FOCAL POINT

Cannabinoids and the Eye

OTCQB: SKYE
December 2022

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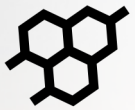
skye BIOSCIENCE

INVESTMENT SUMMARY

Innovation in ophthalmology to unlock the potential of novel cannabinoid derivatives



Phase 1: dosing started for CB1R agonist program in Dec-22
Phase 2: Received FDA okay to proceed for its Investigational New Drug application; plan to start in USA H1 2023

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

Preclinical foundation for glaucoma with strong ocular R&D capability and pipeline

Multiple academic collaborations to expand pipeline of novel cannabinoid derivatives

Pursuing collaboration and partnership opportunities for programs

STRATEGY FOR GROWTH AND VALUE CREATION

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

Seeking to affect the endocannabinoid system for therapeutic outcomes via the development of cannabinoid derivatives and small molecule drugs

Expand ophthalmology-focused pipeline with new target indications/products in 2023

Clinical plan designed for relevant outcomes with optimized time and cost

GLAUCOMA: LARGE, WITH UNMET NEEDS

World's leading cause of irreversible blindness

$7B drug market

~80M patients worldwide

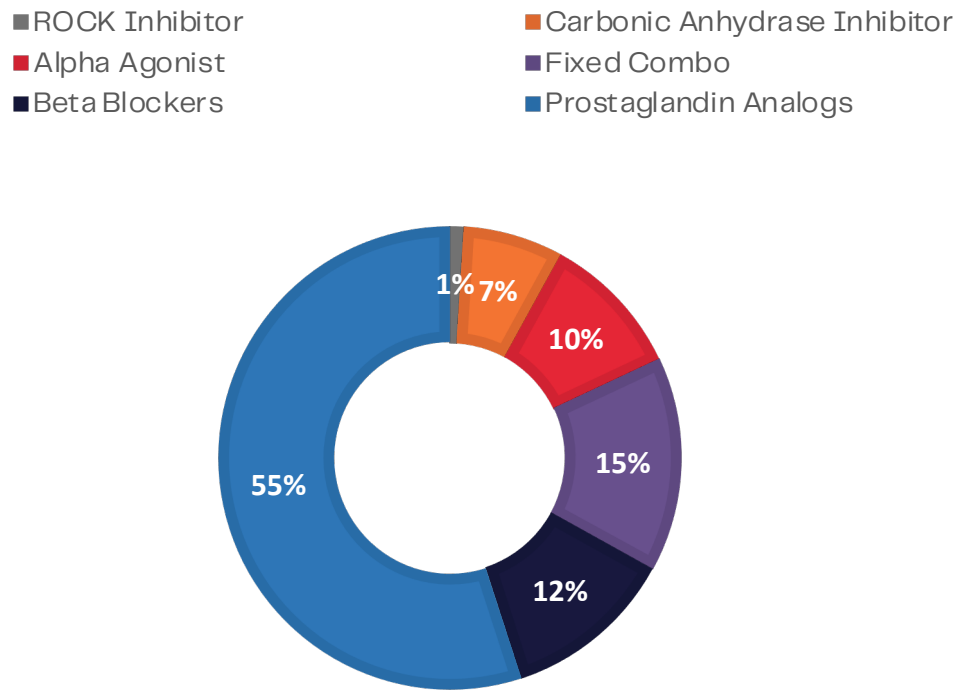
~110M patients by 2026

40% fail 1st line therapy[1]

50% require 2 therapies[1,2]

1 Kass et al, Delaying treatment of ocular hypertension: the ocular hypertension treatment study. Arch Ophthalmolgy, 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 PREDOMINATLY LEGACY CLASSES OF DRUGS AND GENERIC COMPOUNDS



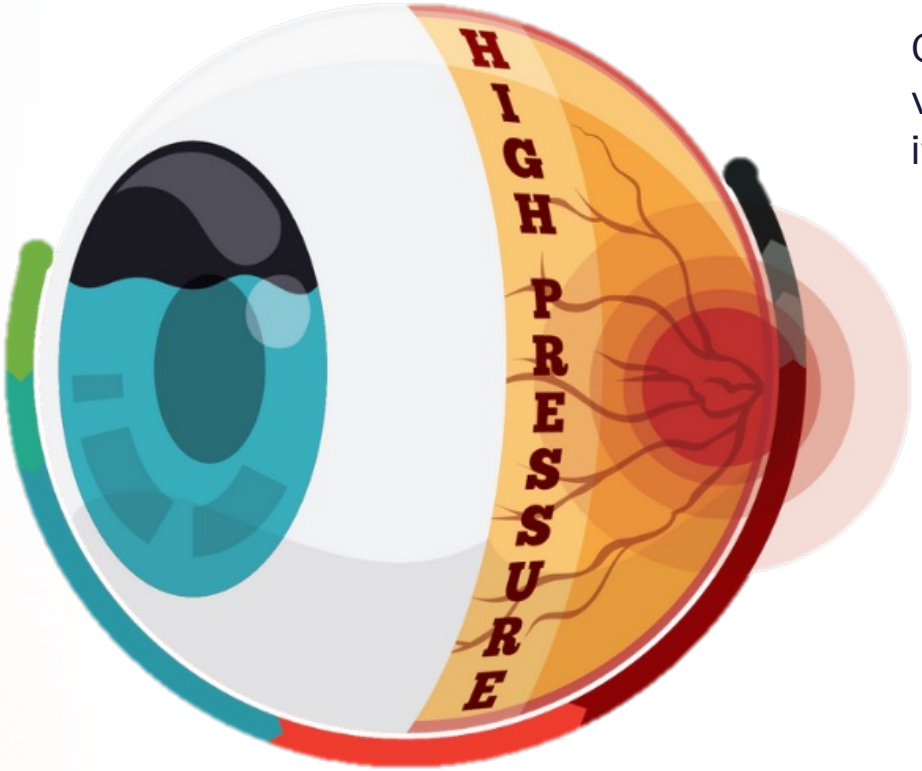
PATHOPHYSIOLOGY OF GLAUCOMA

Intraocular pressure (IOP) 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...



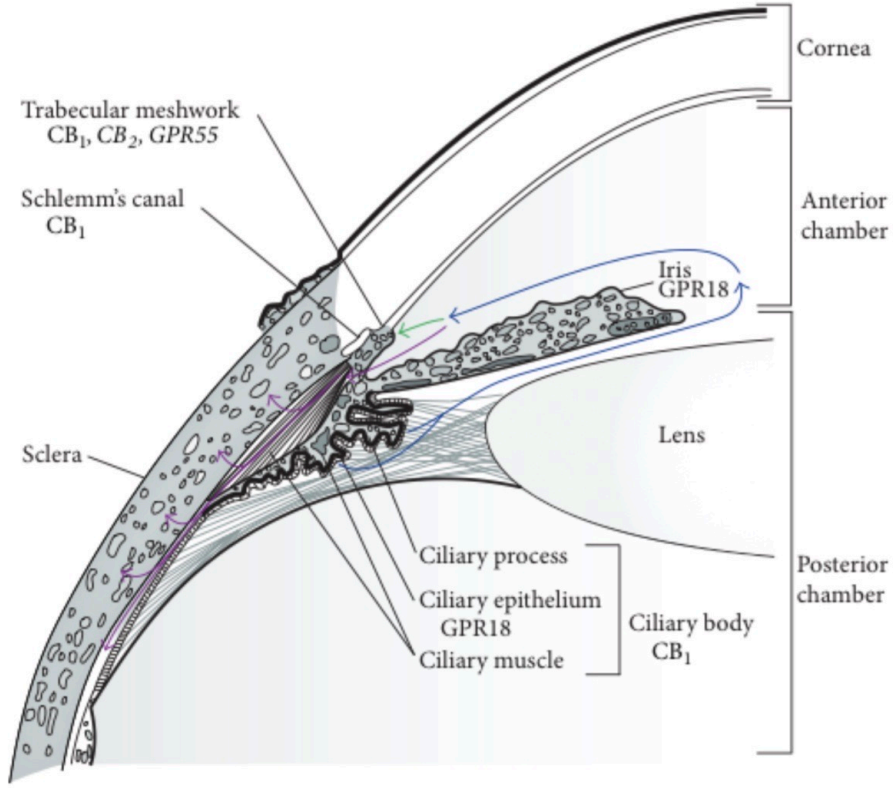
Increasing pressure inside the eye...

Generating progressive vision loss and blindness if not treated

Damaging blood vessels and optic nerve...

NEW FRONTIER FOR GLAUCOMA

- CB1 receptors are in tissue 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



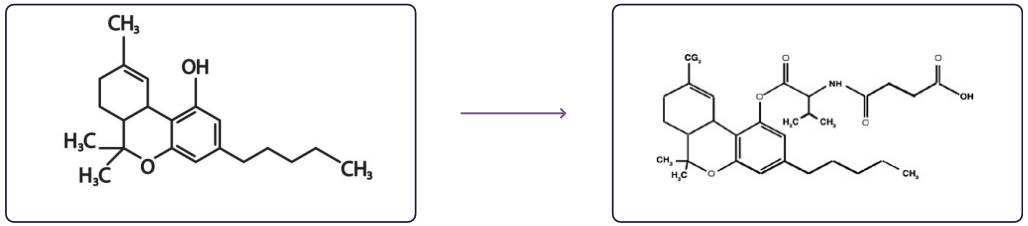
Circulating aqueous humor (blue), flowing from the ciliary body in the posterior chamber to the anterior chamber, is filtered out of the eye through two different outflow pathways: the trabecular meshwork pathway (green) and the uveoscleral pathway (purple).

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

DESIGNING AN EFFECTIVE THERAPY

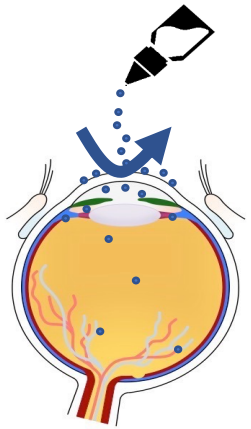
Cannabinoid prodrug enabling local delivery into the eye, with increased efficacy and limiting systemic exposure

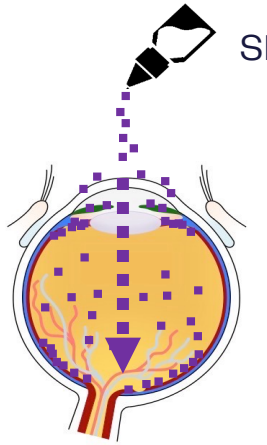
- THC is lipophilic and not easily delivered into the eye topically
- SBI-100 is a prodrug of THC that increases solubility and polarity of THC, allowing it to better penetrate ocular tissue
- Inside the eye, SBI-100 is converted back into THC
- SBI-100 OE proprietary nanoemulsion formulation further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



THC

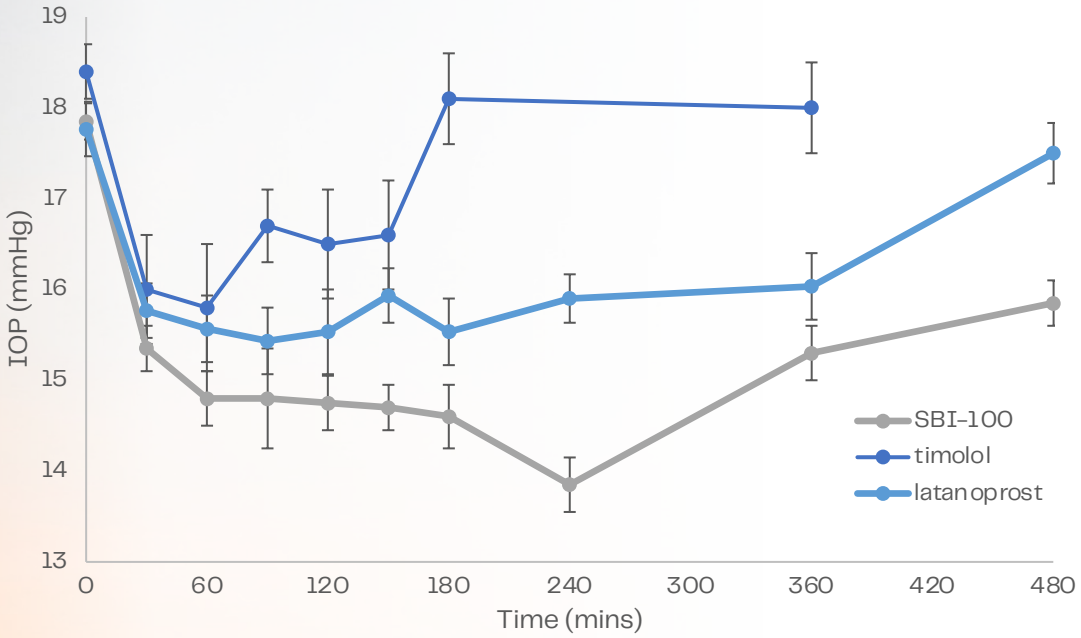
SBI-100

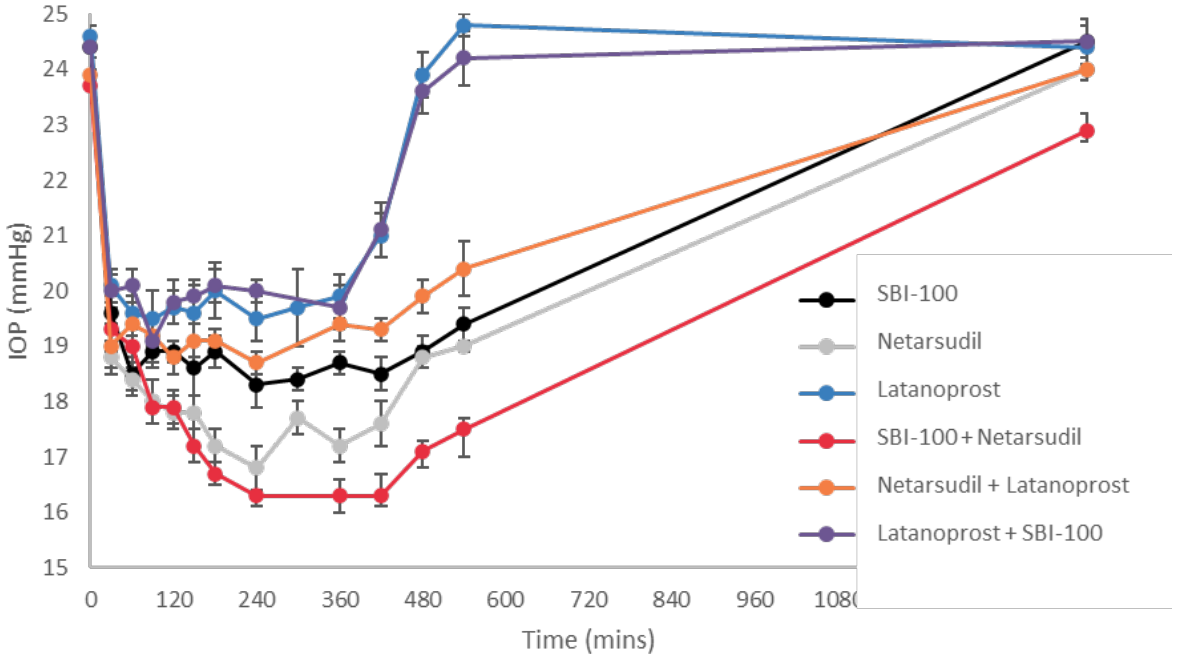




SBI-100 OE

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



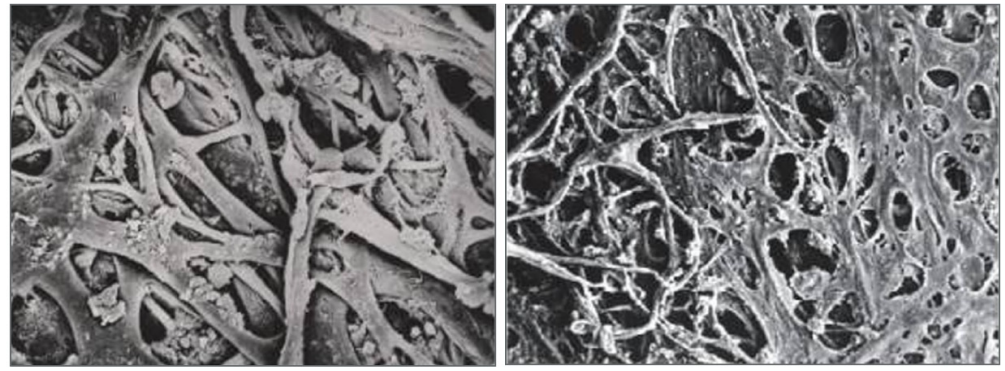


In multiple preclinical studies, SBI-100 demonstrated superior IOP lowering compared to leading therapies as a single agent

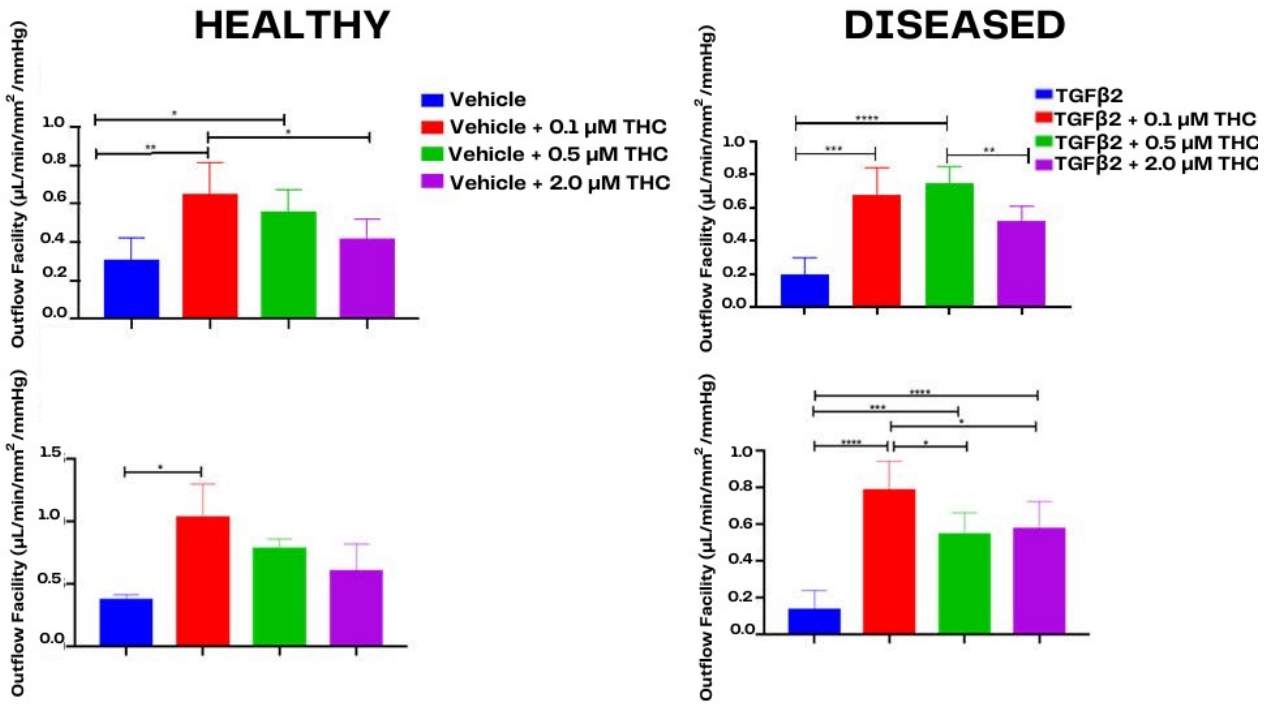
In preclinical studies, SBI-100 demonstrated enhanced efficacy when combined with other approved therapies

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

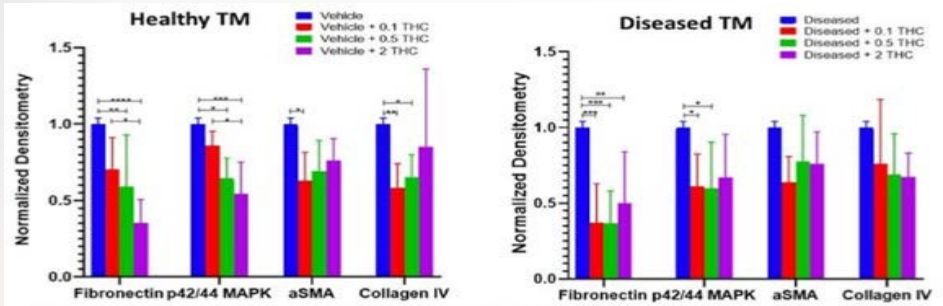


Figure 2. Protein analysis of markers linked to fibrosis at the 3D HTM after 6 days of treatment with THC. All samples of three donors were analyzed using Two-way ANOVA ****P<0.0001, ***P<0.001, **P<0.01, *P<0.05, N ≥ 4 per donor.

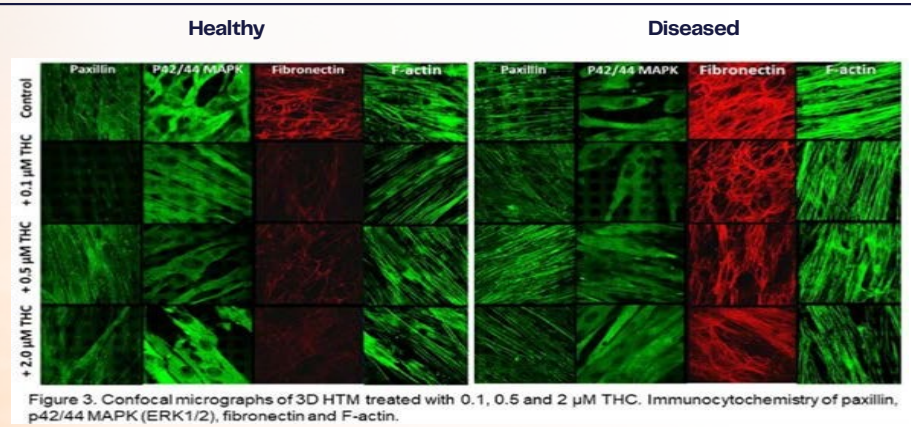


Figure 3. Confocal micrographs of 3D HTM treated with 0.1, 0.5 and 2 µM THC. Immunocytochemistry of paxillin, p42/44 MAPK (ERK1/2), fibronectin and F-actin.

- SBI-100 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
- Potential 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**

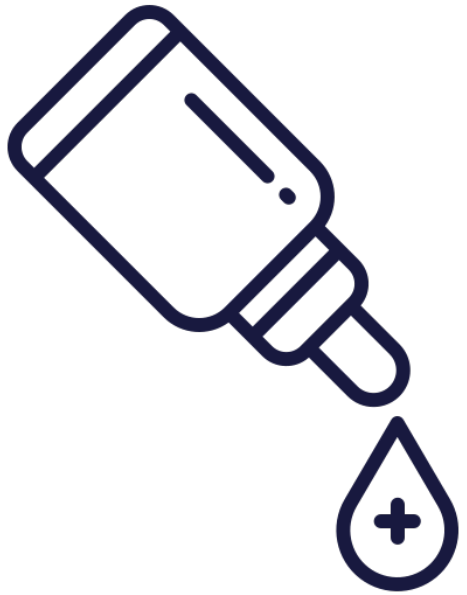
- Most drugs do not target the main site of disease-causing increased IOP -- the trabecular meshwork (TM)
- SBI-100 OE directly targets the TM and may increase flow through the eye as well as uveoscleral pathways
- SBI-100 OE may decrease fibrosis in the TM, the main cause of blockage to flow

✓ **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**

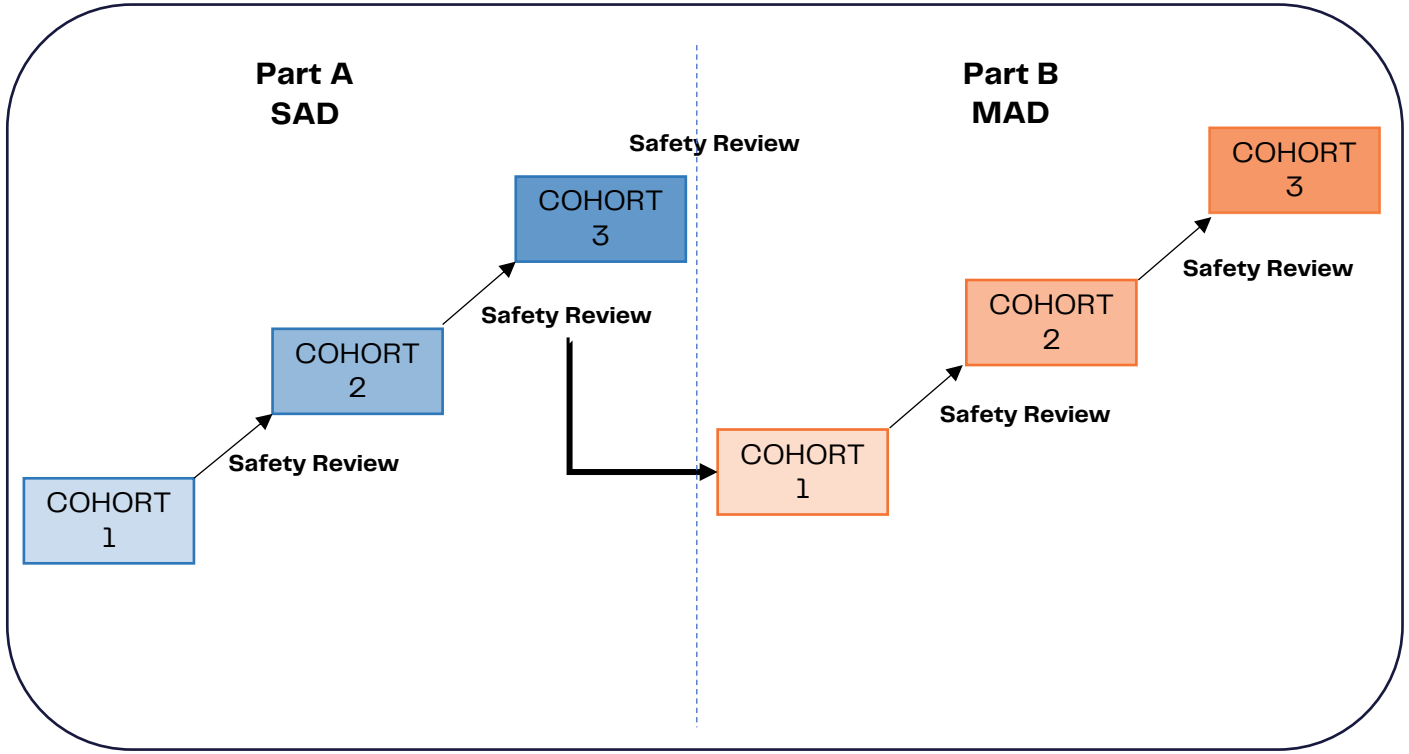
- This class of molecule has shown potential benefits to promote health and survival of optic nerve cells – sparing of retinal ganglion cells (RGCs) – in glaucoma models



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

Dosing for first cohort completed; second cohort planned for February 2022

- Randomized, double-masked, placebo-controlled
- Objectives: Evaluate safety, tolerability, and effect on intraocular pressure (IOP) in healthy subjects in single and multiple ascending dose arms
- ~48 subjects topically administered SBI-100 OE or placebo on a single eye in SAD and MAD arms
- 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



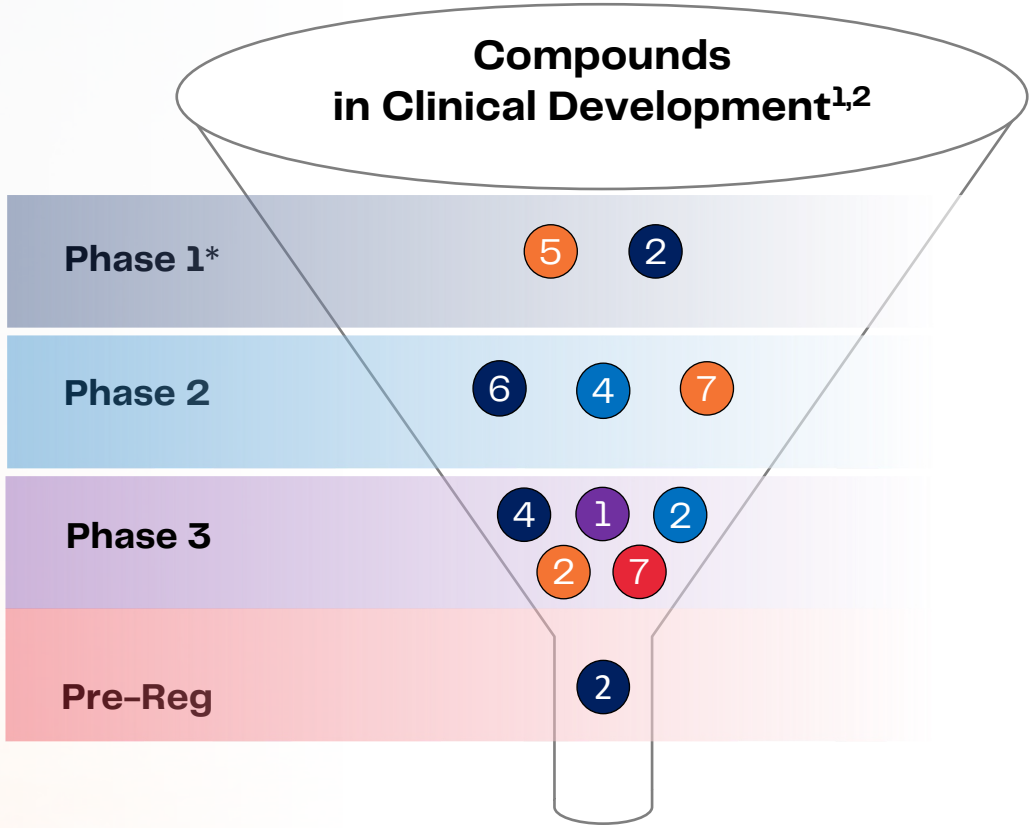
The study comprises 2 arms of 3 cohorts with 8 participants each (6 receiving SBI-100 OE and 2 placebo)

SBI-100 OE – CLINICAL DEVELOPMENT PLAN

Preclinical Proof-of-Concept	Phase 1 Safety & Tolerability	Phase 2 Clinical Proof-of-Concept	Phase 2/3 Efficacy & Safety
Nonclinical and CMC			
✓ Nonclinical MOA POC ✓ Nonclinical efficacy POC ✓ Formulation development	✓ Nonclinical safety and toxicology work completed ✓ Manufacture drug product for Phase 1	▪ Long-term chronic toxicology ▪ Safety pharmacology ▪ Manufacturing process development and optimization ▪ Manufacture P2 drug product	▪ Reproductive toxicology ▪ Carcinogenicity toxicology ▪ Biodistribution ▪ Manufacturing optimization
Clinical			
✓ Target product profile ✓ Protocol design and development	✓ Dosed first cohort of first-in-human SAD/MAD P1 study ▪ Complete dosing of P1 ▪ Phase 1 data analysis	▪ Begin enrolling Phase 2 proof-of-concept study ▪ Complete dosing of P2 ▪ Phase 2 data analysis	▪ Phase 2b efficacy & safety ▪ Phase 3 efficacy & safety
Regulatory			
✓ Regulatory strategy ✓ Pre-IND Meeting	✓ Australian Human Research Ethics Committee approval to start Phase 1	✓ FDA IND authorization	▪ FDA end-of-Phase 2 meeting ▪ FDA NDA submission

INDUSTRY GLAUCOMA PIPELINE LACKS INNOVATION

Late-stage assets dominated by legacy MOAs or combinations

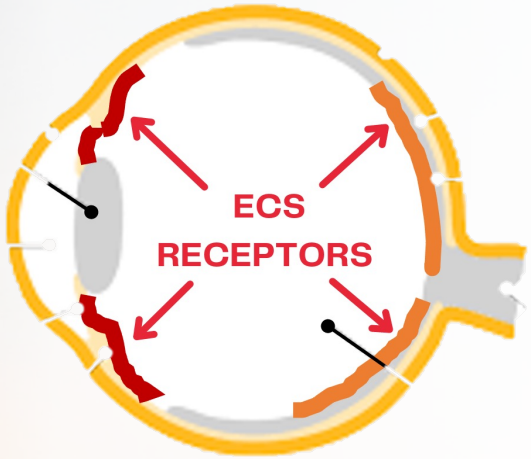


- Prostaglandins
- Adrenergic
- Rho Kinase
- Combinations
- Other**

**Carbonic Anhydrase 2 Inhibitor, Receptor Type Tyrosine Protein Phosphatase Beta Inhibitor, Cholinergic Muscarinic Receptor Agonist, Sulfonamide Protein Kinase Inhibitor, C1q Inhibitor, Potent Corticosteroid Agent, Ciliary Neurotrophic Factor (CNTF), KATP Channel Vessel Relaxer

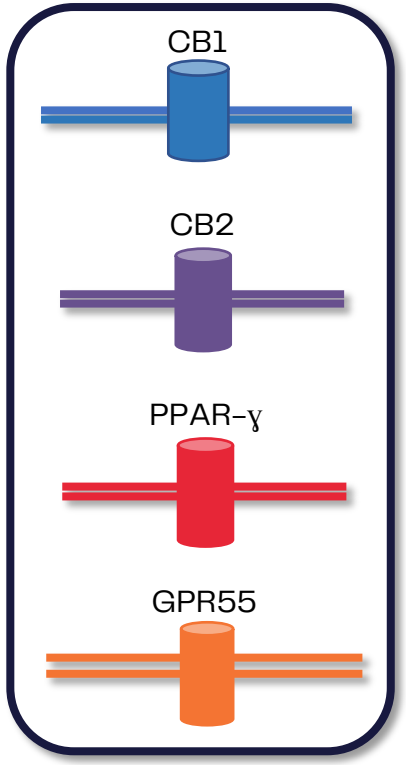
[1] GlobalData; [2] Clinicaltrials.gov
* Compounds listed based on the most recent trial completed or initiated

NOVEL CLASS OF TARGETS 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

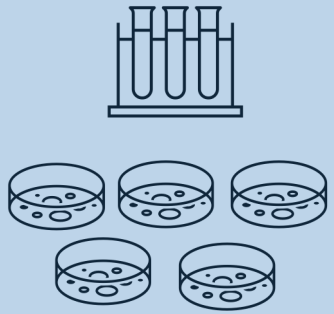
PROPRIETARY IN VITRO SCREENING PLATFORM FOR OCULAR DISEASES

Cannabinoid Pharmaceutical Innovation Program (CPIP)

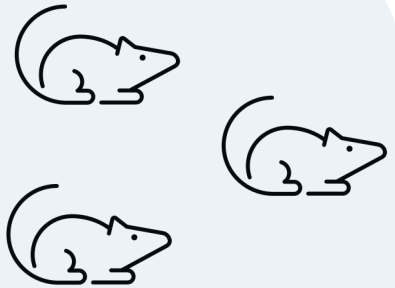
DISCOVERY

80+ novel compounds

IN VITRO SCREENING

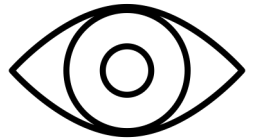


IN VIVO MODELS



OCULAR INDICATIONS

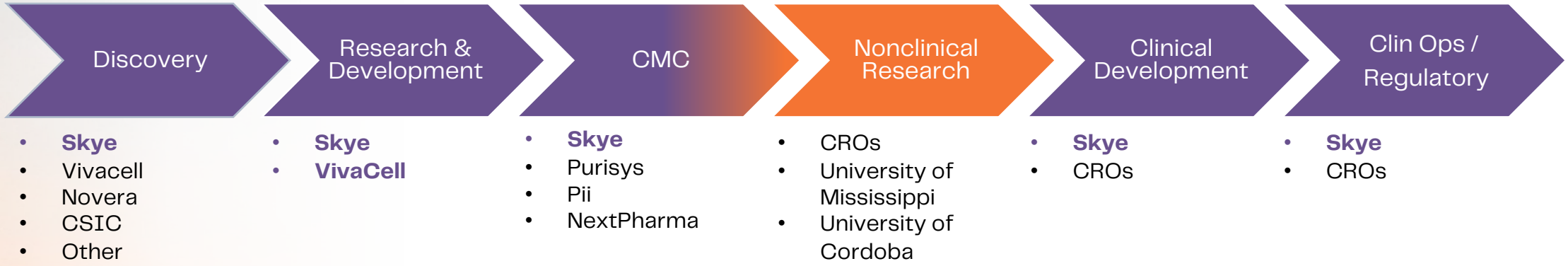
Dry eye
Ocular pain
Uveitis



AMD
Diabetic retinopathy
Uveitis

EXPERT DRUG DEVELOPMENT CAPABILITY

Internal/external resources provide knowledge/flexibility to advance controlled substances through the pharmaceutical drug development path



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
- ✓ Q4-22: Begin Phase 1 enrollment
- ✓ Q4-22: Begin P1 dosing
- ❑ Q2-23: Phase 1 data

SBI-100 OE: PHASE 2

- ✓ Q4-21: Pre-IND meeting with the FDA
- ✓ Q4-22: Submit Investigational New Drug application to FDA
- ✓ Q1-23: IND authorization
- ❑ H1-23: Phase 2 initiation
- ❑ Q1-24: Phase 2 data

STRATEGIC MILESTONES

- ✓ Q4-21: Neuroprotection study to assess SBI-100 potential to spare vision loss
- ✓ H2-22: Close corporate acquisition for capital resources
- ❑ Early-stage research & pipeline expansion (including in Canada)
- ❑ H1-23: Phase 2 efficacy study initiation. New product-driven intellectual property

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

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

Chris Twitty, PhD

Chief Scientific Officer

- 25+ years in R&D, drug pipeline expansion, CMC, non-clinical, regulatory, biomarker discovery and clinical biomarker strategies

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, BPharm RPh

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.

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

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

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

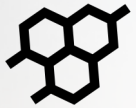
Giovanni Appendino, PhD

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

INVESTMENT SUMMARY

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



Enrolling Phase 1 for CB1R agonist program; Received FDA okay for IND to start studies in US, enabling planned Phase 2

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

Capitalization

Cash and securities[1]

Common shares o/s	912.2 M
Options, warrants and RSUs	247.2 M
Common shares f/d	1,165 M
Cash	$8.6 M
Working capital	$7.5 M

OTCQB SKYE
Market cap: $11.6 M[2]

Incremental capital: sale of non-core asset for $9.3M

Entered share purchase agreement for non-core operating facility for aggregate purchase price of $9.3M on 22/11/10

- ($0.5 M deposit already reflected in cash figure)
- ~$6.0 M to be paid at close
- 3 installments of ~$0.9M to be paid on 18, 30, 42-month anniversaries of closing date

[1]Skye and EHT figures combined on proforma basis as of 22/09/30 [2]22/12/22

THANK YOU

To learn more, please contact:
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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 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 suffering glaucoma	Single oral dose of nabilone (0.5 mg)	**IOP decreased** by 27.9%, 2-6h after administration, no visual side effect
32 patients suffering 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.

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