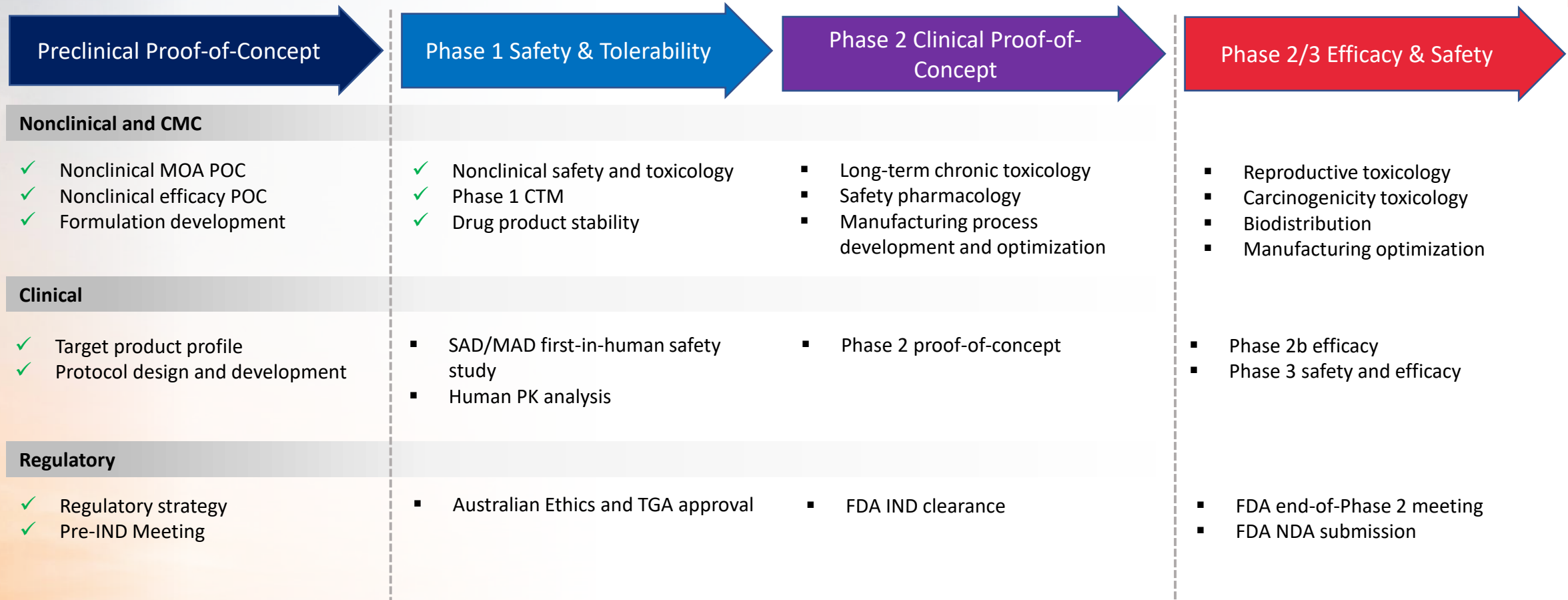


SBI-100 OE: PHASE 1 SAFETY SAD/MAD DESIGN IN HEALTHY VOLUNTEERS

- **Objectives:** Evaluate safety, tolerability, PK of SBI-100 OE/THC/metabolite, and effect on intraocular pressure (IOP) in healthy subjects in single and multiple ascending dose arms
- The study will be conducted in 2 parts consisting of 3 cohorts of 8 subjects
- Safety review committee meetings held prior to each dose escalation and between SAD/MAD
- As a new chemical entity and regulated controlled substance, demonstrating safety in a controlled healthy volunteer study is important for development of SBI-100 OE

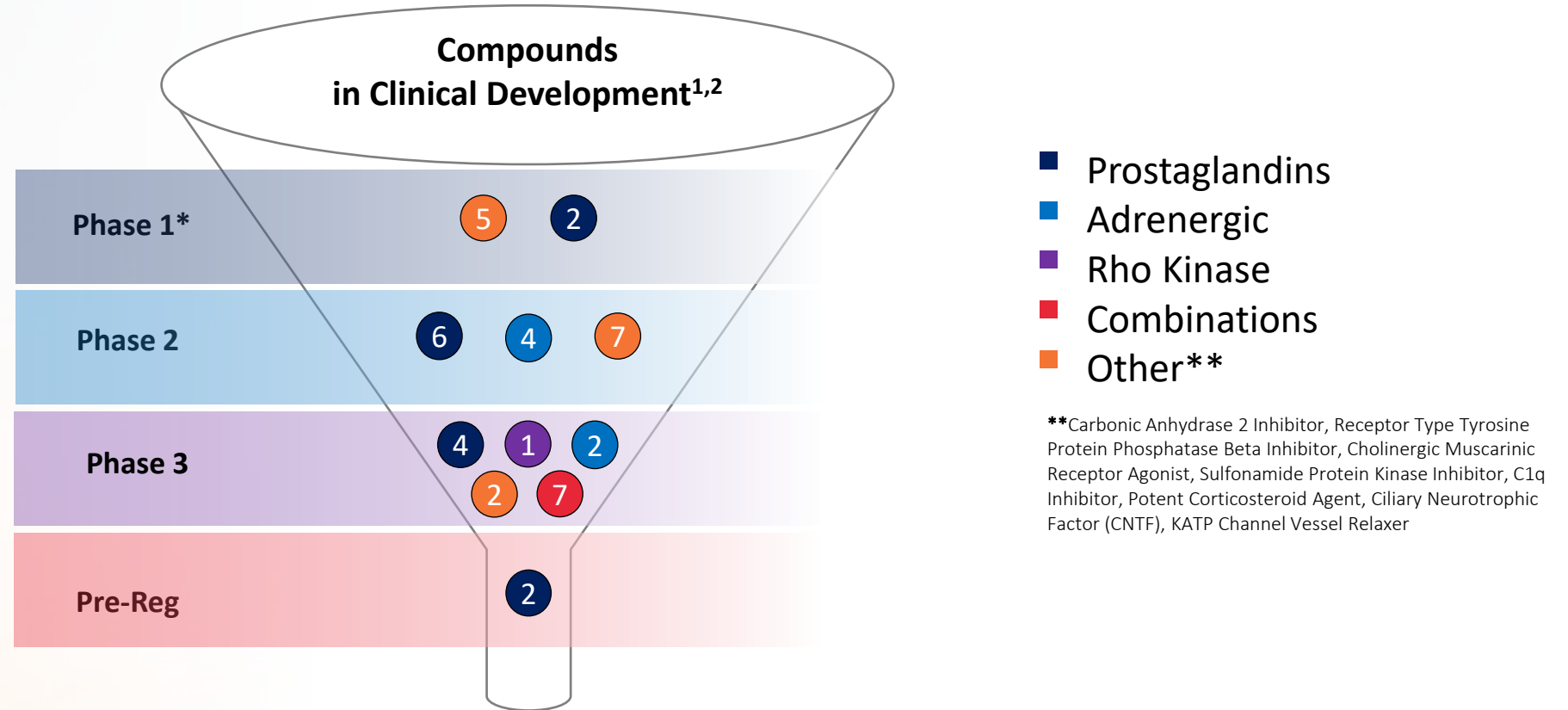


SBI-100 OE – CLINICAL DEVELOPMENT PLAN



INDUSTRY GLAUCOMA PIPELINE LACKS INNOVATION

Late-stage assets dominated by legacy MOAs or combinations

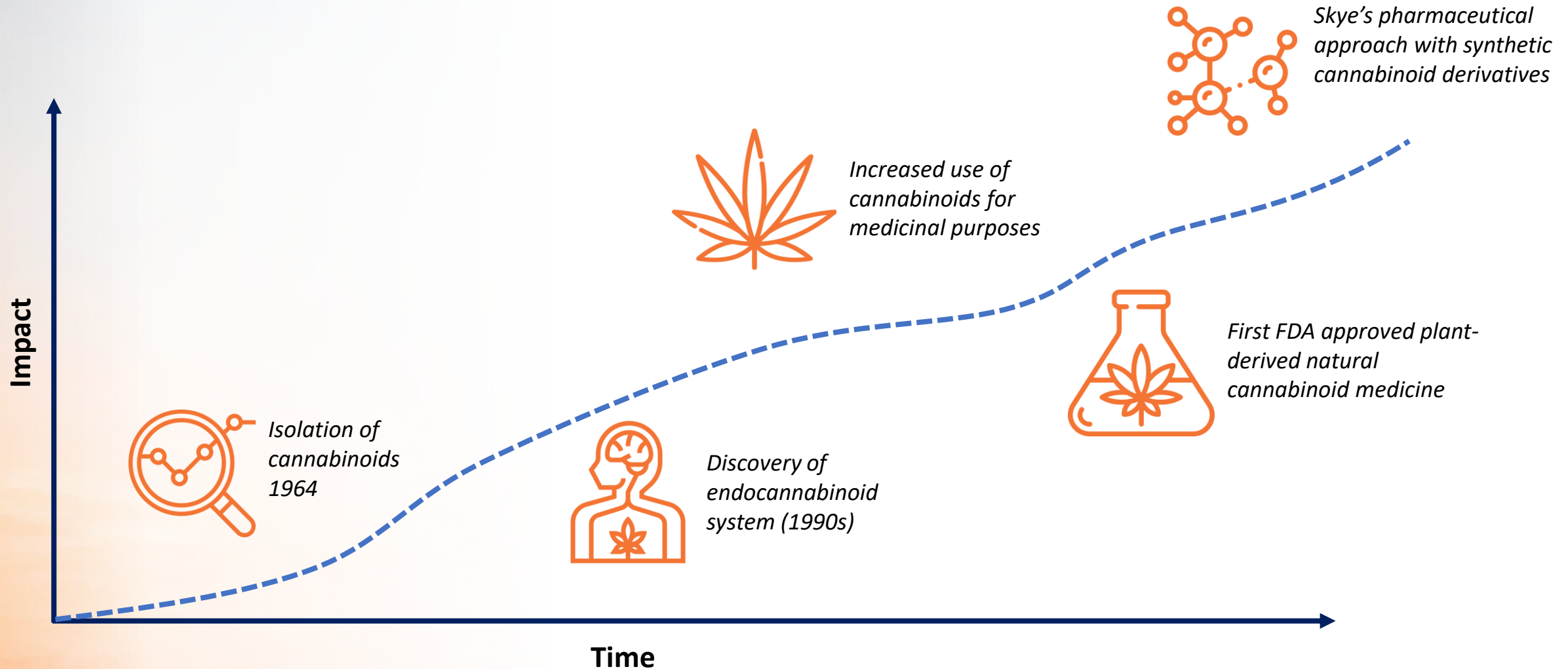


¹ GlobalData; ² Clinicaltrials.gov

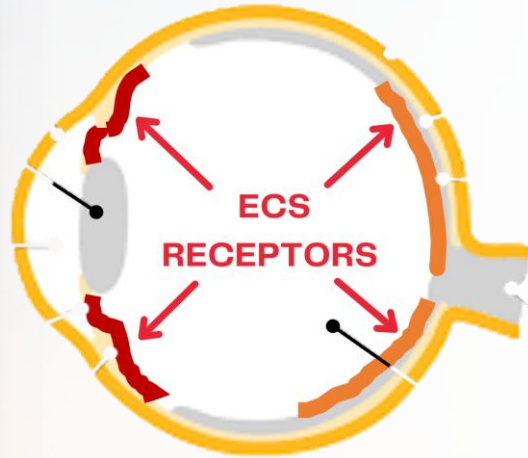
* Compounds listed based on the most recent trial completed or initiated

UNLOCKING PHARMACEUTICAL POTENTIAL OF CANNABINOIDS

Decades of research merging with modern biotechnology techniques

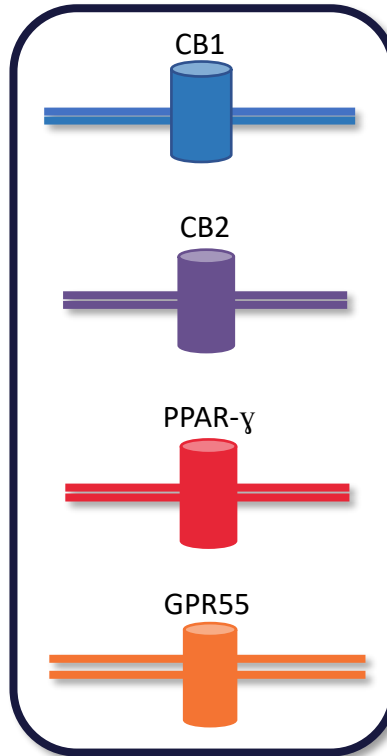


BUILDING CANNABINOID PLATFORM FOR OPHTHALMOLOGY



- Endocannabinoid system (ECS) plays vital role in controlling an array of functions in the body
- Affecting the ECS may provide therapeutic benefit for multiple diseases, including in the eye
- ECS receptors found throughout the eye shown to be involved in a broad set of ocular functions and pathologies

ECS receptors in the eye



Relate to many ocular pathologies

- Intraocular pressure
- Nociception (pain)
- Inflammation
- Neovascularization
- Wound healing
- Neuroprotection
- Fibrosis

Cannabinoid receptor-rich environment of eye creates ripe opportunity for drugs targeting these receptors to affect ocular diseases and specifically glaucoma

CANNABINOID PHARMACEUTICALS: A CLASS OF NEW THERAPIES

FDA approval of a natural cannabinoid



✿ Epidiolex®
(cannabidiol)

1st FDA approval of natural cannabinoid product



\$269M in 2019
\$510M in 2020
\$658M in 2021



Neurological disorder pipeline



Jazz Pharmaceuticals

Acquired for **\$7.2B** in 2021

New chapter: synthetic novel cannabinoid derivative



Synthetic Cannabinoid Derivatives

- Patented new chemical entities
- Reliable manufacturing
- Improved delivery
- Better targeting



Skye is developing drugs to treat diseases of the eye

CATALYSTS TO ADVANCE OUR GROWTH

Bold innovation in ocular applications to unlock full potential of novel class of cannabinoid derivatives

SBI-100 OE: PHASE 1

- ✓ Q1-22: Completion of GLP toxicology studies
- ❑ Q2-22: AUS Human Research Ethics Committee (HREC) approval to start Phase 1 study
- ❑ Q3-22: Phase 1 interim data
- ❑ Q1-23: Phase 1 final data

SBI-100 OE: PHASE 2

- ✓ Q4-21: Pre-IND meeting with the FDA
- ❑ Q2-22: Study protocol
- ❑ Q3-22: Complete IND-supporting studies
- ❑ Q4-22: IND clearance
- ❑ Q4-22: Phase 2 efficacy study initiation

STRATEGIC MILESTONES

- ✓ Q4-21: Neuroprotection study to assess SBI-100 potential to spare vision loss
- ❑ Q2-22: Close strategic transaction
- ❑ Q3-22: Complete wind-down and integration
- ❑ Early-stage research & pipeline expansion (including in Canada)
- ❑ New product-driven intellectual property
- ❑ Efficient corporate growth to support objectives



MANAGEMENT TEAM

SENIOR MANAGEMENT

Punit Dhillon

Chief Executive Officer & Chair

- Co-founded and led OncoSec (NASDAQ: ONCS), a cancer immunotherapy company, through early development and partnership with Merck to launch Phase 2/3 multi-center trial. Previously VP, Finance & Operations for Inovio Pharmaceuticals (NASDAQ: INO).

Kaitlyn Arsenault, CPA

Chief Financial Officer

- Over 14 years of experience in accounting, auditing, financial reporting, mergers and acquisitions, as well as business operations in the life science and technology sectors

Tu Diep, MSc

Chief Development Officer

- Over 15 years' experience in research, clinical and strategic operations, business process, CMC, regulatory affairs, and business development

Karam Takhar

VP, Corporate Development

- Over 15 years of life sciences experience in research, sales, project management, strategic operations, finance, investor relations and business development

Tom Kim, Esq

General Counsel & Director of IP

- Over 20 years' experience counseling biotech companies. Previously SVP and Corporate Secretary for Inovio Pharmaceuticals. Built global patent portfolio, led M&A transactions, closed license and partnering deals with large pharma.

Rhea Williams, MPH

Head of Regulatory Affairs & Quality Assurance

- Over 25 years in drug development, regulatory affairs and quality assurance. Supported development of small and large molecules in the areas of neurology, hematology, oncology, women's health, cardiology, and ophthalmology

BOARD OF DIRECTORS

Punit Dhillon

Chair

- Co-founded and led OncoSec (NASDAQ: ONCS), a cancer immunotherapy company, through early development and a partnership with Merck to launch a Phase 2/3 multi-center registration clinical trial. Previously VP, Finance & Operations for Inovio Pharmaceuticals (NASDAQ: INO).

Margaret Dalesandro, PhD

Director

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

Praveen Tyle, PhD

Director

- Over 37 years of broad pharmaceutical executive leadership. Currently President, CEO, and Director of Invectys, Inc. Experienced in ocular disorders with a wealth of academic insight. Previous senior leadership positions at Novartis and Bausch & Lomb.

Keith Ward, PhD

Director

- Over 25 years of experience in the biotech and pharmaceutical industry. Currently President and CEO of InterveXion Therapeutics. Previously served as Global Vice President of Pharmaceutical R&D at Bausch & Lomb.

Bobby Rai*

Director

- Over 20 years' experience operating The Medicine Shoppe Pharmacies in Vancouver, Canada. Introduced HIV point-of-care testing as well as lab testing (including chronic kidney disease screening using HealthTab technology) into community pharmacies.

**Post closing of Plan of Arrangement*

ADVISORS

CLINICAL

Robert Ritch, MD

Prof. 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

Louis Pasquale, MD

Prof. 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

Eduardo Muñoz, MD, PhD

Prof. 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

Jeffery Goldberg, MD, PhD

Prof. of Ophthalmology, Stanford

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

Miguel González-Andrades, MD, PhD

Clinician-Scientist of Ophthalmology

- Clinician-scientist, ophthalmologist at Reina Sofia University Hospital, Assistant Professor and Research Scientist at Maimonides Biomedical Research Institute of Córdoba - University of Córdoba

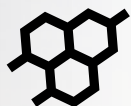
Giovanni Appendino, PhD

Prof. 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

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Pursuing partnership opportunities for programs

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THANK YOU

To learn more, please contact:

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COMPETITORS IN THE CANNABINOID SPACE

Skye is leading the field and will be in the clinic before competitors



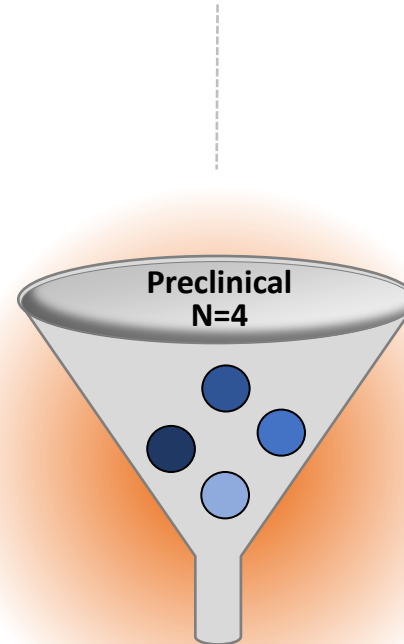
LBI-1026

- **Mechanism of Action:** CB₁/CB₂ receptor agonist
- **Highlights:** Indicated for pain, nausea, vomiting, epilepsy, neuropathy, and **glaucoma with several possible ROAs including IVT, inhalation, oral, and ophthalmic dosage forms**; although CBD formulation is complete, further development is paused until funding is secured



INM-088

- **Mechanism of Action:** CB₁/CB₂ receptor agonist
- **Highlights:** **CBN eye drop formulation* that may offer neuroprotection while simultaneously reducing IOP**; completed extensive safety studies of CBN, which unearthed no concern, and exhibited an anti-apoptotic effect on differentiated RGCs



TA-A002

- **Mechanism of Action:** CB₁/CB₂ receptor agonist
- **Highlights:** **Targets activation of CB₁ and CB₂ receptors**; however, **TA-A002 has a bias towards the CB₁ receptor** and is indicated as a topical treatment for chronic back-of-eye diseases such as **glaucoma** and age-related macular degeneration

ADTECH PHARMA, INC.

NB-110

- **Mechanism of Action:** CB₁/CB₂ receptor agonist
- **Highlights:** Ophthalmic solution is comprised of **synthetic cannabinoid Nabilone**, designed to mimic human tears; Nabilone exemplifies crystalline structure and has been **formulated to lower IOP** while also **potentially** providing neuroprotective effects

GLAUCOMA: MAJOR EYE DISEASE WITH SIGNIFICANT NEED

Irreversible and progressive eye disorder with a continued need for more effective treatment options

Description

- “Open angle glaucoma”: **chronic, progressive optic neuropathy** characterized by acquired atrophy of the optic nerve and loss of retinal ganglion cells and their axons; **associated with an open anterior chamber angle**^{1,2}

Symptoms & Patient Outcomes

- Symptomatic patients commonly exhibit **blurred vision, eye pain, high IOP, haloed vision, nausea, and blind spots in vision**³
- **6 – 12% of patients** with primary open-angle glaucoma, the predominate subtype of glaucoma, **progress to blindness** at an incidence rate of ~1% per year⁴

Patient Characteristics

- Major risk factors include **age (>60 yrs.), family history, ethnicity, certain medical conditions** (diabetes, heart disease), and **eye injury**³
- Glaucoma is **often undiagnosed in patients** as symptoms usually do not appear until advanced stages⁵

Etiology & Classification

- **Primary open-angle glaucoma (POAG)** is characterized by increased resistance to drainage of the aqueous humor in the trabecular meshwork, even though the angle between the cornea and the iris remain open
- **Secondary open-angle glaucoma**, a less common subtype of OAG, is a result of other secondary causes such as eye injury, side effects of medication, diabetes, etc.

