Skye Bioscience Investor Day

CB1 Axis: Unlocking the Potential of the Endocannabinoid System

October 25, 2023

Speakers

Skye Executive Management

Punit Dhillon
CEO & Chairman

Tu Diep, MSc
Chief Development Officer

Chris Twitty, PhD
Chief Scientific Officer

Kaitlyn Arsenault, CPA
Chief Financial Officer

KOLs

Sameh Mosaed, MD

Brian Levy, OD

Glenwood Gum, Ph.D.

Investor Day Agenda

	Presenter
Corporate Strategy & Clinical Path forward	Punit Dhillon I CEO
Historical Perspectives of Cannabis/THC in Preclinical Research: Past Challenges and Why it May Work Now	Glenwood Gum, Ph.D.
SBI-100 OE Nonclinical Data and Biomarker Program Overview Pipeline & Research Update	Christopher Twitty, Ph.D. I CSO
Clinical Perspectives on the Use of Cannabis/THC in the Management of Glaucoma	Sameh Mosaed, M.D.
SBI-100 OE Phase 1 Data and Phase 2 Update	Tu Diep I CDO
Physician Commercial Perspective	Brian Levy, O.D.
SBI-100 OE KOL Feedback: Market Opportunity & Positioning	Punit Dhillon
Q&A Session	All

Safe Harbor and Forward-looking Statements

Any discussion of the potential use or expected success of our product candidates is subject to our product candidates being approved by regulatory authorities. In addition, any discussion of clinical trial results for SBI-100 Ophthalmic Emulsion relates to the results in its Phase 1 clinical trial.

The information in this presentation is current only as of its date and may have changed or may change in the future. We undertake no obligation to update this information in light of new information, future events or otherwise. We are not making any representation or warranty that the information in this presentation is accurate or complete.

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Any future clinical trial results may not demonstrate safety and efficacy sufficient to obtain regulatory approval related to the preclinical research findings discussed in this presentation. These risks and uncertainties are described more fully in the quarterly and annual reports that we file with the SEC, particularly in the sections titled "Risk Factors" and "Management's Discussion and Analvsis of Financial Condition and Results of Operations." Such forward-looking statements onlv speak as of the date they are made. We undertake no obligation to publicly update or revise any forward-looking statements, whether because of new information, future events or otherwise, except as otherwise required by law.

Punit Dhillon,
CEO & Chairman

Corporate Strategy and Clinical Path Forward

Skye is Building an Endocannabinoid Pharmaceutical Company

Our Mission

To pioneer and lead the development of new medicines that unlock the pharmaceutical potential of the endocannabinoid system, initially through modulation of the CB1 receptor, to advance the standard of care and treatment alternatives for patients worldwide to treat diseases with neuropathic, inflammatory, and metabolic processes.

Our Strategy

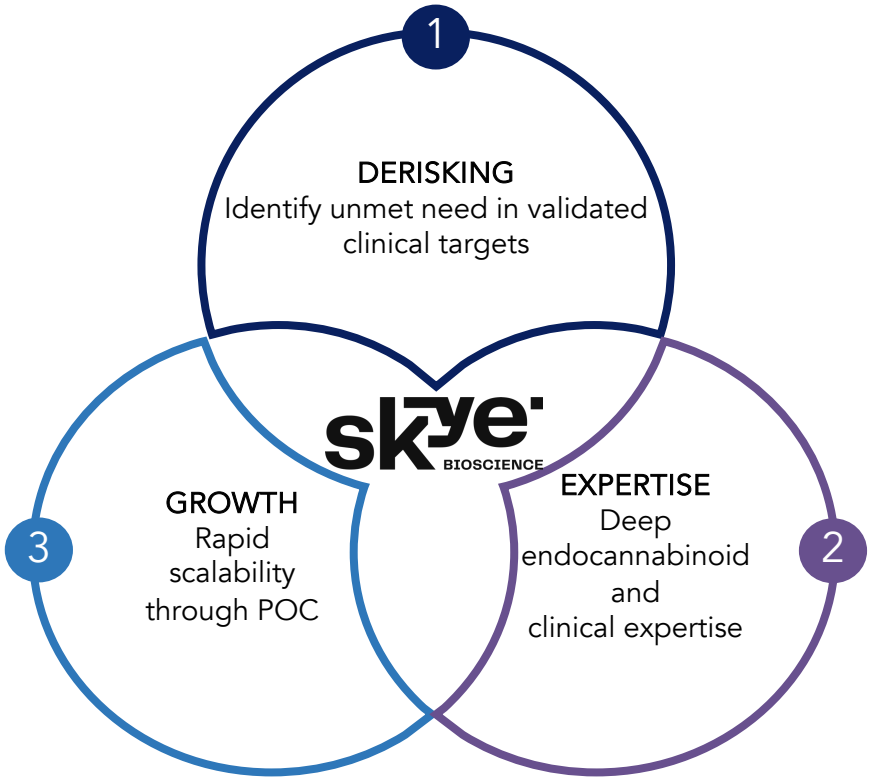
DERISKING	Advance clinical targets that are validated with large markets and have high probability of success
GROWTH	Accelerate clinical development through POC stage and build KOL participation in high-quality clinical execution
EXPERTISE	Build on science and understanding of ECS to support R&D pipeline

Highly Productive Clinical Development Strategy Optimized for Speed, Probability of Success

Pipeline focused on CB1 axis and potential best-in-class molecules

In Three Years, Skye Bioscience…

- SBI-100 OE – Clinical formulation, IND, delivered on first-in-human trial
- SBI-100 OE – Phase 2 glaucoma study initiation
- Nimacimab – Acquired Phase 2-ready asset being developed for cardio-metabolic indication(s)
- Pre-clinical research with new drug candidates generated from CPIP[1] engine



All drugs are investigational and subject to regulatory approval. For investor audiences only.
1: CPIP: Cannabinoid Pharmaceutical Innovation Program announced October 2021

Strong Execution Track Record and Clear Clinical Path Forward

2021

- Execution and advisory team buildout and rebranding
- CFO appointed
- Appointed Head of RA & QA, and Director of R&D
- Pre-clinical work required to advance SBI-100 OE for the treatment of glaucoma into the clinic largely completed
- Ophthalmic drug development expertise expanded through addition of new board member
- Cannabinoid Pharmaceutical Innovation Program (CPIP) R&D program launched

2022

- Australian Ethics Committee approval for first-in-human Ph. 1 study of SBI-100 OE
- Drug production for Ph. 1 study completed
- First-in-human clinical trial of lead asset SBI-100 OE in Australia initiated
- CSO appointed
- First patient dosed in Ph. 1 SBI-100 OE trial
- Open US IND for SBI-100 OE to study the treatment of glaucoma

2023

- Ph. 2a clinical trial protocol approved from central Institutional Review Board (IRB) for SBI-100 OE
- Receive positive safety review for final cohort in Ph. 1 study of SBI-100 OE (Australia)
- 5AM Ventures Versant Ventures Investment BOD additions
- SBI-100 OE Ph.1 Final Results
- Ph. 2a (US) glaucoma study first patient dosed
- IND submission for nimacimab to study cardio metabolic indication

2024

- SBI-100 OE Ph. 2a interim readout glaucoma
- Anticipated initiation of nimacimab Ph. 2 clinical study in cardio metabolic indication[1]
- SBI-100 OE Ph. 2a final data
- Ph. 2 interim readout for nimacimab clinical study[1]
- SBI-100 OE 3-month toxicity completed
- Anticipated initiation of SBI-100 OE Ph. 2b (US) glaucoma clinical study[1]

2025

- Ph. 2 final readout for nimacimab clinical study[1]
- SBI-100 OE Ph. 2b interim data[1]
- SBI-100 OE 6-month toxicity completed[1]
- IND submission for new ocular indication SBI-300[1]
- EOP2 meeting with FDA for SBI-100 OE[1, 2]

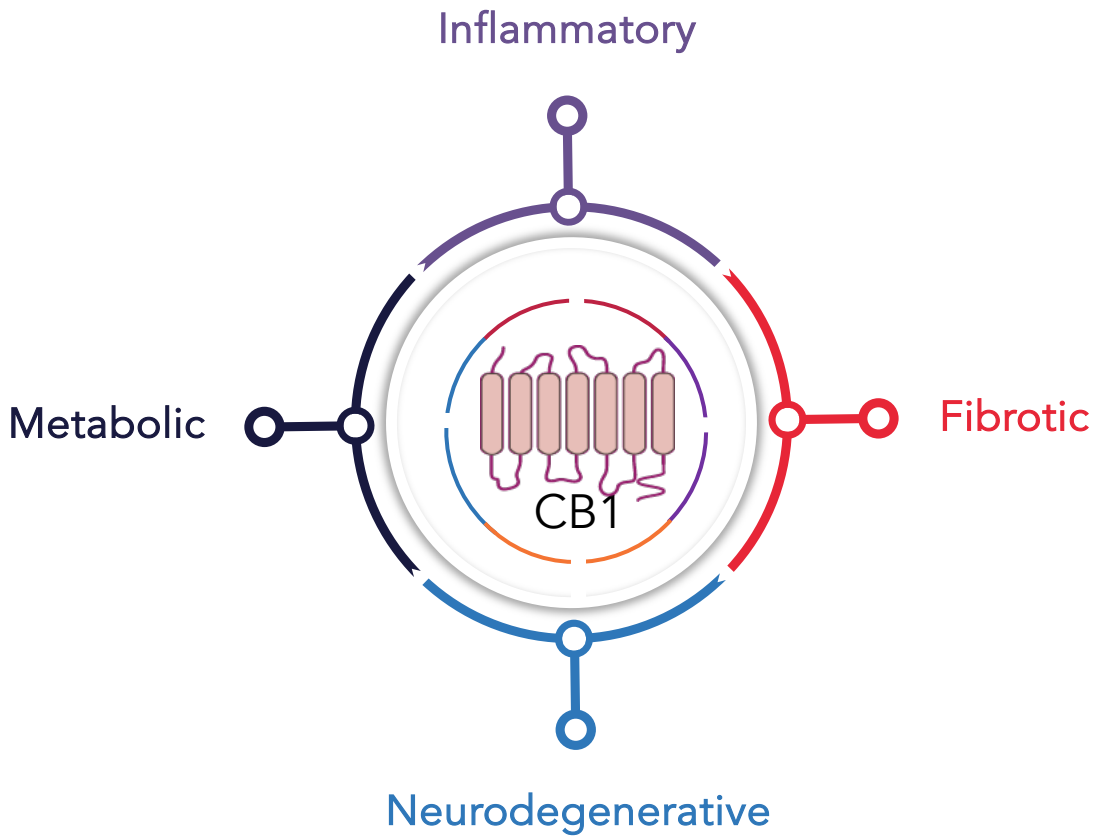
skye BIOSCIENCE

References are to calendar years. All drugs are investigational and subject to regulatory approval. For investor audiences only.
1: Pending additional funding;
2: Assuming P2b completed

CB1: High-potential Target for Physiological Regulation

CB1 involved in many disease processes

- CB1 (cannabinoid receptor 1) a renewed target of interest for drug discovery.
- Modulation of CB1 signaling can impact key biological processes including:
  - Inflammatory, metabolic, fibrotic, and neurodegenerative pathways.
- CB1 plays an important role in promoting/blunting disease progression in peripheral tissues and their associated disease pathologies including:
  - Glaucoma
  - Chronic kidney disease
  - Obesity



Barutta F, Bruno G, Mastrocola R, Bellini S, Gruden G. The role of cannabinoid signaling in acute and chronic kidney diseases. Kidney Int. 2018 Aug;94(2):252-258. doi: 10.1016/j.kint.2018.01.024. Epub 2018 Apr 27. PMID: 29706358.
Dao Myriam, François Helene Cannabinoid Receptor 1 Inhibition in Chronic Kidney Disease: A New Therapeutic Toolbox. Front. Endocrinol. 2021 July; 12 DOI=10.3389/fendo.2021.720734

Key Milestones Position Skye for Near Term Value Generation

Multiple data catalysts across two key programs through end of 2024

References are to calendar years. All drugs are investigational and subject to regulatory approval. For investor audiences only.
1: Unaudited estimate
2: Forecast for FY2024 pending additional funding
3: In reference throughout presentation to Primary Open Angle Glaucoma & Ocular Hypertension

Nimacimab

Novel CB1-targeting mAb therapeutic

NIMACIMAB

MOA	Disease	R&D	Phase 1	Phase 2
CB1 Receptor Inhibitor *Sub-cutaneous*	**Cardio-Metabolic Indication**			

Best–in-class and Only-in-class Monoclonal Antibody	**Phase 2 ready** molecule with three open INDs. **Only CB1** negative allosteric modulating humanized monoclonal antibody (mAB) in **clinic**. A highly selective inhibitor of CB1, with no detectable binding to CB2 or other GPCRs. Mechanism of action has therapeutic potential in fibrotic, inflammatory and metabolic diseases.
Past Clinical Development History	Rimonabant validated CB1 receptor as effective target for obesity. **Past safety challenge: depression, anxiety and suicidal ideations due to CNS exposure.**
Favorable Safety Profiles	Next generation drug design. Unprecedented safety and tolerability identified through preclinical and Phase 1 data Nimacimab designed to minimize safety issues associated with previous CB1 modulators, while maximizing clinical benefit.

SBI-100 Ophthalmic Emulsion

Improving CB1-targeting drug design for glaucoma

SBI-100 OE

MOA	Disease	R&D	Phase 1	Phase 2
CB1 Receptor Agonist *Topical*	Glaucoma			

Best–in-class and Only-in-class Molecules	First/only prodrug of THC developed and currently in the clinic for glaucoma.
Clear Clinical Endpoint	Lowering intraocular pressure (IOP) prevents subsequent progression of functional damage in the retina and is accepted as an approvable clinical endpoint.
Past Clinical Development History	THC known to reduce intraocular pressure since 1970s.[1,2,3,4] Also known to protect against neurodegeneration.[5,6] **Past safety challenge: psychotropic effects due to CNS exposure.**
Next Generation Drug Design/Improvements	Next generation drug design, local delivery with eye drop in a novel formulation. Prodrug design for improved bioavailability in the eye. Designed for minimal or no psychotropic effect.

All drugs are investigational and subject to regulatory approval. For investor audiences only.

1: Hepler RS, Frank IR. Marihuana smoking and intraocular pressure. JAMA. 1971 Sep 6;217(10):1392. PMID: 5109652.
2: Hepler R.S., Petrus R.J. Experiences with administration of marihuana to glaucoma patients. In: Cohen M., editor. *The Therapeutic Potential of Marihuana*. Springer; New York, NY, USA: 1976. pp. 63–75
3: Hepler R.S., Frank I.M., Petrus R. Ocular effects of marihuana smoking. In: Braude M.C., Szara S., editors. *The Pharmacology of Marihuana*. Raven Press; New York, NY, USA: 1976.
4: Tiedeman J.S., Shields M.B., Weber P.A., Crow J.W., Cocchetto D.M., Harris W.A., Howes J.F. Effect of synthetic cannabinoids on elevated intraocular pressure. *Ophthalmology*. 1981;88:270–277. doi: 10.1016/S0161-6420(81)35052-0.
5: Crandall J., Matragoon S., Khalifa Y.M., Borlongan C., Tsai N.T., Caldwell R.B., Liou G.I. Neuroprotective and intraocular pressure-lowering effects of (-)Delta9-tetrahydrocannabinol in a rat model of glaucoma. *Ophthalmic Res.* 2007;39:69–75. doi: 10.1159/000099240.
6: Pinar-Sueiro S., Zorrilla Hurtado J.A., Veiga-Crespo P., Sharma S.C., Vecino E. Neuroprotective effects of topical CB1 agonist WIN 55212-2 on retinal ganglion cells after acute rise in intraocular pressure induced ischemia in rat. *Exp. Eye Res.* 2013;110:55–58. doi: 10.1016/j.exer.2013.02.009.

Historical Perspectives of Cannabis/THC in Preclinical Research:

Past Challenges and Why it May Work Now

Cannabinoids for Glaucoma

October 25, 2023

Dr. Glenwood Gum, MS, PhD

Ophthalmology Department: Pharmaron (US Lab) Services, San Diego

Early Studies with Cannabinoids

- Early systemic studies with cannabinoids assumed the decrease in IOP effects was centrally derived[1]
- Mid 1970s studies in rabbits noted an increase in aqueous outflow through the Trabecular Meshwork[2,3]
- Different cannabinoid derivatives were tested for their ability to reduce IOP[4]
  - Δ 9- and Δ 8- tetrahydrocannabinol (THC) were more active in lowering IOP than the parent cannabinoids
- Reduction in aqueous humor production has been shown in glaucomatous monkeys[5]

[1]Purnell WD, Gregg JM. Delta(9)-tetrahydrocannabinol,, euphoria and intraocular pressure in man. Ann Ophthalmol. 1975 Jul. 7(7):921-3
[2]Green K, Podos SM. Antagonism of arachidonic acid-induced ocular effects by delta 1-tetrahydrocannabinol. Invest Ophthalmol 1974;13:422-429.
[3]Green K, Pederson JE. Effect of 1-tetrahydrocannabinol on aqueous dynamics and ciliary body permeability in the rabbit. Exp Eye Res 1973;15:499-507.
[4]ELSohly MA, Harland EC, Benigni DA, Waller CW. Cannabinoids in glaucoma II: the effects of different cannabinoids on intraocular pressure of the rabbit. Curr Eye Res 1984 Jun; 3(6) 841-50.
[5]Chien FY, Wang R-F, Mittag TW, et al. Effects of WIN 55212-2 a cannabinoid receptor agonist, on aqueous humor dynamics in monkeys. Arch Ophthalmol 2003;121:87-90.

Cannabinoids in the Normotensive and Glaucomatous Beagles

University of Florida College of Veterinary Medicine

- Dr.s Kirk N. Gelatt and Glenwood G. Gum tested a Δ 9- tetrahydrocannabinol (THC) compound in the glaucoma dog model

Formulation (supplied from Federal agency)

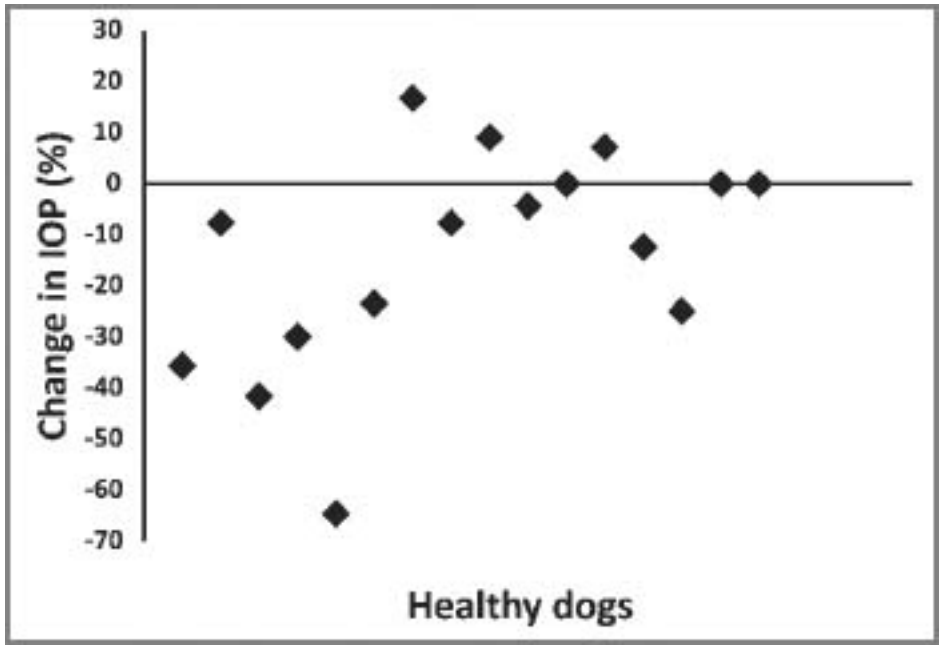
2% Δ 9- tetrahydrocannabinol (THC) solution

Excipient: mineral oil

Stored in an amber vial to protect from light degradation

- **Results:** No significant difference was observed in both the normotensive and glaucomatous beagles

Glaucomatous Beagle Results Similar to Other Canine Studies



Scatterplot showing the percentage change from baseline (pretreatment) values in evening (5:00 pm) IOPs following topical administration of a 2% THC ophthalmic solution in 16 clinically normal adult dogs. Each diamond represents the value for 1 animal. One drop was administered every 12 hours (for a total of 9 doses) to 1 randomly selected eye in each dog. Intraocular pressures were measured via applanation tonometry. Most dogs had decreased IOP in the treated eye, but responses varied substantially among individual dogs, suggesting that some were more responsive to THC treatment than others.

Fisher KM, Ward DA, Hendrix DVH. Effects of a topically applied 2% delta-9-tetrahydrocannabinol ophthalmic solution on intraocular pressure and aqueous humor flow rate in clinically normal dogs. AJVR, vol 74, No. 2, February 2013.

Possible Reasons why Δ 9- THC was not Successful in the Glaucomatous Beagles

Problems with the formulation was the largest concern

- Being an oily formulation, pipetting was more difficult than other glaucoma compounds
- Light sensitivity with Δ 9- THC formulation, required amber vials for protection, other glaucoma compounds did not require this
- Uniformity of the Δ 9- THC formulation was a concern
- Excipients used in the formulation, being an oily compound would cause blurring of the visual axis

Other Glaucoma Drug Development at the Time

All of the following glaucoma drugs, including older marketed drugs, were effective in the glaucomatous beagle model

- Beta blockers (Timolol)
- Topical carbonic anhydrase inhibitors (Tom Maren, University of Florida, Depart. Pharmacology)
- Alpha adrenergic agonists
- Prostaglandins
- Rock inhibitors (developed much later)

$PGF_{2\alpha}$ Effects in the Normotensive and Glaucomatous Beagles

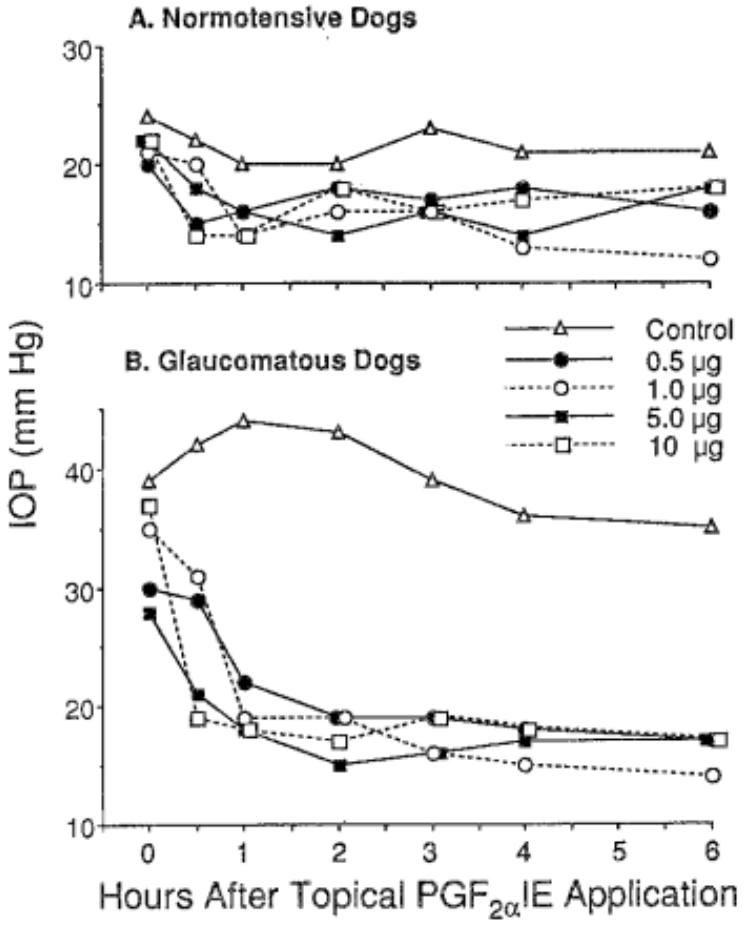


Figure 2: The ocular hypotensive effect of topically applied $PGF_{2\alpha}$-IE on normotensive (panel A) and glaucomatous (panel B) dogs in the dose range of 0.5 µg to 10 µg of $PGF_{2\alpha}$ equivalent.

Bito LZ, Camras CB, Gum GG, Resul B. The ocular hypotensive effects and side effects of prostaglandins on the eyes of experimental animals. The ocular effects of prostaglandins and other eicosanoids, Alan R. Liss, Inc., NT 1989, 349-368

New Role of Cannabinoids as Neuroprotection in Glaucoma

Table 2. Main effects of ECS on retinal neuroprotection.

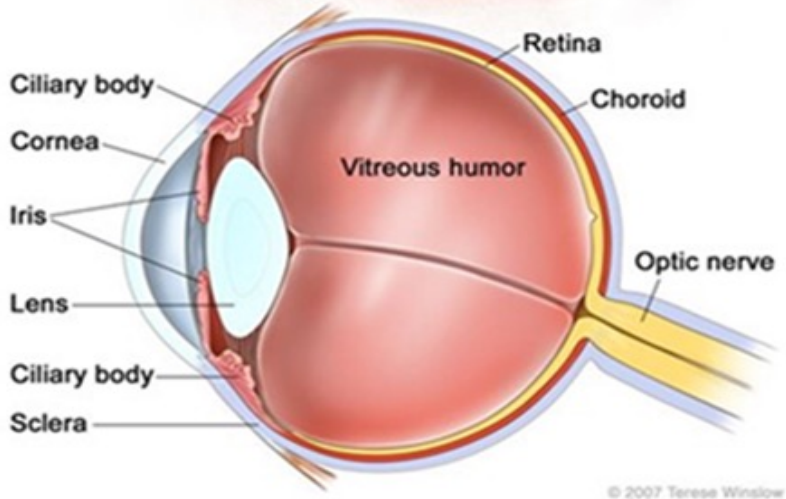
Animal/Human/Cell Model	Target	Molecular Effect	Effect on eCB-Binding Receptors	Overall Effect	References
Retinal ischemia mice model	Retinal Ganglion Cells	FAAH inhibition	↓ CB_1, TRPV1	IOP reduction	Nucci *et al.*, 2007
Knockout mice (-/-) for β_1 AR, β_2 AR, CB_1, or CB_2	Anterior Eye	NE release Inhibition	↑ CB_1	IOP reduction	Hudson *et al.*, 2011
Rat model of axotomy	Retinal Ganglion Cells	FAAH inhibition	↑ CB_1	Cell protection	Slusar *et al.*, 2013
AMPA excitotoxicity animal model	Amacrine Cells	PI3K/AKT and MEK/ ERK1/2 signalling pathway	↑ CB_1	Cell protection	Kokona *et al.*, 2015
Ocular hypertensive subjects	Vascular Endothelium	Inhibition of AEA degradation (?)	Receptor-independent	IOP reduction	Strobbe *et al.*, 2013
Knockout (-/-) mice for CB_1, CB_2, or MAGL	Nonpigmented Ciliary Epithelium	MAGL blockage	↑ CB_1	IOP reduction	Miller *et al.*, 2016
Knockout (-/-) mice for TRPV1	Retinal Ganglion Cells	Enhanced excitability by Ca^{2+} efflux	↑ TRPV1	Cell protection	Sappington *et al.*, 2015
Streptozotocin-induced diabetics rat model Human retinal endothelial cell	Retinal Endothelial Cells	Suppression of oxidative stress and inflammation	↑ CB_1	Cell protection	El-Remessy *et al.*, 2008
Animal/Human/Cell Model	Target	Molecular Effect	Effect on eCB-binding Receptors	Overall Effect	References
NMDA excitotoxicity rat model	Retinal Ganglion Cells	Activation of CGRP and tachykinin NK1 receptors	↑ TRPV1	Cell protection	Sakamoto *et al.*, 2014
Xenopus leavis	Retinal Ganglion Cells	Enhanced excitability by chloride channel current	↑ CB_1	Visual response protection	Miracourt *et al.*, 2016
Light-induced damage mice model	Murine Retinal Cone Cells	Suppression of oxidative stress and inflammation	↑ CB_2	Photoreceptor protection	Inamura *et al.*, 2017
Human retinal pigmental epithelial cells	Retinal Pigment Epithelium	Downregulation oxidative stress	↑ CB_1	Cell protection	Wei *et al.*, 2013
Light-induced photoreceptor damage rat model	Retinal Section	Mediated by saffron	↓ CB_1, CB_2	Photoreceptor protection	Maccarone *et al.*, 2016

Rapino C, Tortolani D, Scipioni L, Maccarrone M. Neuroprotection by (Endo) Cannabinoids in Glaucoma and Retinal Neurodegenerative Diseases. Curr NeurophRMacology 2018,16, 959-970.

In Vivo Ocular Modalities

- Ophthalmic examination
  - Slit-lamp biomicroscopy
  - Indirect ophthalmoscopy

- Anterior Chamber
  - Tonometry
  - Pupillometry
  - Pachymetry
  - Slit-Lamp Biomicroscopy
  - Oculus Pentacam
  - Konon Specular Microscope
  - Heidelberg spectralis Cornea OCT

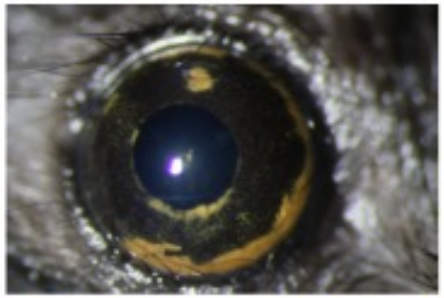


- Posterior chamber
  - Zeiss Fundus Photography
  - Heidelberg spectralis (IR,FA, ICGA & OCT)
  - VERIS Electroretinogram (Full field and multifocal ERG)

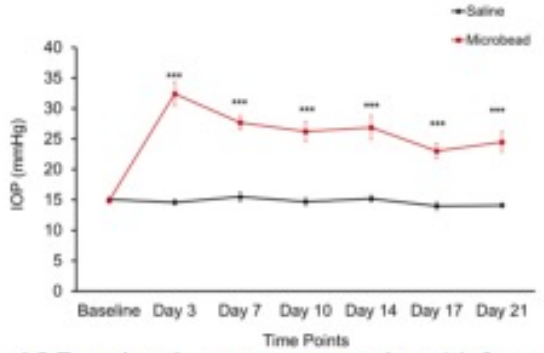
New imaging modalities added are Heidelberg Anterion and HRT3 RCM, Zeiss CLARUS fundus camera, and available OcuMetrics Fluorotron. The Pharmaron Ophthalmology team has many decades of experience in glaucoma research and develpoment.

Microbeads Model can be Used to Test Cannabinoid Neuroprotection

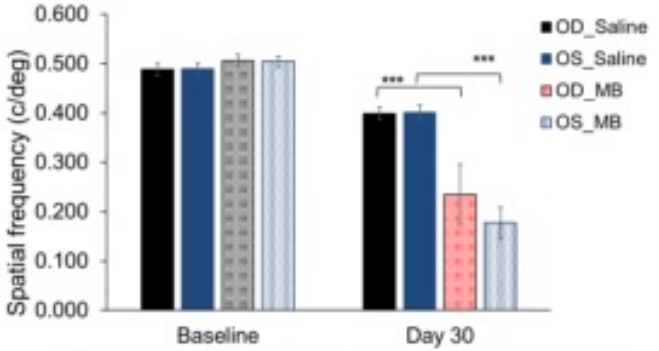
Glaucoma Mouse Model: Neurodegeneration



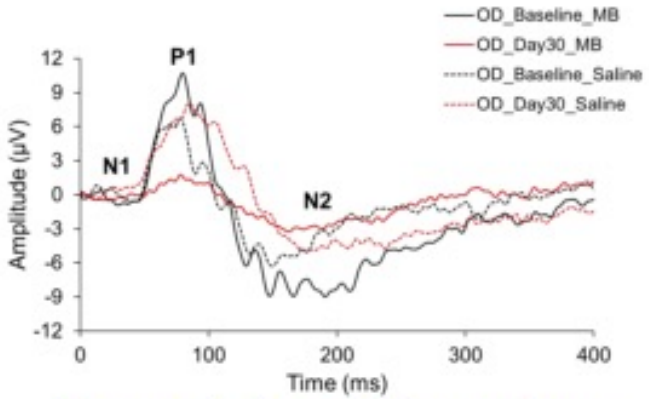
Intracameral injection of yellow magnetic microbeads



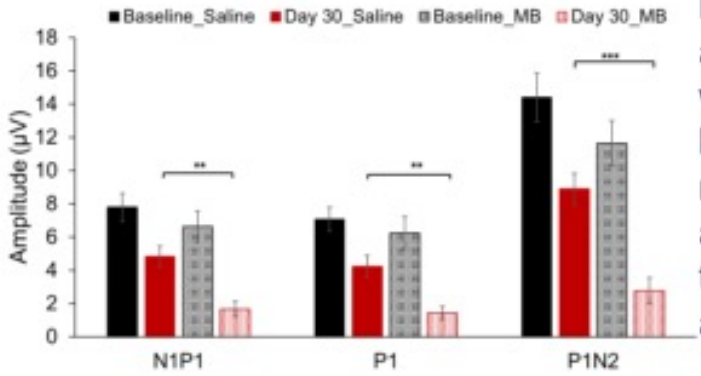
IOP raised on average by 11.8 ± 6.0 mmHg in microbeads injected animals.



Reduced visual acuity on Day 30 for both eyes



Representative pERG waveforms



Both N1P1 and P1N2 amplitudes at Day 30 were significantly lowered in the microbeads injected animals compared to the saline injected animals

Question: where do cannabinoids fit in the crowded market of glaucoma drugs?

Thank you !

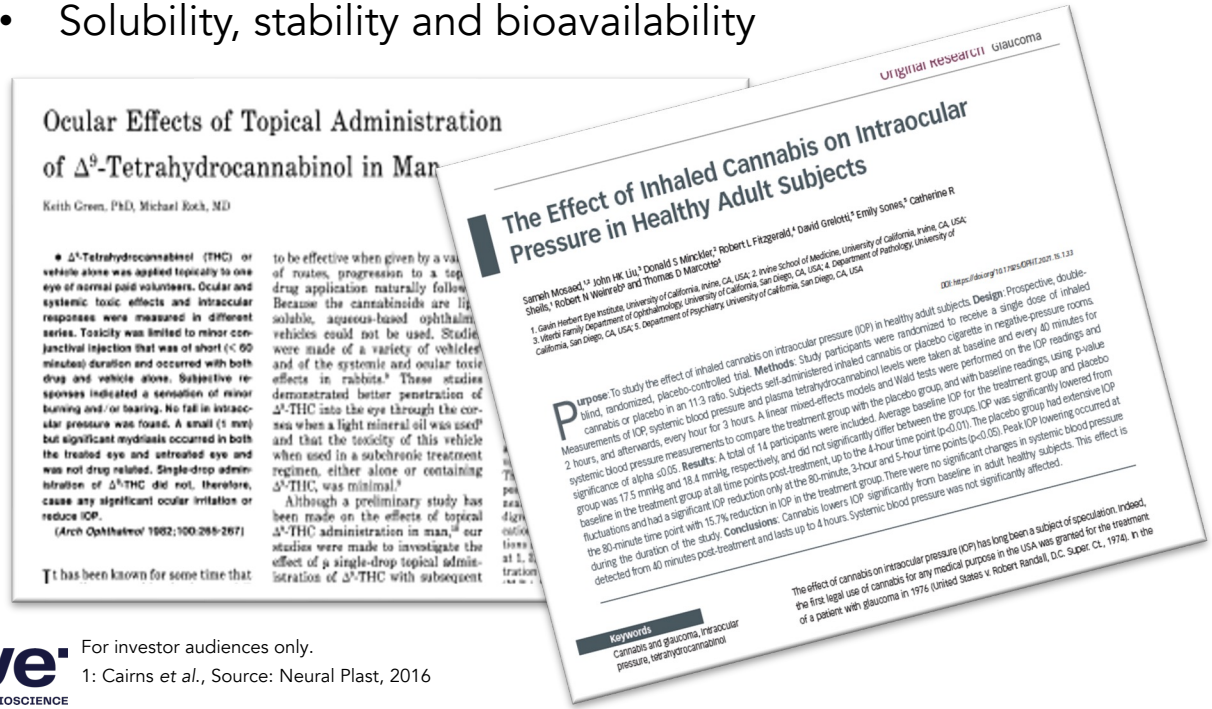
SBI-100 OE: Pipeline and Research Update

Nonclinical Data and Biomarker Program Overview

CB1 Agonism as New Therapeutic Class to Treat Glaucoma

Reduced IOP and associated mechanisms suggest potential for a novel therapeutic

- Research with THC and other CB1 agonists have highlighted relevant mechanisms to support the use of cannabis as a treatment option
- Multiple clinical trials demonstrate the use of cannabis to reduce IOP
- *Significant hurdles* have prevented meaningful development
  - Side effects with inhalation/systemic delivery
  - Solubility, stability and bioavailability



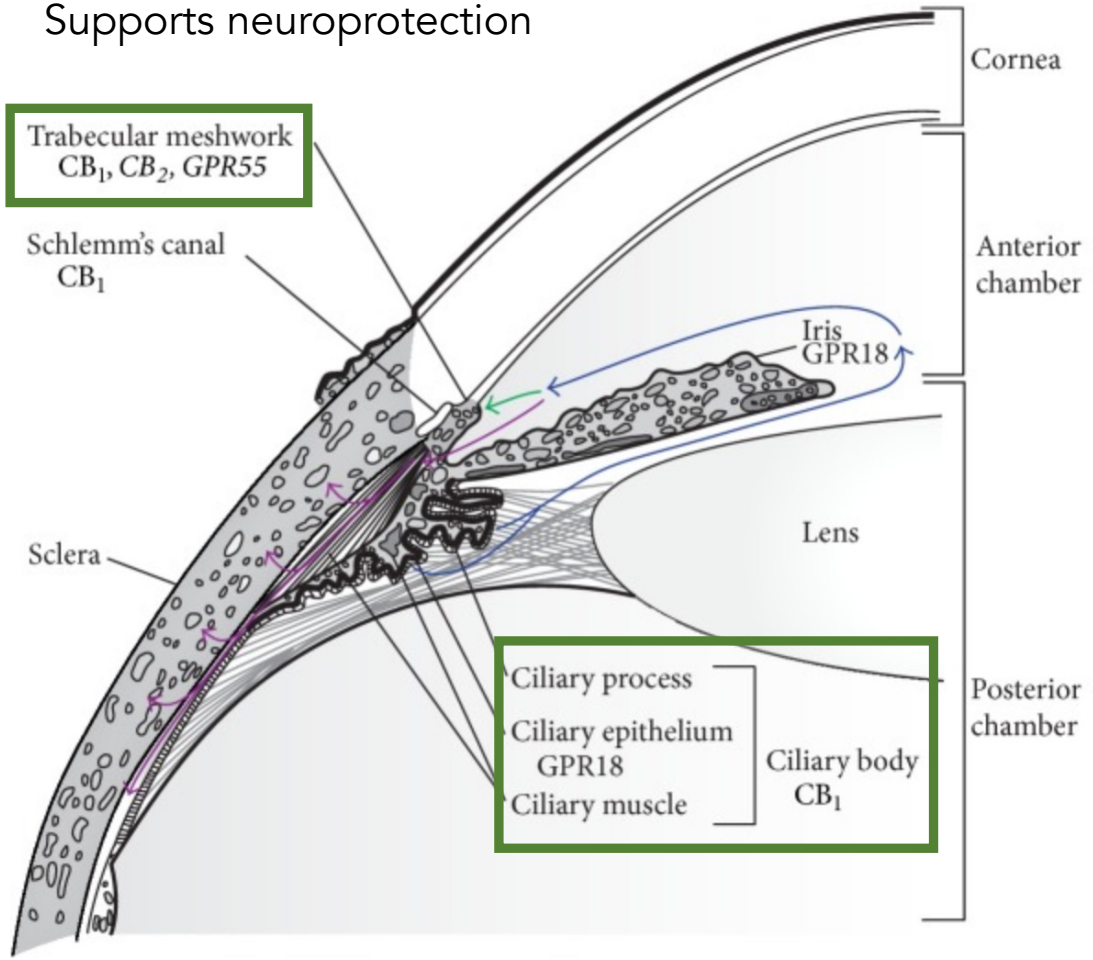
Ocular Effects of Topical Administration of Δ^9-Tetrahydrocannabinol in Man

Keith Green, PhD; Michael Roch, MD

The Effect of Inhaled Cannabis on Intraocular Pressure in Healthy Adult Subjects

CB1 is expressed in key ocular tissues and its engagement[1]:

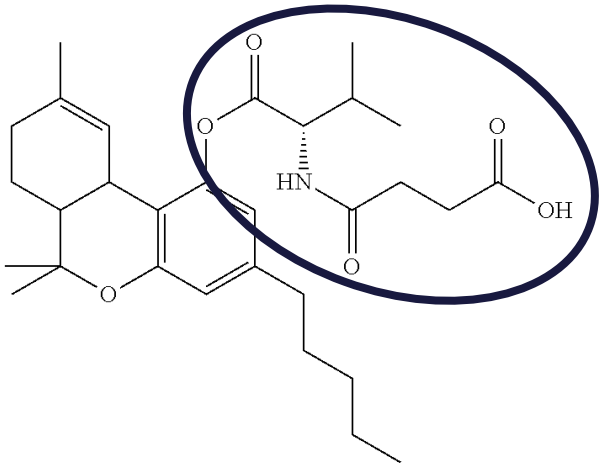
- Reduces aqueous humor ("AH") production
- Promotes AH outflow
- Supports neuroprotection



1: Cairns *et al.*, Source: Neural Plast, 2016

SBI-100 Ophthalmic Emulsion: Synthetic THC-based Prodrug

Prodrug technology and novel formulation addresses hurdles with THC therapeutics

DESIGN FACTOR	RATIONALE	SBI-100 STRUCTURE
Tetrahydrocannabinol (THC)	Therapeutic backbone is not water soluble and has poor bioavailability.	
Prodrug design	Improves solubility, stability and bioavailability. Prodrug moiety is rapidly released once inside the eye.	
Prodrug moiety (valine-hemisuccinate)	Valine-hemisuccinate is added to THC in a scalable and proprietary synthetic method under GMP control.	
Nanoemulsion formulation (ophthalmic emulsion)	Improved delivery of SBI-100 into multiple structures of the eye.	

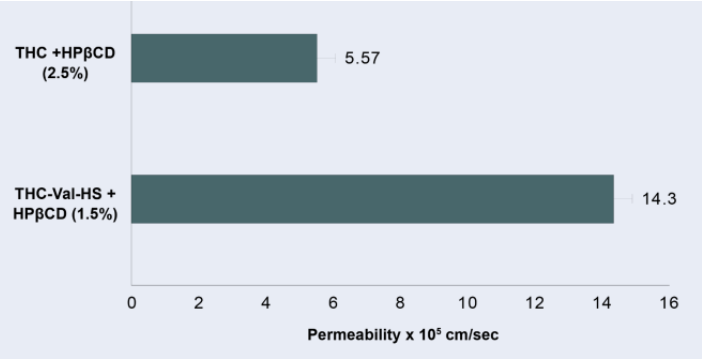
Chemical Formula: $C_{30}H_{43}NO_6$
Molecular Weight: 513.6655
THC-valinate-hemisuccinate (15)

Adelli et al., Invest Ophthalmol Vis Sci, 2017

Prodrug Strategy Enhances Ocular Biodistribution of THC

THC amino dicarboxylic acid prodrugs further enhance bioavailability

- Different prodrug strategies were functionally evaluated *in vitro* and *in vivo*
- Solubility, stability and bioavailability were associated with control of IOP



Increased permeability with THC Val-HS

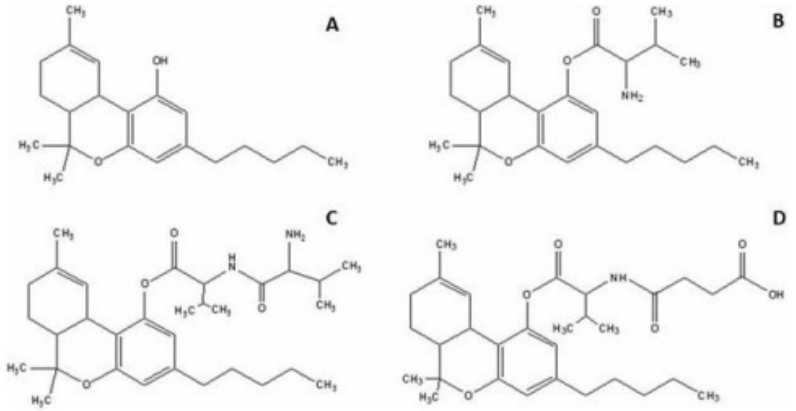


Figure 1. Chemical structures of (**A**) (THC), (**B**) THC-Val, (**C**) THC-Val-Val, and (**D**) THC-Val-HS.

THC Val-HS has superior biodistribution regardless of formulation or dose

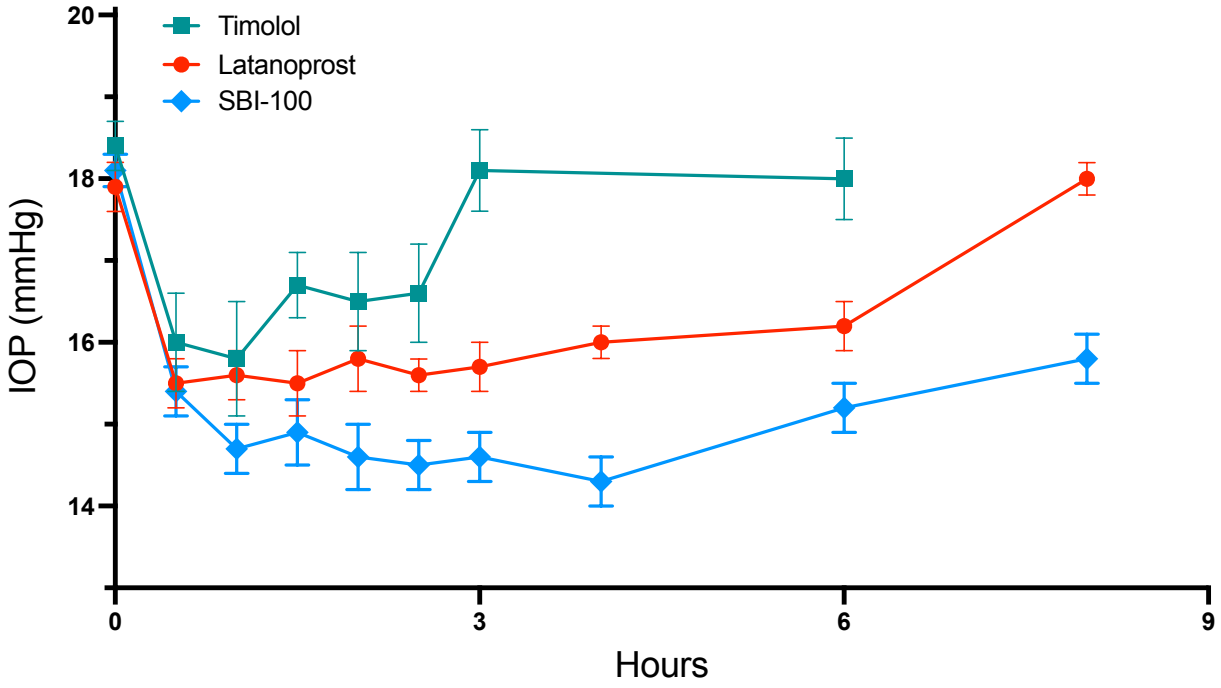
	THC			THC Val-HS		
	Light Mineral Oil	Emulsion	Micellar Solution 1	Cyclodextrin Solution		Micellar Solution 1
Tissue	1 Hour	1 Hour	1 Hour	1 Hour	3 Hours	1 Hour
Drug concentration in terms of THC, % w/v	0.1	0.37	0.125	0.26		0.25
Dose, µg	50	185	62.5	130		125
Cornea, ng/50 mg tissue	68.8 (14.5)	300.6 (79.6)	553.9 (87.4)	1677.1 (172.1)	1142.3 (415.9)	1191. 7 (231.1)
Aqueous humor, ng/100 µL	ND	ND	ND	69.4 (16.7)	38.3 (10.2)	62.1 (12.6)
Iris-Ciliary body, ng/50 mg tissue	ND	ND	ND	65.8 (15.9)	57.9 (16.1)	51.44 (19.5)
Vitreous humor, ng/mL	ND	ND	ND	ND	ND	ND
Retina-Choroid, ng/50 mg tissue	ND	ND	ND	ND	ND	ND
Sclera, ng/250 mg tissue	104.1 (36.1)	171.1 (66.6)	439.3 (280.2)	882.2 (185.8)	241.8 (106.6)	913.4 (432.9)

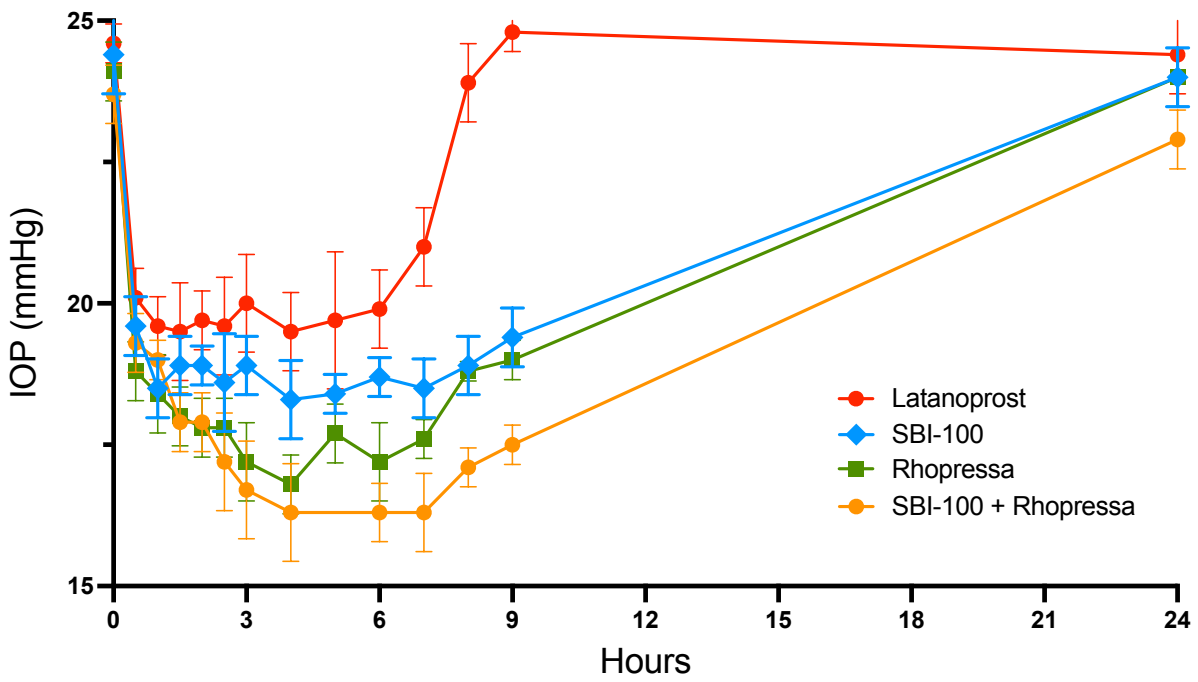
THC Val-HS converts to THC in key tissues

	Molecule			
Tissue	THC-Val-HS		THC	
Time, min	60	120	60	120
Aqueous humor, ng/ 100 µL	9.1*	ND	ND	ND
Iris Ciliary bodies, ng/50 mg	24.2 (8.8)	11.3 (0.9)	53.02 (50.1)	57.4 (32.1)
Retina-Choroid, ng/50 mg	15.5 (11.6)	7.6†	5.2 (0.3)	5.3*

SBI-100 OE Demonstrates Superior IOP Lowering

Nonclinical studies highlight favorable comparison with standard of care drugs





SBI-100 demonstrated superior IOP lowering compared to the leading therapies timolol and latanoprost as a **single agent**

Single dose study with normotensive New Zealand rabbits

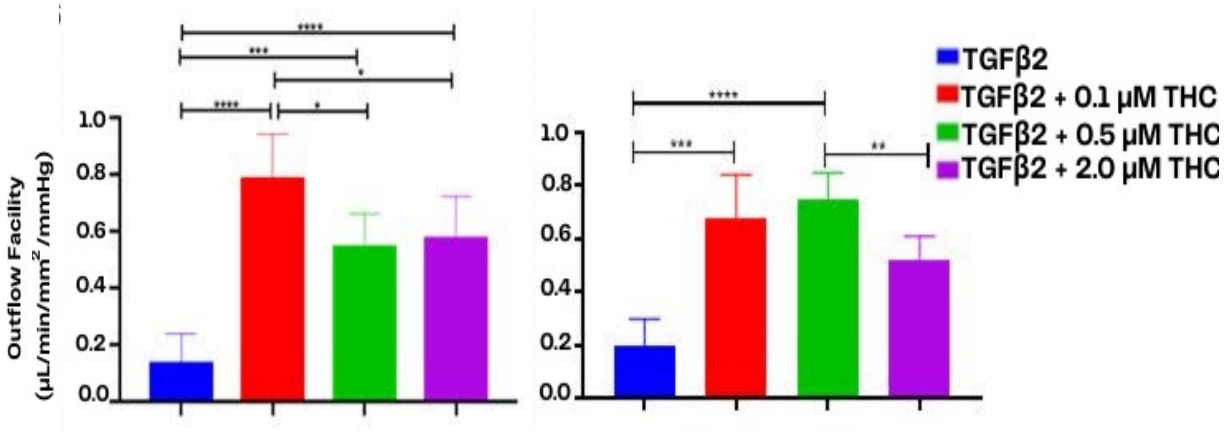
In **combination**, SBI-100 + Rhopressa demonstrated enhanced efficacy, suggesting the potential for clinical combinations

Day 5 multidose study with normotensive New Zealand rabbits

Human Trabecular Meshwork Model Highlights Key Mechanism of Action

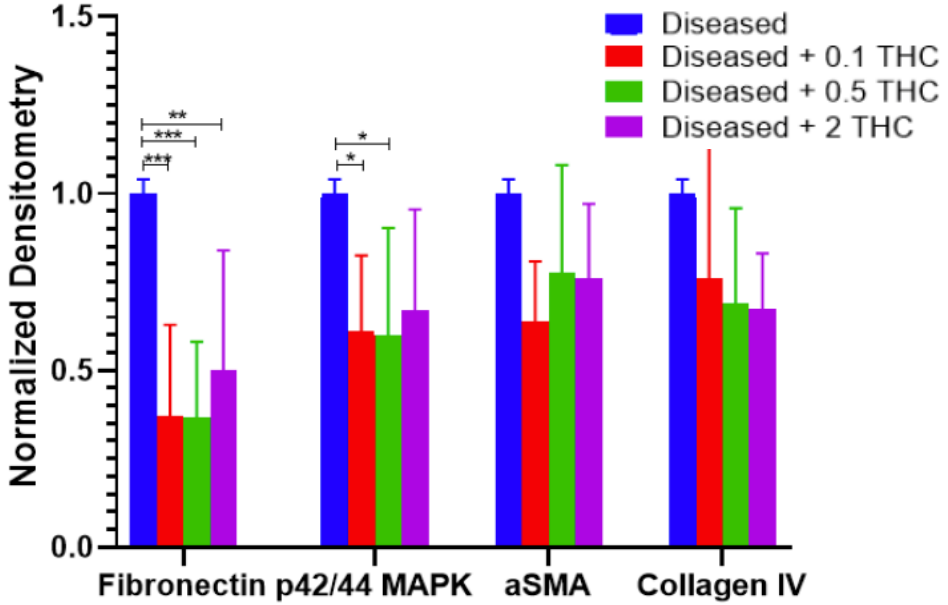
Measuring outflow facility via trabecular meshwork

- Both human 3D models demonstrated a significant increase of outflow with SBI-100's active pharmaceutical agent across all doses
- Outflow of aqueous humor via TM is a principal driver of maintaining physiological levels of IOP



Reduced markers of inflammation & fibrosis

- Significant reduction in fibrotic and inflammatory proteins after 6 days of treatment
- Suggest a complementary disease-modifying mechanism distinct from existing IOP-lowering drugs



Source: IOP lowering ability of SBI-100 active moiety, THC, in a human tissue model. Torrejon et al., Glauconix Biosciences. 2019 Oct
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Potential Neuroprotective Benefits with SBI-100

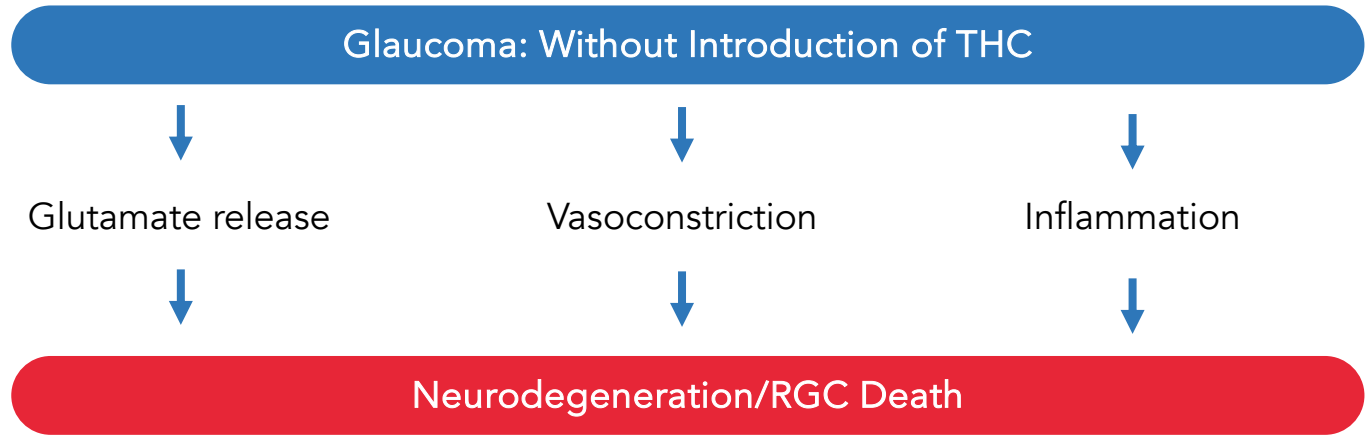
Additional complementary therapeutic mechanism to address associated neuropathy

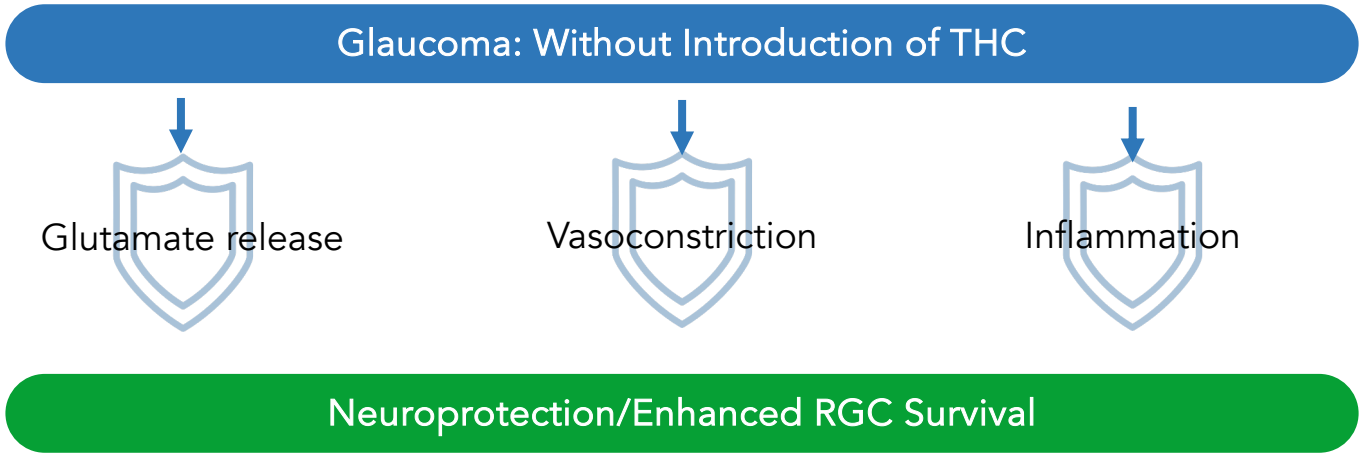
Biodistribution studies demonstrated the presence of SBI-100 OE in the back of the eye

SBI-100 OE's active ingredient, THC, can reduce neurodegenerative mechanisms and preserve RGCs

Potential to modulate 3 key processes that promote neurodegeneration and death of retinal ganglion cells:

- Destructive glutamate release[1]
- Vasoconstriction of optic nerve[2]
- Inflammation[3]





Crandall et al., Ophthalmic Res 2007;39:69-75
1: El-Remessey et al., Am. J. Pathol. 2003 Nov;163(5):1997-2008
2: Green et al., Exp.Eye Res. 1978;26:65-69
3: Krishnan et al., Neuroscience. 2015;284:536-545

Clinical Biomarker Program to Support SBI-100 OE

Analyses of immunological and neuroprotective markers in tear and blood components

Unlike a typical biomarker program, our rationale is not to develop patient selection or early response markers but to support a differential MOA relative to other classes of therapeutics

Serum/Tear Analyses

- Multiplex proteomics
  - Olink - target 96 inflammation/neurology panels
  - Cytokine analysis – MSD inflammatory panel (Th1/Th2/Th17 + TGFb/IL-1/IL-6)
- ELISA
  - Neuroprotection: endothelin-1/myelin basic protein
  - Inflammatory: HSP60 + anti-SSA/B, anti-αfodrin, and anti-nucleic acid antibodies

PBMC Analyses

- Frequency and activation status (phenotype) of $CD8^+/CD4^+$ T cells, Treg and B cells.
- Functional immune response: cytokine production with HSP, retinal ganglion cells and polyclonal stimulations

Lommatzsch et al., Sci Rep 2022
Yang et al., Invest Ophthalmol Vis Sci. 2019
Grus et al., Invest Ophthalmol Vis Sci 2006
Wax et al., Am J Ophthalmol 1998
Shin et al., Diagnostics 2021

Near-term R&D Efforts Support Pipeline Development

Glaucoma

- Biomarker program: analysis of bio-samples from Ph2 glaucoma clinical trial
- Preclinical studies to further SBI-100 development
  - Combination studies with 1L/2L glaucoma drugs in normotensive and glaucomatous models
  - Mechanistic studies to interrogate contribution of AH production/outflow and neuroprotection

Other Ocular Diseases

- Cannabinoid Pharmaceutical Innovation Program (CPIP)
  - Skye has designed/screened a library of novel molecules for the treatment of chronic ocular pain and dry eye disease
  - Currently selecting lead clinical candidates:
    - Disease-specific mechanistic studies *in vitro/ex vivo* (2D and 3D models)
    - *In vivo* models to benchmark efficacy
- Skye is developing this class of therapeutics for chronic ocular pain post-corneal refractive surgery as well as to treat keratopathies associated with specific oncology treatments.

SBI-100 OE: Development Plan for Glaucoma and Ocular Hypertension

Phase 1 Clinical Data and Phase 2 Update

Overview

Phase 1 Study Design, Purpose and Rationale

Inclusion/Exclusion Criteria

Safety Assessments

SAD/MAD Safety Data

PK Data

Intraocular Pressure Analysis

Phase 2a Study and Next Steps

History and Safety of THC/Cannabis

- Marinol (dronabinol) approved in 1985 for use anorexia associated weight loss in patients with AIDS and nausea and vomiting associated with chemotherapy.
- The side effects of systemic THC are well characterized.
- Cannabis has been used both recreationally and medicinally for centuries and the effects of smoking cannabis or ingesting it in other ways are also well established.

Dronabinol/THC

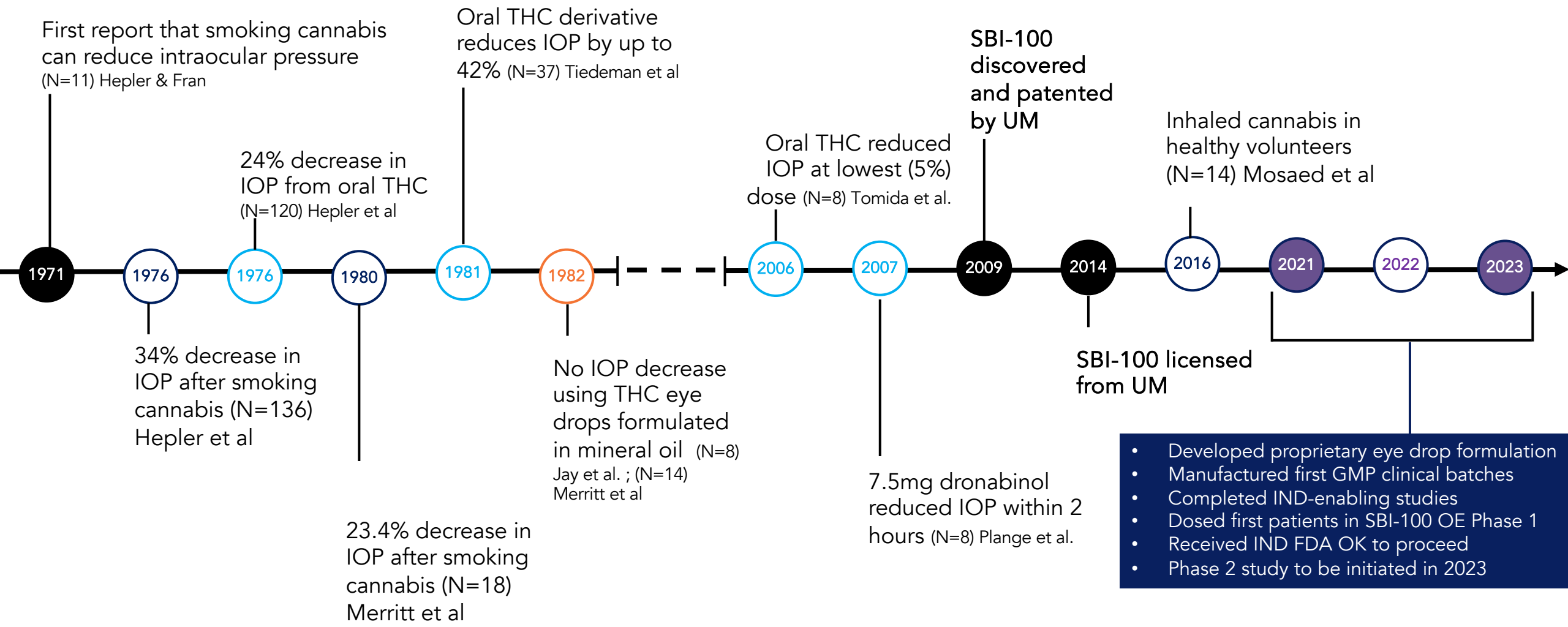
Common Side Effects
Nausea and vomiting
Anxiety
Confusion
Sleepiness
Difficulty concentrating
Unsteady walking
Feeling outside of your body
"High" elevated mood
Hallucinations
Depression
Headaches
Vision problems
Weakness
Stomach pain

Potential Serious Adverse Effects
Seizures
Fainting
Tachycardia

The purpose of this Phase 1 study was to evaluate both local (ocular) and systemic (non-ocular) safety of SBI-100 OE when given to healthy volunteers as a topical eye drop.

History of Cannabis in Glaucoma

Since 2021 Skye has rapidly progressed SBI-100 OE into the clinic

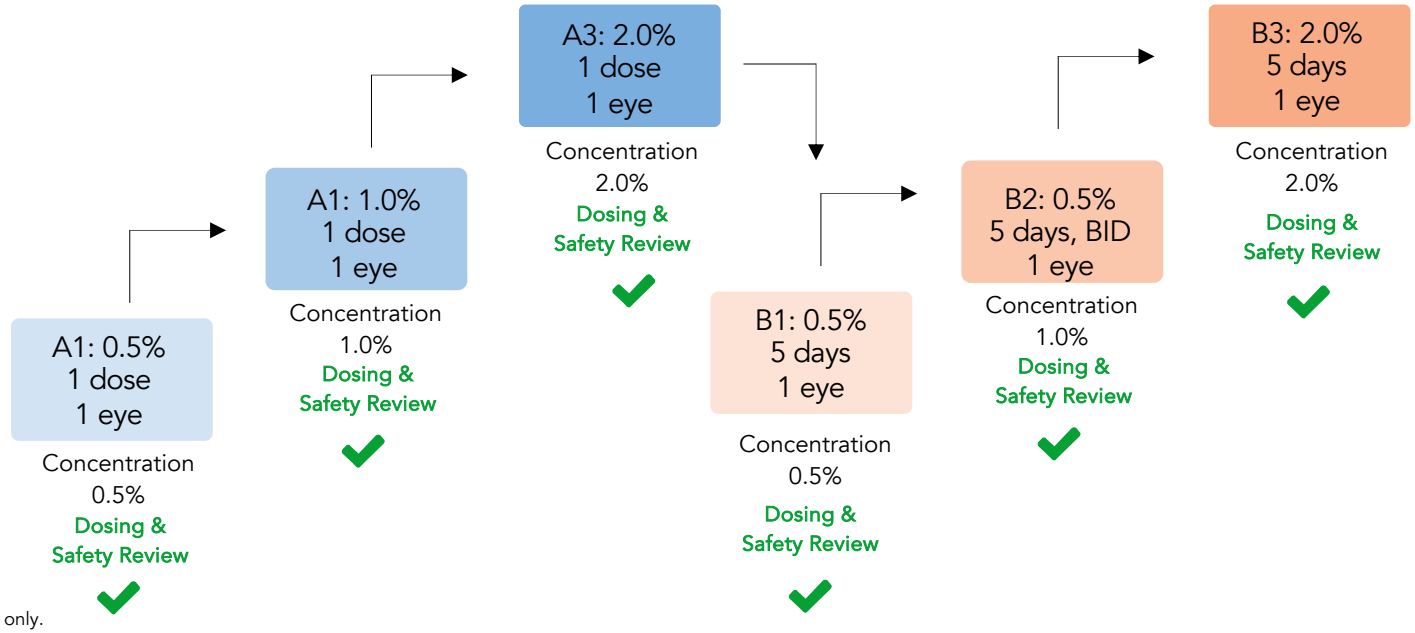


Clinical Trial Design– SAD/MAD Randomized Placebo-Controlled

- Randomized, placebo-controlled study in up to 48 healthy volunteers across 6 treatment cohorts.
- Primary objective: establish safety and tolerability of single ascending and multiple ascending doses of SBI-100 Ophthalmic Emulsion relative to placebo

SAD
1 single dose in right eye of starting at 5.0 mg/mL (0.5%) SBI-100

MAD
5 days of twice daily dosing in right eye starting at 5.0 mg/mL (0.5%) SBI-100



Dose Escalation Scheme

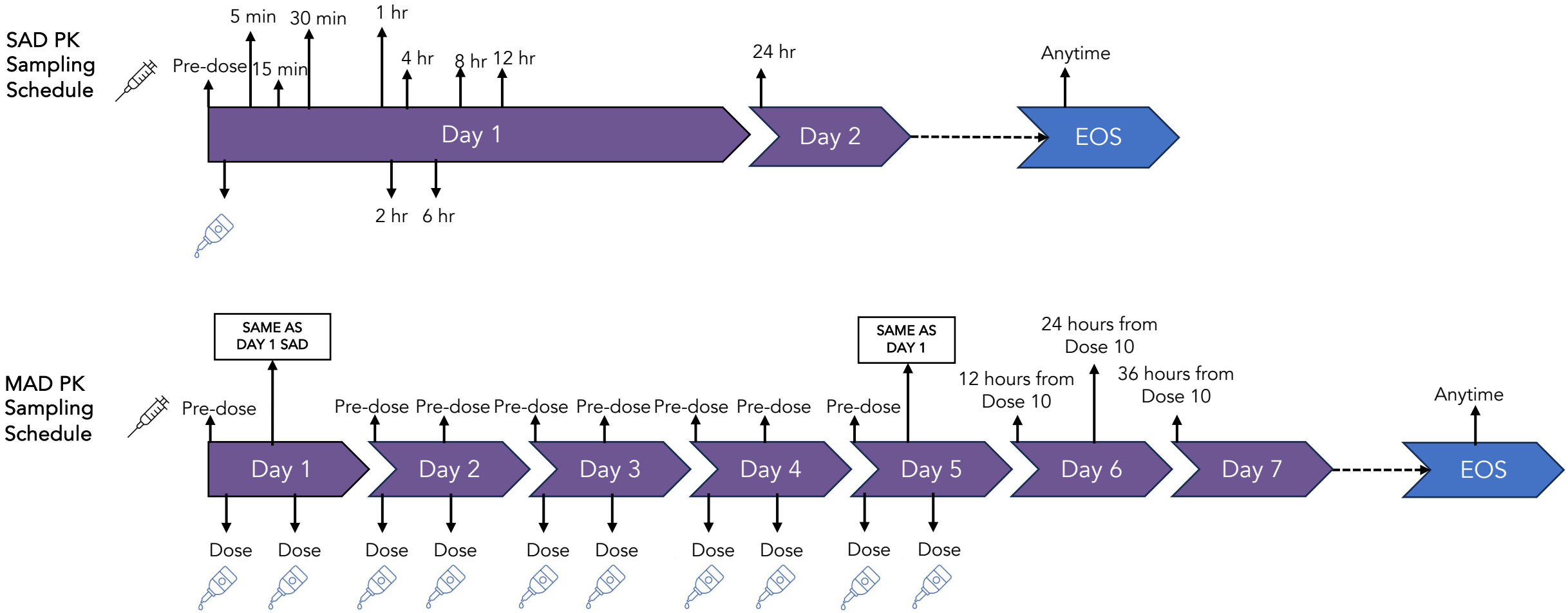
Cohort	Dose Level & Frequency	Number of Participants (N)
A1 (SAD)	1 single dose (1 drop) in right eye of 5.0 mg/mL (0.5%)	8
A2 (SAD)	1 single dose (1 drop) in right eye of 10.0 mg/mL (1.0%)	8
A3 (SAD)	1 single dose (1 drop) in right eye of 20.0 mg/mL (2.0%)	8
B1 (MAD)	5 days x 1 drop BID in right eye of 5.0 mg/mL (0.5%)	8
B2 (MAD)	5 days x 1 drop BID in right eye of 10.0 mg/mL (1.0%)	8
B3 (MAD)	5 days x 1 drop BID in right eye of 20.0 mg/mL (2.0%)	8

Each SAD cohort had 8 participants with 2 sentinels (1 placebo, 1 active). The remaining 6 participants were dosed upon PI assessment of safety and tolerability of the sentinels. If the PI determined there were no clinically significant issues (this will be documented in an email format), the remaining participants were dosed at least 48 hours after dosing of the sentinels.

SRC meeting: data up to Day 2 for SAD and Day 7 for MAD from at least 6 of the 8 participants were required to be available for the safety review committee to approve the next cohort.

Pharmacokinetics – Dosing and PK Sampling Plan

Plasma samples analyzed for SBI-100, THC and 11-OH-THC



Key Inclusion Criteria

1. Male or female, 18 to 60 years of age at screening.
2. IOP as measured by iCare tonometer in each eye of ≥ 10 to ≤ 21 mmHg with a difference of ≤ 3 mmHg between each eye at screening and Day -1 (pre-dose).
3. Central corneal thickness in each eye ≥ 500 µm and ≤ 600 µm as measured by optical coherence tomography (OCT) at Screening.
4. Habitual visual acuity (VA) in each eye of 20 /40 or better at screening and Day -1.
5. Medically healthy with no clinically significant findings on medical history, physical examination, vital signs, ECGs, or laboratory tests, in the opinion of the Investigator or designee at Screening that would interfere with the study.
6. Medically healthy eye condition with two normal (non-diseased) eyes, with no clinically significant or anatomical ocular abnormalities in the opinion of the Investigator or designee that would interfere with the study.

Key Exclusion Criteria

1. Unable to discontinue contact lens use during study visits including confinement at the study site.
2. Previous ocular surgery: glaucoma surgery, glaucoma laser procedures, cataract or refractive surgery (e.g., radial keratotomy, photorefractive keratectomy, or laser in situ keratomileusis), and post-YAG laser capsulotomy after cataract surgery, within past 12 months.
3. Recent (within 3 months prior to screening) or current evidence of ocular infection or inflammation in either eye (such as current evidence of clinically significant blepharitis, conjunctivitis, or keratitis).
4. History of clinically significant optic nerve disease (eg, optic neuritis, papilledema, glaucomatous optic neuropathy, ischemic optic neuropathy, etc.).
5. Visual field defect in either eye as determined by automated visual field analysis
6. Use of ophthalmic topical steroids, topical non-steroidal anti-inflammatories, or ocular hypotensive medications within past 3 months prior to screening
7. Unable to abstain from the use of cannabis and other cannabinoid compounds (other than the study drug) from the time of Screening until after the EOS visit.
8. Known hypersensitivity reaction or allergy to cannabinoids or cannabis or to any component of the SBI 100 formulation including sesame seed/oil.

Ocular Assessments – Slit Lamp

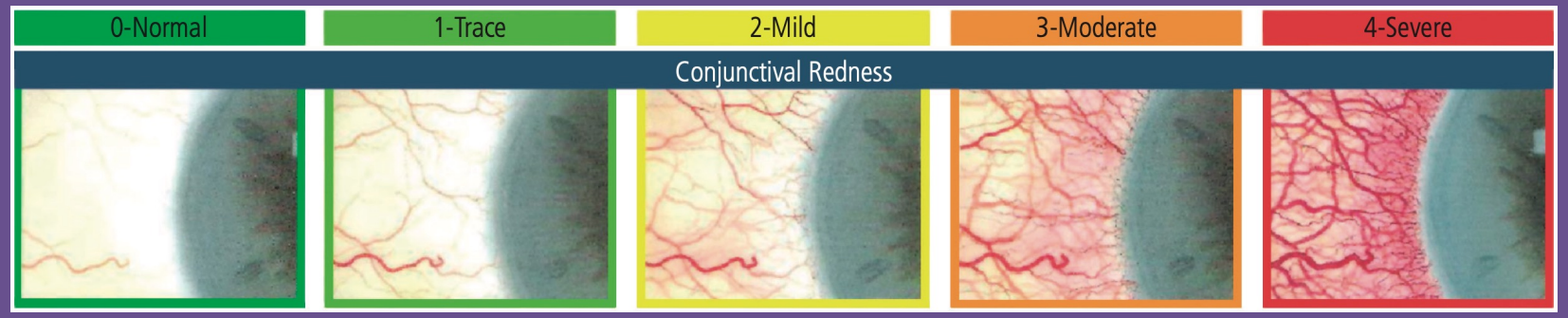
Evaluation of anterior segment of the eye:

- Lids
- Cornea
- Conjunctiva
- Anterior chamber
- Iris
- Lens
- Posterior capsule

Ocular Assessments – Conjunctival Hyperaemia

Conjunctival hyperaemia was assessed using the Efron grading scale[1].

Efron Grading Scales for Contact Lens Complications



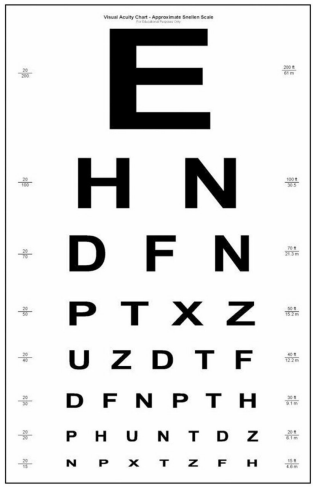
Hyperaemia is one of the main reasons that patients stop treatment.

Hyperaemia results in increased overall costs for patients, almost doubling the costs for some patients[2].

Source:
1: Efron N, Morgan PB, Katsara SS. Validation of grading scales for contact lens complications. Ophthal Physiol Opt. 2001; 21:17-29.
2. Schwartz et al., Hyperemia-associated costs of medication changes in glaucoma patients treated initially with prostaglandin analogs. J Ocul Pharmacol Ther. 2009 Dec;25(6):555-61.

Ocular Assessments – IOP, Visual Acuity, Visual Field, Pupil Diameter and Oct

Visual Acuity	Visual Field	Intraocular Pressure	Pupil Diameter	Optical Coherence Tomography (OCT)



Clinical Trial Partners

Partner	Role
innovative EYE CARE	Ophthalmology assessments
Government of South Australia Health Central Adelaide Local Health Network	IP management/pharmacy – Royal Adelaide Hospital Pharmacy
AUSTRALIAN Clinicalabs	Local laboratory
AGILEX BIOLABS	Pharmacokinetic analysis
AmerisourceBergen World Courier	Shipping and courier services
TRIALWISE	Data management and biostats
NT NOVOTECH The Asia Pacific CRO	Contract research organization
CMAX CLINICAL RESEARCH I'ROM GROUP	Phase 1 clinical research unit

Patient Demographics - SAD

	SBI-100 Ophthalmic Emulsion Single Ascending Dose (SAD)				
	SBI-100 0.5% (N=6)	SBI-100 1% (N=6)	SBI-100 2% (N=6)	SAD Placebo (N=6)	SAD Overall (N=24)
Sex					
Male	0	4 (66.7%)	1 (16.7%)	4 (66.7%)	9 (37.5%)
Female	6 (100%)	2 (33.3%)	5 (83.3%)	2 (33.3%)	15 (62.5%)
Age					
Mean (SD)	32.5 (12.3)	34.0 (13.2)	29.3 (5.9)	29.2 (12.4)	31.3 (10.8)
Median	32.5	30.0	30.0	24.5	28.5
Corneal Thickness (µm)					
Right Eye					
Mean (SD)	559.5 (16.2)	546.5 (32.4)	561.8 (19.3)	536.8 (18.4)	551.2 (23.4)
Median	561.0	554.0	556.5	530.5	552.5
Left Eye					
Mean (SD)	556.8 (28.9)	546.7 (34.0)	558.8 (17.9)	540.5 (14.8)	550.7 (24.7)
Median	562.0	557.0	552.0	536.0	550.0
Baseline IOP (mmHg)					
Right Eye					
Mean (SD)	14.72 (2.26)	12.45 (1.27)	16.03 (2.63)	13.42 (3.74)	14.40 (2.51)
Median	13.90	12.75	15.95	12.10	13.90
Left Eye					
Mean (SD)	16.73 (2.97)	13.05 (2.28)	14.23 (3.33)	13.30 (3.95)	14.67 (3.14)
Median	16.10	12.15	13.30	11.90	14.40

Study Eye (Low baseline IOP)

Treatment Emergent Adverse Events – by System Organ Class SAD

SYSTEM ORGAN CLASS PREFERRED TERM	Non-Ocular TEAEs by MedDRA System Organ Class and Preferred Term SAD Placebo (N=6)	 SAD Overall (N=24)
General disorders and administration site conditions		
Catheter site pain	1 (16.7%)	2 (8.3%)
Vessel puncture site bruise	1 (16.7%)	2 (8.3%)
Nervous system disorders		
Headache	0	1 (4.2%)
Somnolence	0	1 (4.2%)
Musculoskeletal and connective tissue disorders		
Back pain	0	1 (4.2%)
Skin and subcutaneous tissue disorders		
Dermatitis contact	0	1 (4.2%)

SYSTEM ORGAN CLASS PREFERRED TERM	Ocular TEAEs by MedDRA System Organ Class and Preferred Term SAD Placebo (N=6)	 SAD Overall (N=24)
General disorders and administration site conditions		
Instillation site pain	4 (66.7%)	16 (66.7%)
Instillation site foreign body sensation	0	2 (8.3%)
Instillation site discomfort	0	1 (4.2%)
Eye disorders		
Corneal oedema	1 (16.7%)	2 (8.3%)
Punctate keratitis	0	2 (8.3%)
Asthenopia	0	1 (4.2%)
Blepharitis	0	1 (4.2%)
Conjunctival hyperaemia	0	1 (4.2%)
Eye pain	1 (16.7%)	1 (4.2%)

Not related to treatment.
Occurred after end of therapy visit.

Discomfort due to instillation of eye drop was main drug-related adverse event

Patient Demographics - MAD

	SBI-100 Ophthalmic Emulsion Multiple Ascending Dose (MAD)				
	SBI-100 0.5% (N=6)	SBI-100 1% (N=6)	SBI-100 2% (N=6)	MAD Placebo (N=6)	MAD Overall (N=24)
Sex					
Male	4 (66.7%)	3 (50.0%)	5 (83.3%)	5 (83.3%)	17 (70.8%)
Female	2 (33.3%)	3 (50.0%)	1 (16.7%)	1 (16.7%)	7 (29.2%)
Age					
Mean (SD)	31.8 (4.0)	30.3 (7.2)	36.0 (7.9)	33.2 (9.0)	32.8 (7.1)
Median	31.5	28.0	36.0	35.5	33.0
Corneal Thickness (µm)					
Right Eye					
Mean	538.5 (28.3)	575.5 (20.9)	545.7 (24.1)	543.5 (26.4)	550.8 (27.7)
Median	531.5	581.5	541.0	545.5	550.0
Left Eye					
Mean	537.5 (33.2)	571.2 (21.5)	544.7 (29.9)	541.5 (29.9)	548.7 (30.2)
Median	532.5	574.0	541.0	537.5	545.0
Screening IOP (mmHg)					
Right Eye					
Mean	16.40 (2.76)	15.38 (3.69)	14.15 (1.72)	14.60 (3.14)	15.31 (2.83)
Median	17.00	16.45	14.00	14.45	15.65
Left Eye					
Mean	16.77 (2.12)	14.42 (2.71)	14.45 (2.66)	14.43 (3.49)	15.21 (2.62)
Median	16.85	15.00	13.70	13.95	15.15

Study Eye (Low baseline IOP)

Treatment Emergent Adverse Events – by System Organ Class MAD

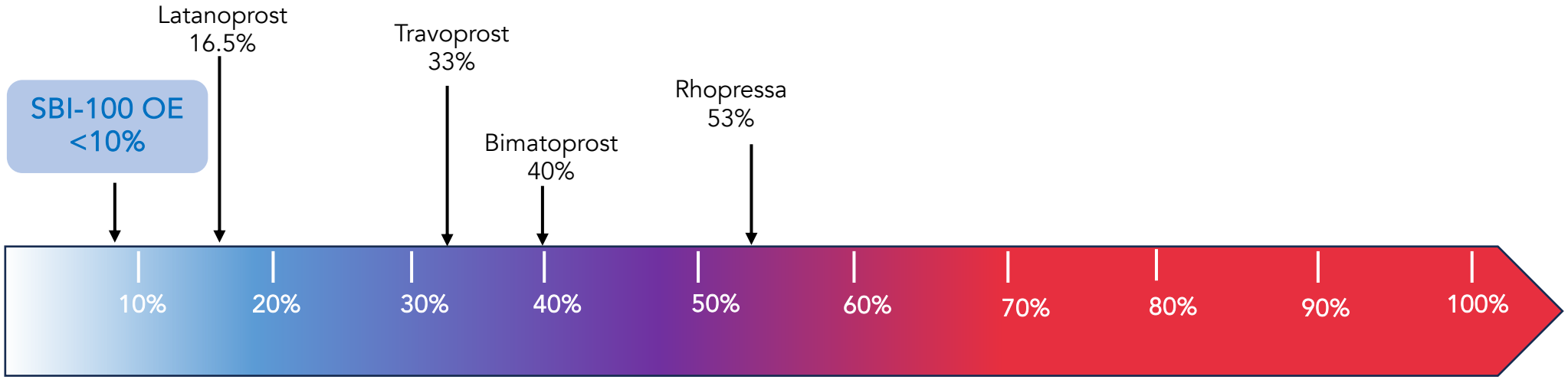
SYSTEM ORGAN CLASS PREFERRED TERM	Non-Ocular TEAEs by MedDRA System Organ Class and Preferred Term MAD Placebo (N=6)	 MAD Overall (N=24)
General disorders and administration site conditions		
Catheter site pain	1 (16.7%)	2 (8.3%)
Fatigue	0	1 (4.2%)
Vessel puncture site bruise	0	1 (4.2%)
Vessel puncture site erythema	0	1 (4.2%)
Nervous system disorders		
Headache	0	3 (12.5%)
Amnesia	0	1 (4.2%)
Somnolence	0	1 (4.2%)
Infections and infestations		
COVID-19 and/or Flu	1 (16.7%)	2 (8.3%)
Musculoskeletal and connective tissue disorders		
Back pain	0	1 (4.2%)
Pain in extremity	0	1 (4.2%)
Skin and subcutaneous tissue disorders		
Dermatitis contact	1 (16.7%)	2 (8.3%)

SYSTEM ORGAN CLASS PREFERRED TERM	Ocular TEAEs by MedDRA System Organ Class and Preferred Term MAD Placebo (N=6)	 MAD Overall (N=24)
General disorders and administration site conditions		
Instillation site pain	3 (50.0%)	19 (79.2%)
Instillation site discomfort	3 (50.0%)	13 (54.2%)
Instillation site foreign body sensation	1 (16.7%)	7 (29.2%)
Instillation site erythema	0	3 (12.5%)
Instillation site pruritis	0	1 (4.2%)
Eye disorders		
Conjunctival hyperaemia	0	2 (8.3%)
Abnormal sensation in the eye	0	1 (4.2%)
Asthenopia	0	1 (4.2%)
Blepharospasm	0	1 (4.2%)
Eyelid irritation	0	1 (4.2%)
Lacrimation increased	0	1 (4.2%)
Ocular discomfort	0	1 (4.2%)
Ocular hyperaemia	0	1 (4.2%)
Punctate keratitis	0	1 (4.2%)
Visual acuity reduced	0	1 (4.2%)

Two cases of hyperaemia
Pain on instillation of eye drop was most reported AE

SBI-100 OE Demonstrates Significantly Less Hyperaemia Compared to Other Therapies

Incidence of Hyperaemia in Currently Approved Drugs vs. SBI-100 OE

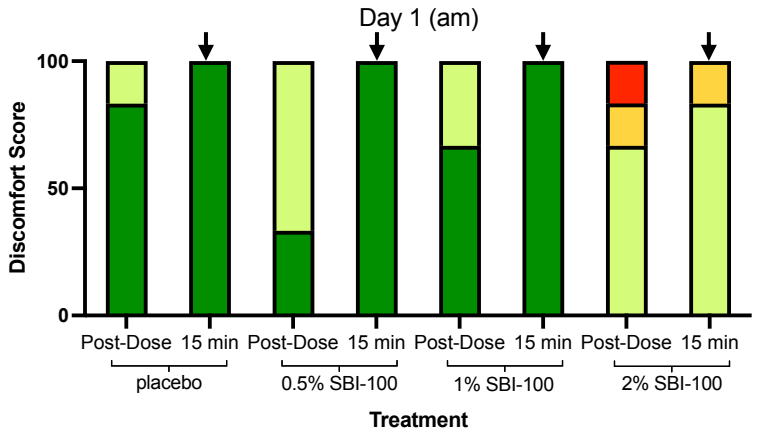


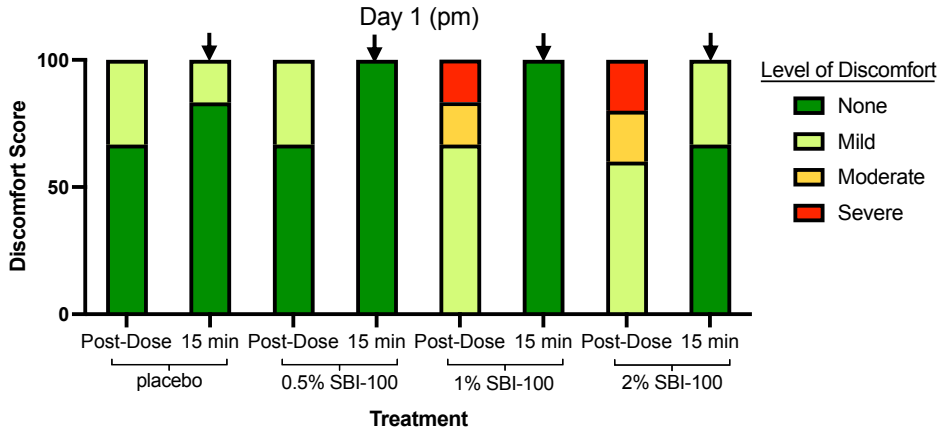
For investor audiences only.

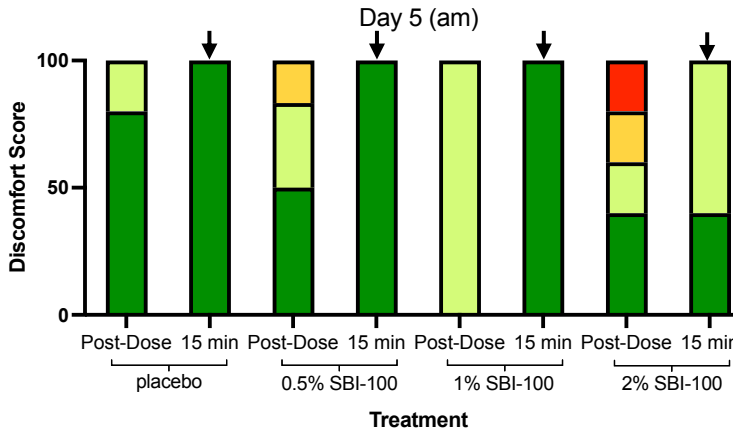
Honrubia et al., Br J Ophthalmol. 2009 Mar; 93(3): 316–321

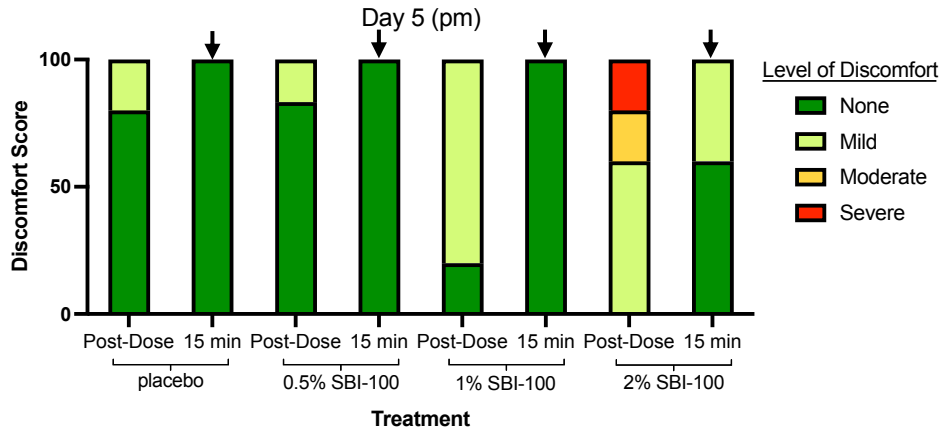
Rhopressa® (netarsudil ophthalmic solution) 0.02% Prescribing Information, Aerie Pharmaceuticals, Inc., Irvine, Calif. 2019

MAD Day 1 & 5 – Discomfort is Transient and Quickly Resolves









Discomfort/pain upon instillation was usually mild and any discomfort was transient and resolved on average in less than 15 minutes.

Pharmacokinetics – Little to no Exposure of THC in Plasma

MAD PK population

	0.5% SBI-100 N=6	1.0% SBI-100 N=6	2.0% SBI-100 N=6
Day 1 PK Parameters, Mean (SD)			
AUC (h*ng/mL) SBI-100	0.9184 (0.4252)	0.8252 (0.2533)	2.131 (1.139)
Cmax (ng/mL) SBI-100	0.2742 (0.07336)	0.2973 (0.1103)	0.7202 (0.3403)
Day 5 PK Parameters, Mean (SD)			
AUC (h*ng/mL) SBI-100	3.003 (1.014)	1.948 (0.6637)	4.459 (3.025)
Cmax (ng/mL) SBI-100	0.5066 (0.1285)	0.4875 (0.1587)	0.8672 (0.6459)
Tmax (h) SBI-100	0.500 (0.000)	0.417 (0.129)	0.550 (0.274)

- SBI-100 OE was detected in plasma of all cohorts.
- However, THC and its more psychoactive metabolite 11-OH-THC were not detected across all cohorts (except one patient in the 1.0% SBI-100 OE cohort [M2-04]).
- Lack of THC and 11-OH-THC detected in plasma support the minimal systemic side effects observed.

Intraocular Pressure Analysis – Full Population

Low baseline IOP across all subjects

- Historically, glaucoma drugs do not significantly reduce IOP in healthy volunteers
- Participants receiving placebo and active had similar reductions in IOP.
- This is potentially due to the lower baseline IOP measured across all participants.

Treatment (N)	Mean Baseline IOP (mmHg)	Mean reduction of all IOP Measurements Post-Dose 1 (mmHg)*
Placebo (6)	14.6	-2.02
Active (18)	15.3	-1.99

**Baseline IOP measured on Day 1 prior to first dose (approximately 8am)*
***IOP measured at Pre-dose, 1hr, 2hr, 4hr and 8hr post-dose each day*

Subgroup Analysis[1] – "High IOP"

- Because of the relatively low mean baseline IOP in this healthy volunteer population, we did not see any significant reductions in IOP when evaluating active against placebo.
- A subgroup analysis of participants with "high" baseline IOP was evaluated.
- We evaluated participants with baseline IOP of 17mmHg or greater.
  - 1 placebo participant; 5 active participants

Patient#	Treatment	Baseline IOP (mmHg)	Mean reduction of all IOP Measurements Post-Dose 1 (mmHg)*	% IOP Reduction
M1-01	Placebo	19.2	-2.8	14%
M1-03	0.5% SBI-100	17.7	**-4.5**	**25%**
M1-04	0.5% SBI-100	19.3	**-4.5**	**23%**
M1-07	0.5% SBI-100	18.9	**-5.9**	**31%**
M2-02	1.0% SBI-100	17.4	**-4.2**	**24%**
M2-03	1.0% SBI-100	18.9	**-2.6**	**14%**

***IOP measured at Pre-dose, 1hr, 2hr, 4hr and 8hr post-dose each day**

For investor audiences only.
1: A subgroup analysis of participants, not pre-specified in the trial design, with "high" baseline IOP was evaluated.

SBI-100 OE: Phase 1 Safety Clinical Data Summary

- **Good Safety Profile:** Generally safe and well-tolerated. No participants dropped out due to SBI-100 OE
- **Transient Discomfort:** Main side effect is discomfort/pain upon drop instillation, but average duration of discomfort was less than 15 minutes.
- **Lack of Systemic Side Effects:** Little to no presence of THC in plasma following multi-day dosing supports lack of systemic side effects observed in Phase 1 study.
- **Minimal Hyperaemia:** Little to no hyperaemia compared to other leading classes of drugs.
- **Efficacy:** IOP data suggests encouraging activity in participants with high baseline IOP (>17 mmHg)

SBI-100 OE Phase 2A Glaucoma Proof-of-Concept Study

Primary open-angle glaucoma and ocular hypertension

Key Inclusion Criteria

21mmHg ≥ IOP < 34mmHg

No prior surgical interventions for POAG or OHT

Primary Endpoint

Change in diurnal IOP vs placebo

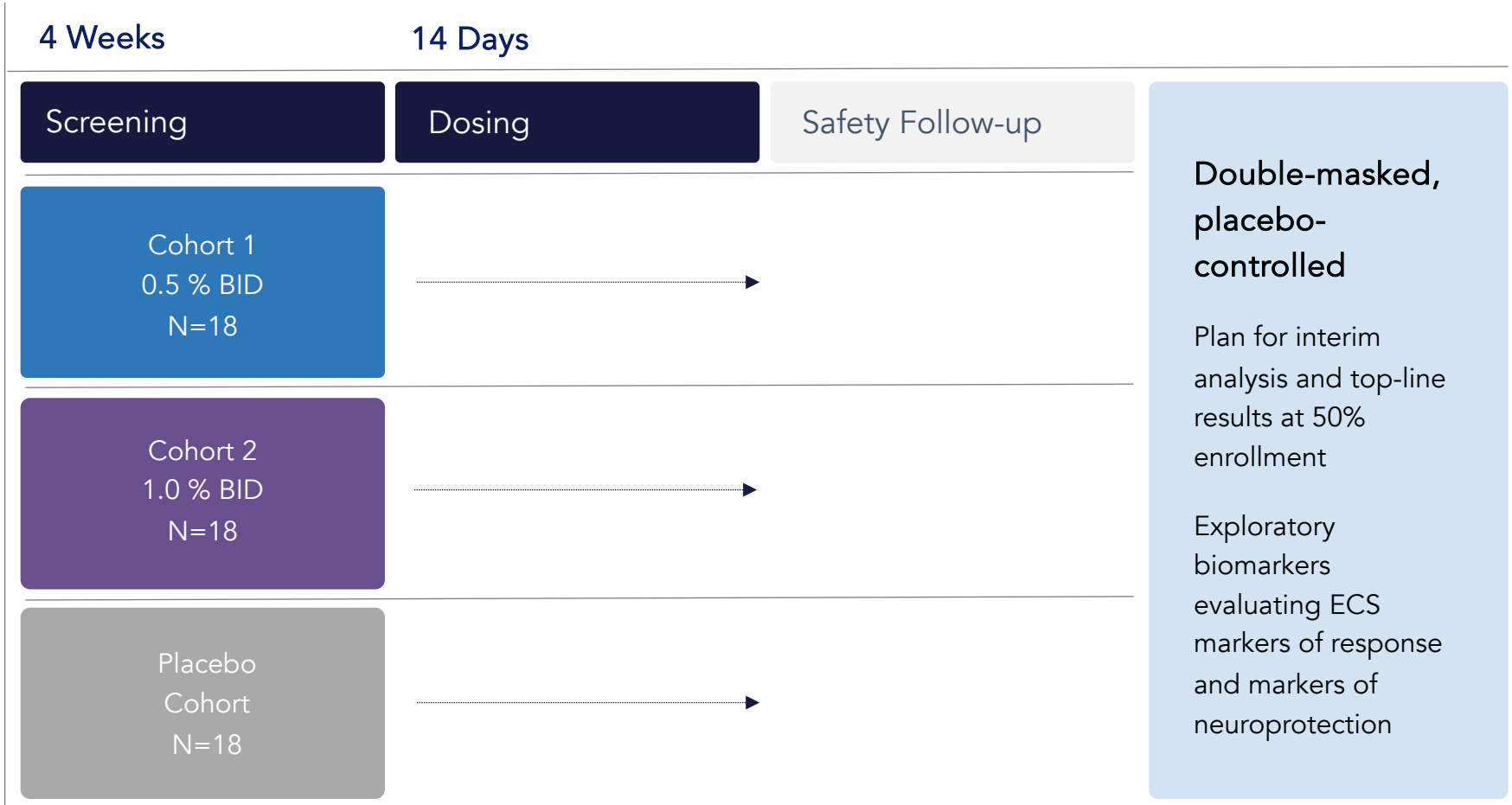
Secondary Endpoint

Safety and tolerability

Evaluation of psychotropic effects

Change in diurnal IOP from baseline

Exploratory biomarkers



Double-masked, placebo-controlled

Plan for interim analysis and top-line results at 50% enrollment

Exploratory biomarkers evaluating ECS markers of response and markers of neuroprotection

Source: Company data. For investor audiences only.

SBI-100 OE – Target Product Profile

POPULATION

Treatment to lower IOP in patients with ocular hypertension and primary open-angle glaucoma following recurrence or failure with first-line therapy

MECHANISM OF ACTION

CB-1 receptor agonist

DOSING & ADMINISTRATION

Single topical drop once per day

PIVOTAL STUDY DESIGN

Non-inferiority study against standard of care second-line therapy (timolol)

EFFICACY

Reduction in IOP of at least 20%

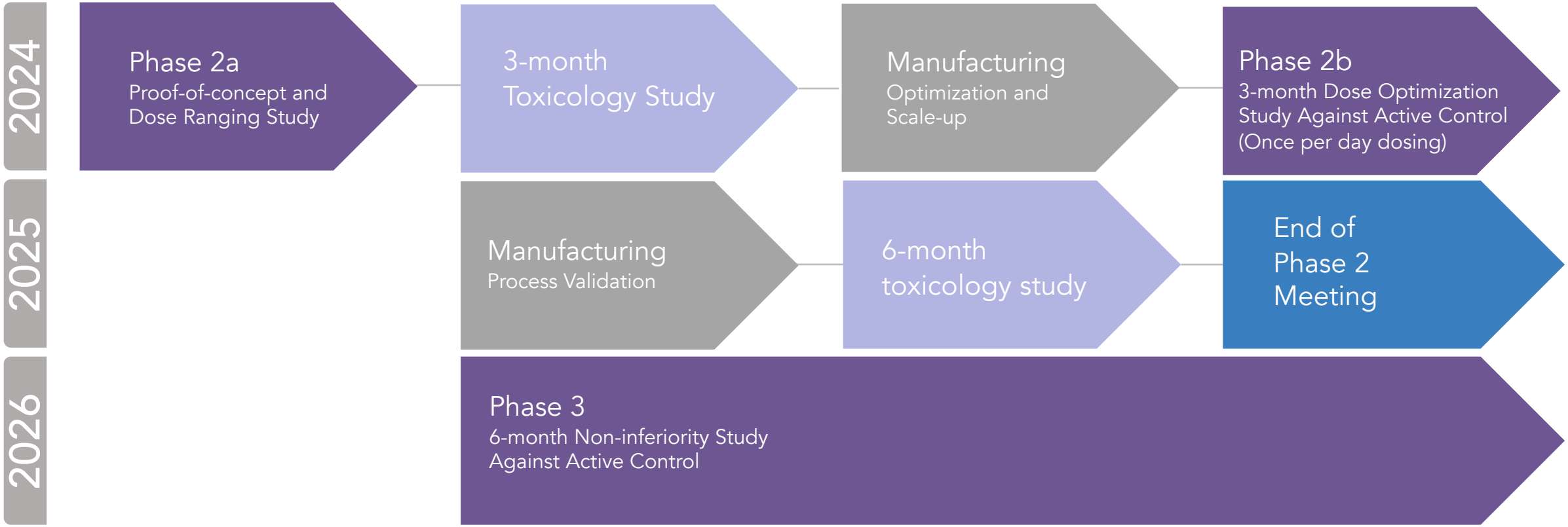
SAFETY & TOLERABILITY

Minimal ocular side effects

No hyperemia

Minimal systemic side effects due to THC

SBI-100 OE Next Steps – Roadmap to Commercialization



SBI-100 OE: Treatment Paradigm and Clinical Data

Physician's Commercial Perspective

Challenges in Treating Glaucoma

Treatments Current State

KOLs view current treatments as satisfactory; overall compliance is a problem regardless of IOP lowering (tolerability, inconvenience). Patients often require "add-on" or fixed combination Tx to lower IOP, which often exacerbates tolerability.

Novel topical therapies that are effective and increase adherence/compliance, either 1st or 2nd line, are needed.

Novel neuroprotective treatments that can prevent visual field loss remain a significant unmet need

Key Unmet Needs in Glaucoma

Patient Adherence: Patient adherence/compliance is a **significant hurdle** facing effective chronic treatment; greater adherence/compliance would provide for enhanced chronic treatment efficacy. (includes instillation and all day comfort, once a day dosing and effective IOP lowering)

More Efficacious 1st and 2nd Line Agents: Physicians generally exhaust all pharmacologic treatments before recommending invasive surgical intervention; added **IOP-reducing 1st or 2nd line agents would be preferred to prevent or prolong the need for risky surgery**

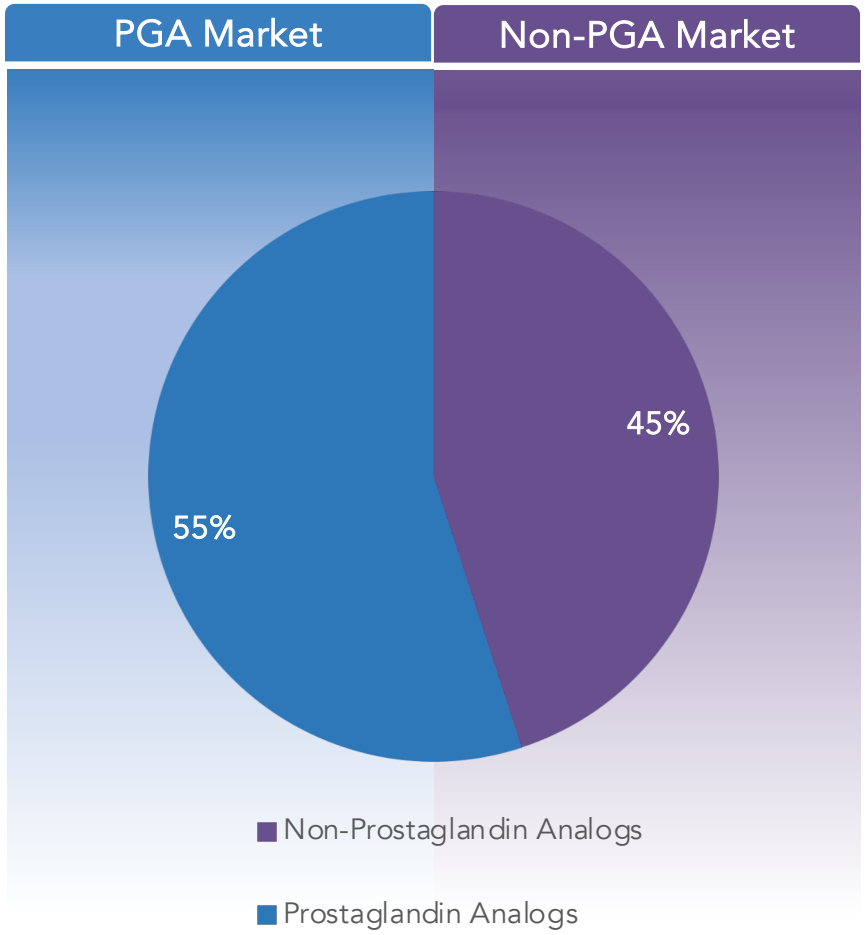
Unique Mechanism of Action: An agent with a **different target** and improved tolerability from current classes of drugs, would allow for **more effective treatment** for patients that require additional IOP lowering

Neuroprotective Agents: An agent that offers optic nerve protection **independent of IOP lowering, is the "holy grail" for the effective treatment of a chronic sight-threatening disease such as glaucoma.**

Source: LifeSci Primary Market Research (N=10 U.S. KOL Ophthalmologists, N=5 U.S. payors, N=3 Strategics); For investor audiences only.

Key Opportunities for SBI-100 OE

1. **Targets the tissue of disease**
   - Current medications either:
     - Inhibit aqueous production from the ciliary body: beta-blockers and carbonic anhydrase inhibitors
     - Increase uveosceral outflow (secondary physiological outflow): prostaglandin analogs
     - Increase trabecular outflow (primary physiological outflow pathway): rho-kinase inhibitors
2. **New class of medication**
   - Only 5 classes of drug available
   - Because of multiple comorbidities in this population, many times patients are only eligible to use 2 or 3 classes of drugs
3. **Safe and more tolerable agent that can be combined with available therapies**



Challenges in Treating Patients with Glaucoma

Achieving and maintaining effective IOP lowering (20-30%) from baseline with existing medications:

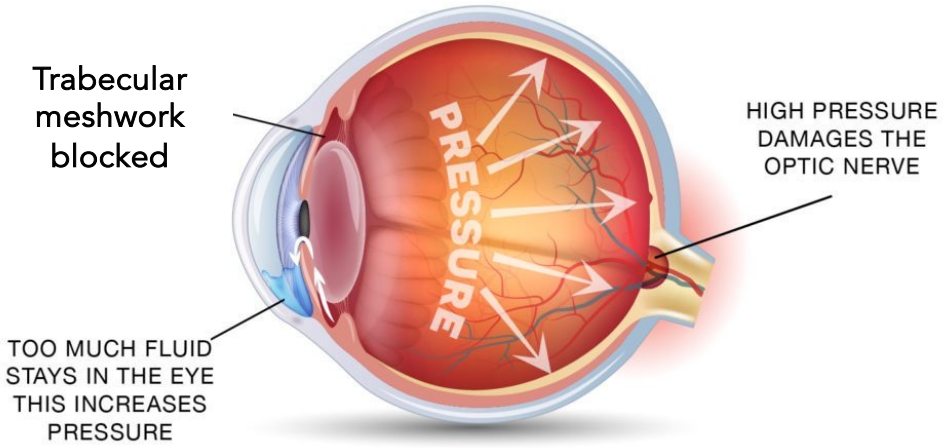
- Magnitude of IOP reduction is often titrated by disease severity and benefit/risk of desired treatment.
- The more severe the disease the more aggressive and riskier the lowering of IOP becomes.
- Current maximal medical therapy may not provide the IOP lowering required to protect from further nerve damage.
- Current medications may cause intolerable ocular and systemic side effects.
- Newer agents with different mechanisms of action and improved tolerability, both ocular and systemic, are needed to meet the needs of patients being effectively treated for this complex disease.

SBI-100 – Encouraging Phase 1 Results

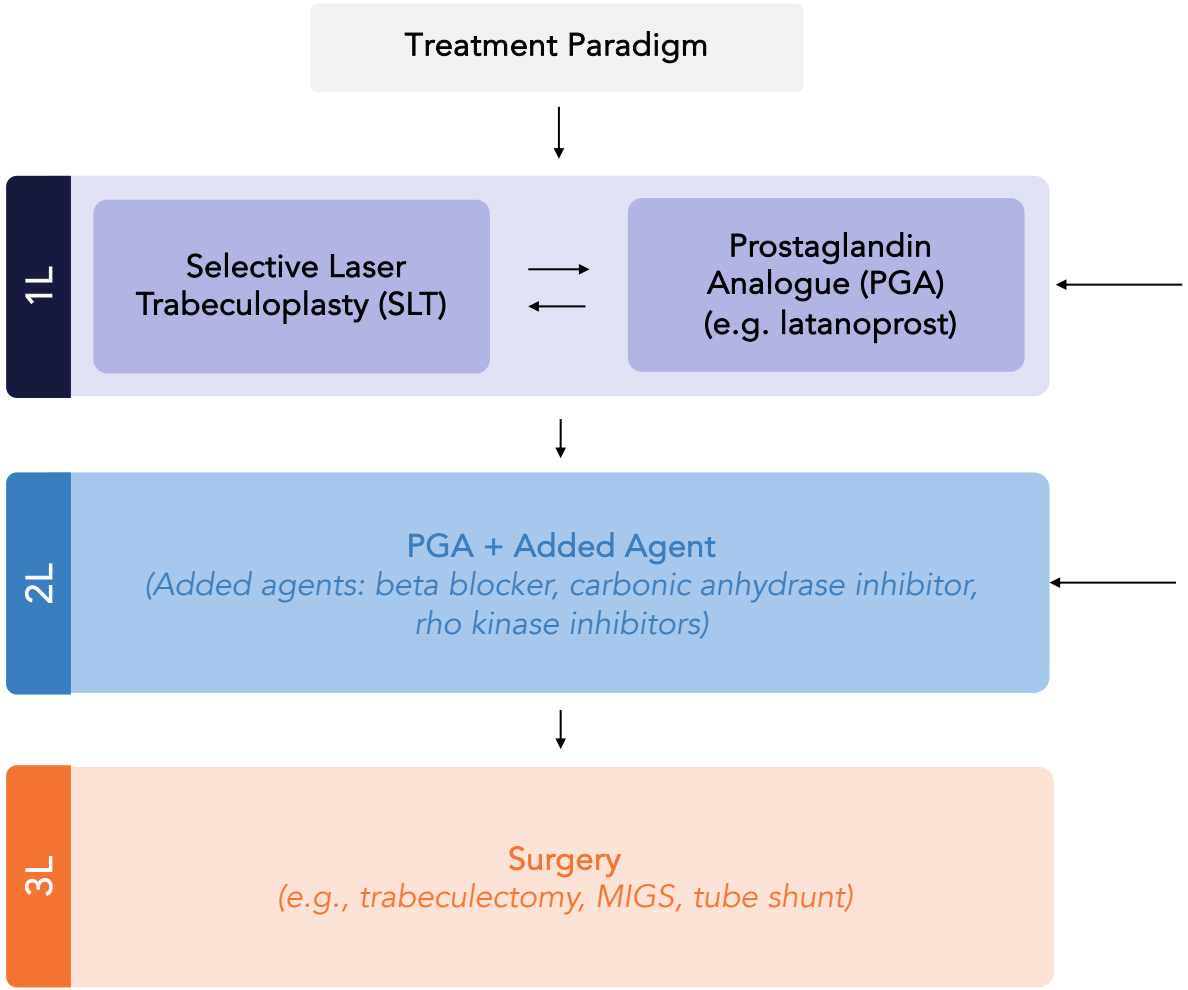
- Directed at primary site of pathology
  - Trabecular meshwork

- Early signs of beneficial safety profile over currently available therapies
  - Low incidence of hyperemia
  - No systemic side effects

- Encouraging IOP lowering effects from Phase 1 study in patients with higher IOP



Current Treatment Paradigm



Depending on data SBI-100 OE could potentially be 1L therapy

Strong safety data and competitive efficacy could secure SBI-100 OE as a 2L therapy

Summary

- SBI-100 OE is well positioned to become a favored option in patients with glaucoma and ocular hypertension.
- Safety data from Phase 1 study shows that the drug is well-tolerated and currently does not present with either ocular or systemic side effects that would hinder future commercial potential (i.e. hyperaemia and Rhopressa).
- Phase 2a for SBI-100 OE is randomized, controlled, double-masked clinical trial, designed to show efficacy (diurnal lowering of IOP), safety and comfort/tolerability in patients with glaucoma and ocular hypertension.
- Skye has clear path forward to NDA with larger controlled Phase 2/3 and Phase 3 pivotal trials that meet the requirements of the FDA for compounds developed for lowering of IOP in patients with glaucoma and ocular hypertension.

SBI-100 OE: KOL Feedback for Glaucoma and Ocular Hypertension

Market Opportunity and Positioning

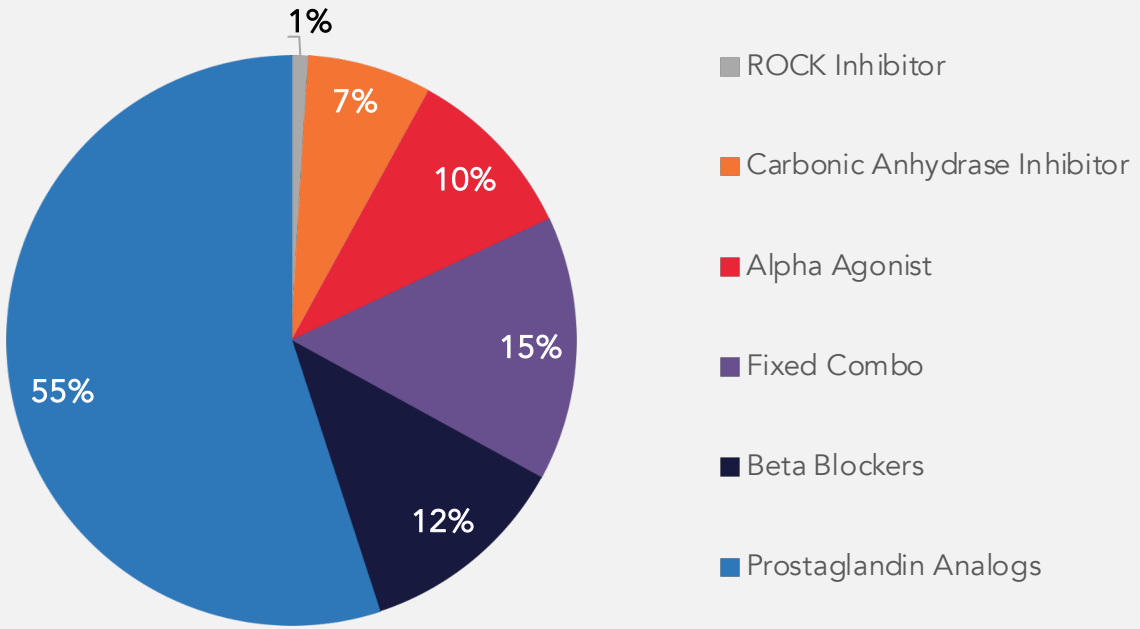
Targeting Glaucoma (POAG & OH): Large Market, Unmet Needs

World's leading cause of irreversible blindness

$7B	drug market worldwide
~60M	patients worldwide
~110M	patients by 2026
40%	fail 1st line therapy[1]
50%	require 2 therapies[1,2]
~7.1M	US prevalence of OH patients[3]

MARKET LACKS INNOVATION

predominantly using legacy classes of drugs and generic compounds.



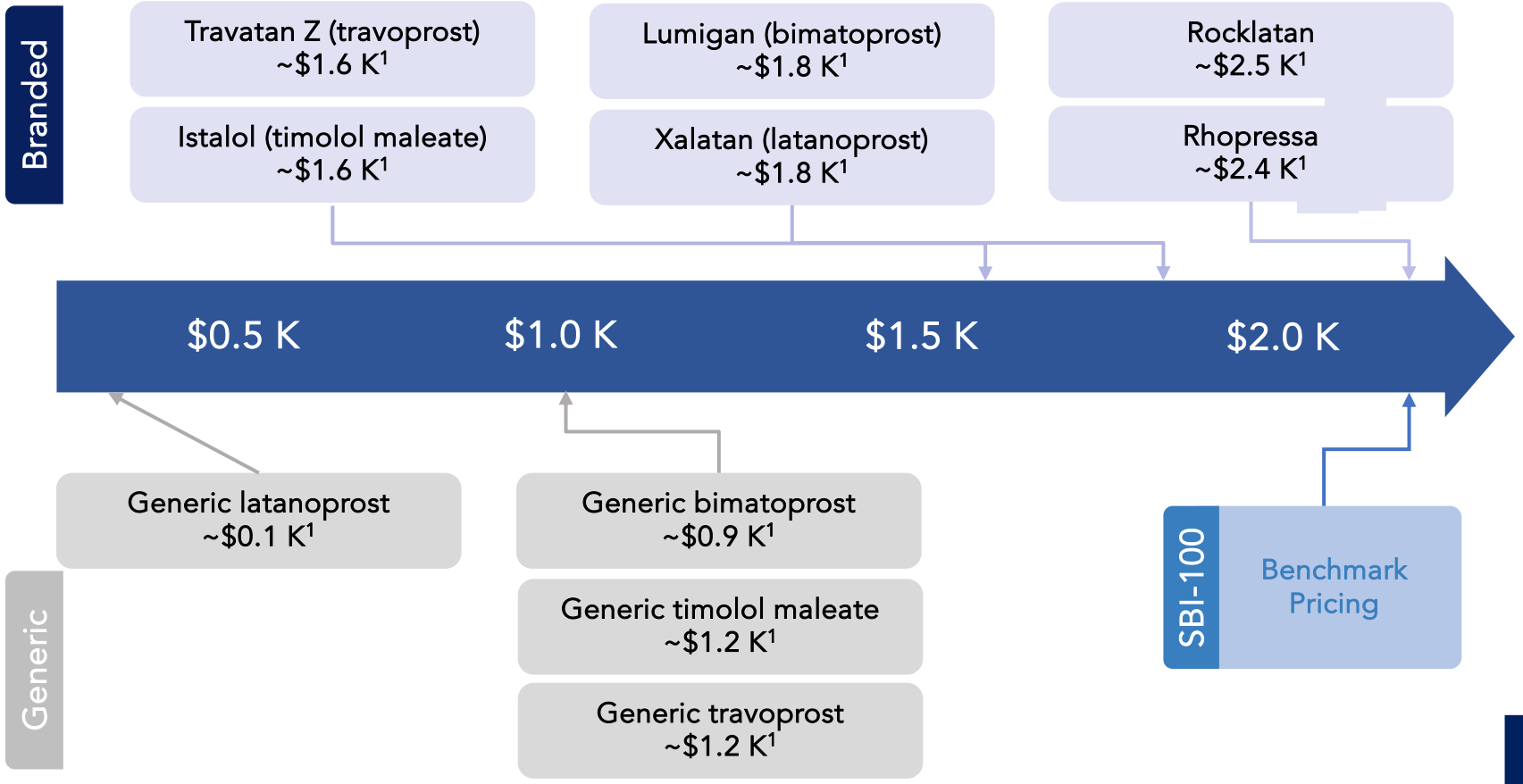
For investor audiences only

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
3: The risk of progression to POAG is 17.5% for treated ocular hypertension patients over a 5-year period.; Kelly. British Journal of Ophthalmology. 2020; 104:1406-1411; Estimated diagnosed prevalence of primary open-angle glaucoma is ~1.5 M

Current Annual Price of Pharmacologic Products

Marketed branded agents for the treatment of glaucoma are priced at <$3 K annually in the U.S.

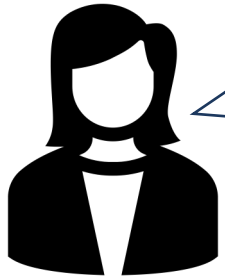
SBI-100 OE: Competitive product profile with significant market opportunity



Current Pricing Landscape

- Consists of **branded and generic IOP-targeting agents**
- **Both generic and branded products are cost effective**, as they are relatively easy-to-manufacture topical small molecules

PAYORS[2]



"SBI-100 could emerge as a common 2L+ treatment and will address the unmet need for additional treatments for the moderate-to-severe patient population."

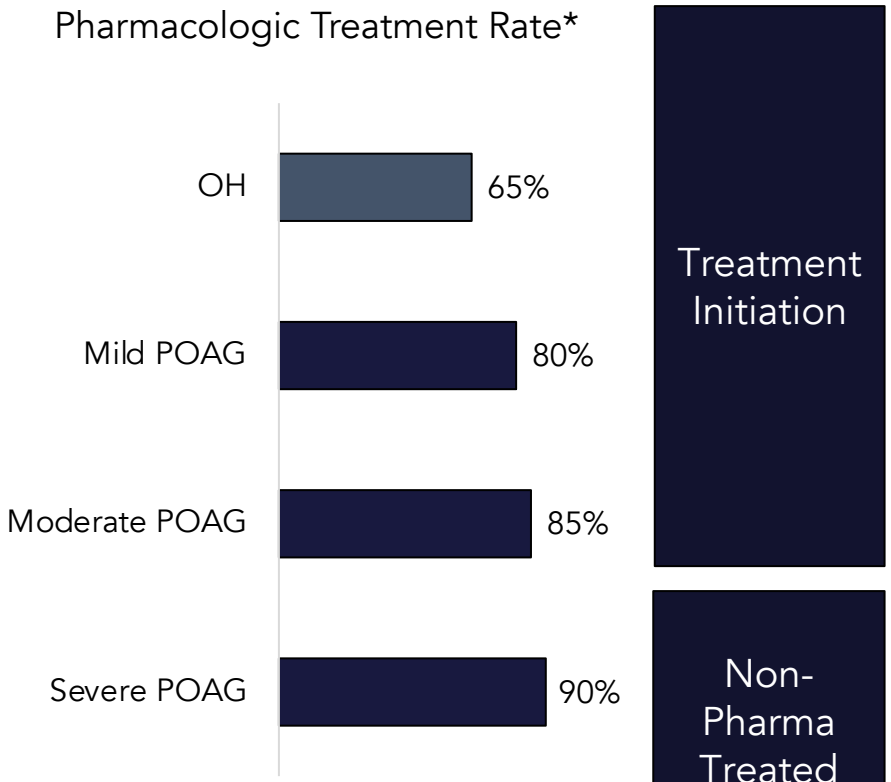
Majority of payors **anticipate a launch price of SBI-100 OE between $2.5 – 3.5 K,** benchmarking to recently approved branded agents (e.g., Rocklatan and Rhopressa)

Source: LifeSci Primary Market Research (N=10 U.S. KOL Ophthalmologists, N=5 U.S. payors, N=3 Strategics); For investor audiences only.
1: RedBook
2: Includes LifeSci prior discussions with payors in ophthalmology
* Prices reflect January 2022 WAC price – Assumes 1 drop per day in each eye, ~90 drops per bottle, 1 bottle per 45 days, 8.1 bottles per year (Queen. Am J Ophthalmol. 2016 Mar; 163: 70–74.e1); Cost of therapy assumes a full 365 days of treatment

Pharmacologic Treatment Rate in POAG and OH

Most patients, regardless of severity, are prescribed pharmacologic treatment to halt disease progression

Pharmacologic Treatment



Treatment Initiation

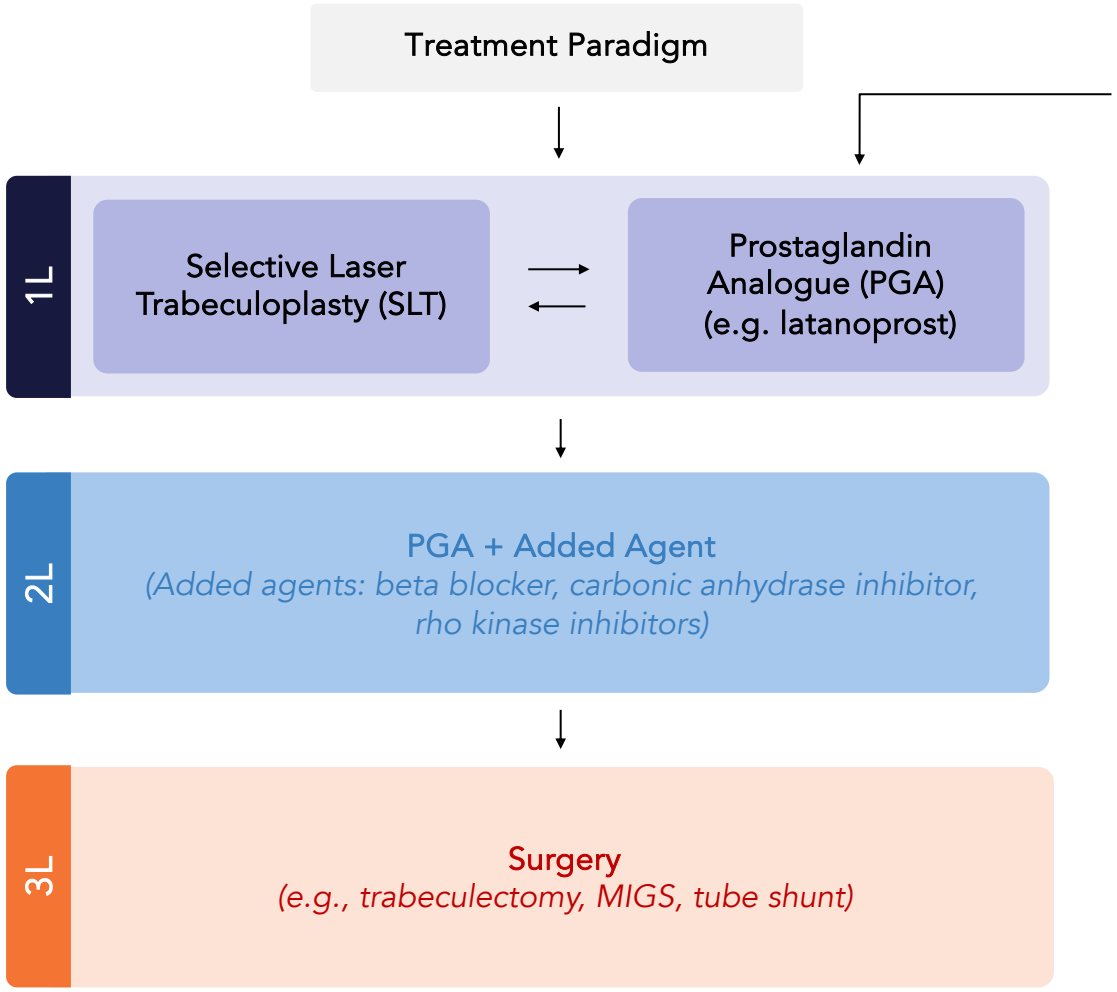
- Regardless of severity, **pharmacologic treatment is commonplace (80 – 90%)** in patients with POAG because of the need to prevent disease progression and irreversible optic nerve degradation
- In OH, initial pharmacologic treatment is stated to be twenty-five percentage points lower than that of POAG; this is because physicians commonly engage in a **"watch-and-wait" technique**, monitoring a patient for signs of progression
- Current indicators used to discern treatment initiation commonly include **optic field testing, IOP level, and optic nerve health via RNFL examinations**
  - For a patient with OH, treatment is commonly initiated at an IOP of >24 mm Hg or the presentation of initial optic nerve damage; however, other factors exist for treatment initiation, such as family history

Non-Pharma Treated

- POAG patients who remain untreated are typically those that receive SLT or a MIGS procedure and do not require follow-on pharmacologic treatment
- KOLs indicate that a MIGS procedure during cataract surgery is a way to efficiently lower IOP; such procedures are performed in order to eliminate poor patient adherence in patients that will likely eventually require multiple IOP-reducing agents

Source: LifeSci Primary Market Research (N=10 U.S. KOL Ophthalmologists, N=5 U.S. payors, N=3 Strategics); For investor audiences only.
RNFL: Retinal Nerve Fiber Layer.

Current Treatment Paradigm for Glaucoma



Once ocular hypertension progresses to the point of requiring treatment, PGA IOP-lowering monotherapy becomes the dominant 1L treatment option

First-line treatment can either be a PGA monotherapy regimen or SLT; use of SLT as an initial treatment option varies by practitioner, but it is suggested that SLT is more effective in mild patients[1,2]; however, SLT procedures have a **failure rate of 50% two years post-procedure**[2,3]

PGA monotherapy is considered effective at reducing intraocular pressure (IOP); treatment is associated with eye irritation and redness

If PGA monotherapy does not sufficiently reduce IOP, then a **PGA + alternative treatment combination therapy** (e.g., beta blocker, rho kinase inhibitor) is prescribed[2]

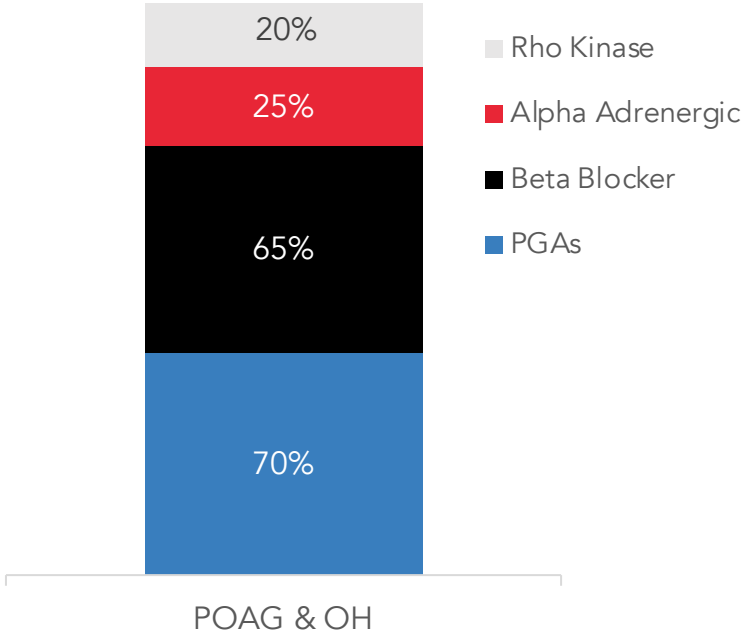
Source: LifeSci Primary Market Research (N=10 U.S. KOL Ophthalmologists, N=5 U.S. payors, N=3 Strategics); For investor audiences only.
1: Huang. Acta Ophthalmol. 2018; 96(3):277;
2: Gazzard. Lancet. 2019; 393(10180):1505–1516;
3: Lusthaus. Med. J. Aust. 2019; 210(4):180.

2L+ Pharmacologic Treatment in POAG and OH

In 2L+, KOLs report adding a pharmacologic treatment (e.g., beta blocker) to the existing PGA regimen

Second Line and Beyond (2L+) Pharmacologic Treatment in POAG

POAG 2L+ Pharmacologic Utilization by Class



** Percentages sum to >100% due to of combination use*

2L+ Treatment Paradigm

- The likelihood of progressing past 1L is directly correlated with increasing severity; **moderate-severe patients, as indicative of the ≥50% 1L relapse / refractory rate, often cycle through combination regimens**
- **PGAs + beta blockers are the 2L treatment of choice** for KOLs; 2L treatment is reported by KOLs to be consistent across severities
- PGAs remain the basis for most 2L+ pharmacologic treatment barring any safety and tolerability concerns during 1L monotherapy regimen
- The greatest difference between the 2L+ pharmacologic treatment of mild, moderate, and severe patients is the percentage of whom require multiple cycles of differing combination therapy and the willingness for a physician and patient to opt for surgery

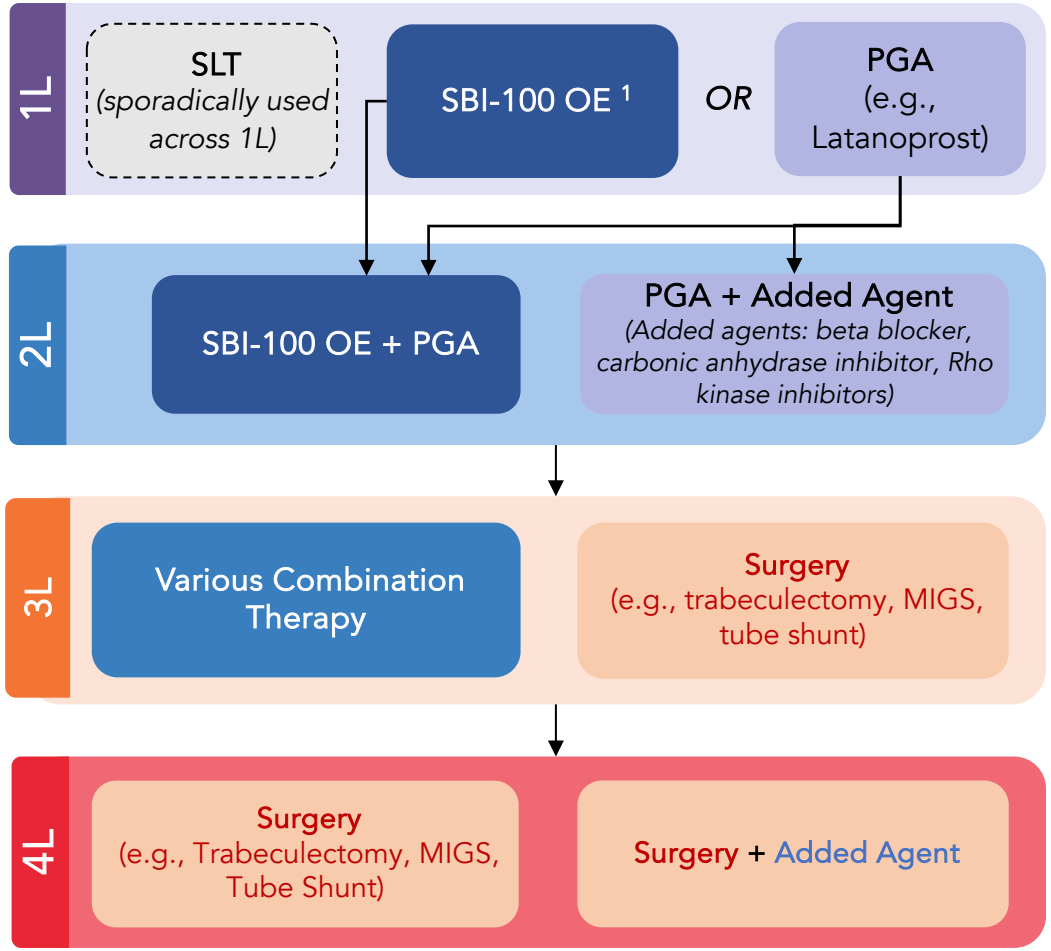
KOL-mentioned payor Dynamics

- KOLs ascribe moderate safety and tolerability concerns to rho kinase inhibitors; however, KOLs shared that the barrier to use is equally dictated by payor coverage requirements, i.e., a two-stage step-edit through PGAs and beta blockers

Source: LifeSci Primary Market Research (N=10 U.S. KOL Ophthalmologists, N=5 U.S. payors, N=3 Strategics); For investor audiences only.

Potential Future Treatment Paradigm – SBI-100 OE

KOLs expect patients will receive SBI-100 OE in 2L in monotherapy



- SBI-100 OE has the potential to be used by some physicians as a first line treatment option, but payor access restrictions are expected to limit 1L use to only patients with plans that do not require a step through generic latanoprost
- **KOLs view SBI-100 OE primarily as a 2L treatment option** prior to use of beta blockers
- The potential for **market leading efficacy, strong safety and tolerability profile, and once daily topical dosing regimen serve as a formidable value proposition**
- **SBI-100 OE + PGA in 2L is a likely scenario** based on physician comfort with decades of use with PGAs
- The novelty and clinical differentiation of the cannabinoid receptor target versus traditional IOP-reducing medications leads KOLs to be willing to prescribe this drug in combination with existing medications given the perceived low risk of drug-to-drug interactions

Source: LifeSci Primary Market Research (N=10 U.S. KOL Ophthalmologists, N=5 U.S. payors, N=3 Strategics); For investor audiences only.
1: Does not account for payor restrictions

SBI-100 OE: Potential to Fulfill Clinical Unmet Needs

Following initial approval of topical drug format, Skye would explore innovative delivery technologies to improve patient adherence

SBI-100 could satisfy multiple key unmet needs expressed by physicians

THC and other cannabinoids have demonstrated neuroprotective benefits in multiple models. [1,2] This could be a future opportunity for SBI-100 OE

Key Unmet Needs in Glaucoma

Patient Adherence: Patient adherence is a **significant hurdle** KOLs face when providing effective long-term care; greater adherence with current pharmacologic options would allow KOLs to properly assess treatment efficacy

More Efficacious 2L+ Agents: **Physicians often exhaust all pharmacologic treatments before recommending invasive surgical intervention; new IOP-reducing 2L+ agents would be preferred to prevent or prolong the need for risky surgery**

Unique Mechanism of Action: An agent with a **different target** from current classes of drugs would allow for **more effective treatment** of "tough-to-treat" patients that often cycle through traditional therapies

Neuroprotective Agents: An agent that offers optic nerve protection **agnostic of IOP dependence** could alleviate moderate to severe patients from aggressive pharmacologic and surgical treatment regimens

Source: LifeSci Primary Market Research (N=10 U.S. KOL Ophthalmologists, N=5 U.S. payors, N=3 Strategics); For investor audiences only.

1: Crandall J., Matragoon S., Khalifa Y.M., Borlongan C., Tsai N.T., Caldwell R.B., Liou G.I. Neuroprotective and intraocular pressure-lowering effects of (-)Delta9-tetrahydrocannabinol in a rat model of glaucoma. *Ophthalmic Res.* 2007;39:69–75. doi: 10.1159/000099240.

2: Pinar-Sueiro S., Zorrilla Hurtado J.A., Veiga-Crespo P., Sharma S.C., Vecino E. Neuroprotective effects of topical CB1 agonist WIN 55212-2 on retinal ganglion cells after acute rise in intraocular pressure induced ischemia in rat. *Exp. Eye Res.* 2013;110:55–58. doi: 10.1016/j.exer.2013.02.009.

Physician Feedback About SBI-100 OE

New drug with novel mechanism of action would be well-accepted by physicians

Mechanism of Action

"I have conducted extensive research about [SBI-100's] mechanism and feel very confident it has a place in the treatment paradigm of OH and POAG. Many of my patients ask me about the IOP-reducing potential of THC."

"I am always willing to try a novel therapy given none of the existing options actually cure the disease. Given the unique mechanism of [SBI-100], I could see all of my patients receiving this option at some point throughout their disease course."

"[SBI-100] is a different mechanism and targeting a different receptor that could offer neuroprotective effect."

Market Opportunity

*"Patients that are intolerant to PGA therapy are subjected to **less effective therapy options** with **greater side effect risk**. Ideally, I would want additional IOP-reducing agents that mechanistically have a different target to **avoid proven ineffective treatment approaches**."*

*"An aging US population represents a growing high-risk patient pool that will require treatment. If we don't **continue to innovate additional therapies** to treat a diverse group of patients, there will be a big problem in this country and globally."*

*"I use PGAs currently, but [SBI-100] **would probably be a second line** to latanoprost or used prior to timolol for patients that are little worried about side effects."*

*"A lot of patients are going to be **extremely happy** if I can provide them with multiple well-tolerated treatment options to reach target IOP reduction. Even if one agent is not enough, the different behaviors of the drugs give me the **added flexibility** I need to treat my patients."*

*"**More medications that are effective and safe will always be a need** until there is a cure for glaucoma. Especially for this product, being as effective as described would release patients from requiring 3 – 4 drops and **would make patient adherence easier**."*

Source: LifeSci Primary Market Research (N=10 U.S. KOL Ophthalmologists, N=5 U.S. payors, N=3 Strategics); For investor audiences only.

Market Analysis Summary

Eye care providers: high level of excitement about CB1 agonist and class of drugs

UNMET NEED

Glaucoma still facing significant unmet need

- Patient adherence, improved second-line therapies, novel mechanisms of action and neuroprotective benefits are seen as key unmet needs in glaucoma

ADOPTION

Cannabinoids, including THC, intriguing to physicians and patients

- Significant interest from both physicians and patients based on the differentiation of the cannabinoid receptor target to treat glaucoma
- Defined pharmaceutical treatment has potential to be prescribed by physicians as 2L monotherapy and in combination with existing medications given perceived low risk of drug-to-drug interactions

MARKET OPPORTUNITY

Anticipate using a potential treatment immediately post-approval and already have patients interested, especially patients unable to take current 1L and 2L options

NOVEL MOA

Novel mechanisms of action viewed as significant benefit for physicians and patients

- Targeting CB1 receptor gives physicians a new option beyond the same classes of current therapeutics offered today

STRATEGIC INTEREST

Strategic partners believe a CB1 receptor agonist can work in glaucoma

Source: LifeSci Primary Market Research (N=10 U.S. KOL Ophthalmologists, N=5 U.S. payors, N=3 Strategics); For investor audiences only.

SBI-100 OE: Phase 1 Safety Clinical Data Summary

- **Good Safety Profile**: Generally safe and well-tolerated. No participants dropped out due to SBI-100 OE
- **Transient Discomfort**: Main side effect is discomfort/pain upon drop instillation, but average duration of discomfort was less than 15 minutes.
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- **Minimal Hyperaemia**: Little to no hyperaemia as compared to other leading classes of drugs.
- **Efficacy**: IOP data suggests encouraging activity in participants with high baseline IOP (>17 mmHg)

Skye Next Steps

- Advance nimacimab clinical trials with longer-term view toward franchise expansion
- Achieve SBI-100 Ophthalmic Emulsion/glaucoma proof-of-concept milestone
- Maintain focused operational and clinical development strategy
- Selectively evaluate business development opportunities to advance product pipeline
- Uplist from OTCQB following successful achievement of upcoming milestones

Expected Upcoming Clinical Development Milestones

2023

- [x] SBI-100 OE Phase 1 study in healthy volunteers - Q4
- SBI-100 OE Phase 2a glaucoma clinical trial Initiation - Q4
- Nimacimab IND submission for cardio-metabolic indication – Q4
- Continued in vivo studies, biomarker development, next-generation efforts

2024

- Nimacimab Phase 2 cardio-metabolic clinical trial initiation - Q1
- SBI-100 OE Phase 2a glaucoma clinical trial:
  - Interim analysis following dosing of 50% of patients - Q1
  - Complete 100% enrollment - Q1
  - Final clinical data - Q3
- Planned SBI-100 OE Phase 2b glaucoma clinical trial initiation - Q4

Q&A Session

Convergence of Right Space, Technology and Team

ENDOCANNABINOIDS	**Two clinical stage Phase 2** first- and only-in class pharmaceuticals in development, targeting the **endocannabinoid system**, a renewed area of interest through next generation engineering. Lead asset acquired through transformational Bird Rock Bio acquisition, supported by **5AM Ventures, Versant** and other dedicated life science shareholders of Bird Rock Bio.
ASSETS IN CLINIC	**Nimacimab:** Next generation ***CB1 inhibitor***, targeting chronic kidney disease, validated target for obesity. **SBI-100 Ophthalmic Emulsion ("OE"):** Next generation ***CB1 agonist/activator*** targeting glaucoma/ocular hypertension.
CLINICAL MILESTONES	**Multiple near term value creating milestones** across pipeline activity through 2024.
EXPERIENCED TEAM	Highly experienced group of experts, leaders, scientists and advisors **guiding clinical development strategy**.
INTELLECTUAL PROPERTY	Robust **intellectual property strategy** including composition of matter protection through 2037 (nimacimab) and 2029 (SBI-100).
LARGE COMMERCIAL OPPORTUNITY	**Significant disease prevalence** in **targeted therapeutic areas**, addressing multi-billion commercial opportunity.

Leadership

Contributed to commercialization of 47+ drugs/diagnostics, led high-value strategic transactions and co-founded multiple companies

Executive Management

Punit Dhillon
CEO & Chair of BOD

Tu Diep, MSc
Chief Development Officer

Chris Twitty, PhD
Chief Scientific Officer

Kaitlyn Arsenault, CPA
Chief Financial Officer

Board of Directors

Andy Schwab
Managing Partner, 5AM Ventures

Deborah Charych, PhD
Co-founder and former CTO, RayzeBio

Keith Ward, PhD
Founder, Pres./CEO, & Chair, Kuria Therapeutics

Paul Grayson
Pres./CEO, Tentarix Bio; Versant partner

Praveen Tyle, PhD
Founder, Potens Pharma

Margaret Dalesandro, PhD
Pharma. Dev. Consultant, Brecon Pharma Consulting

Thank you to the patients, clinical trial investigators and operations staff who participate in our research programs

Learn more, please contact:

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Appendix

Treatment Emergent Adverse Events (TEAE) – SAD Overall

	SBI-100 Ophthalmic Emulsion SAD Ascending Dose (SAD)				
	SBI-100 0.5% (N=6)	SBI-100 1% (N=6)	SBI-100 2% (N=6)	SAD Placebo (N=6)	SAD Overall (N=24)
Total Number of TEAEs	7	9	14	8	38
Total Number of TESAEs	0	0	0	0	0
Number (%) Participants Reporting at Least One:					
TEAE	4 (66.7%)	6 (100.0%)	6 (100.0%)	6 (100.0%)	22 (91.7%)
TEAE by Severity					
Mild	4 (66.7%)	3 (50.0%)	6 (100.0%)	5 (83.3%)	18 (75.0%)
Moderate	0	3 (50.0%)	0	1 (16.7%)	4 (16.7%)
Severe	0	0	0	0	0
TEAE Relationship to SBI-100					
Not Related	3 (50.0%)	2 (33.3%)	3 (50.0%)	2 (33.3%)	10 (41.7%)
Related	1 (16.7%)	4 (66.7%)	3 (50.0%)	5 (66.7%)	12 (50.0%)
TEAE Leading to Early Study Termination	0	0	0	0	0
TEAE Where Drug Withdrawn	0	0	0	0	0
TEAE Where Drug Interrupted	0	0	0	0	0
TEAE Where Drug Interrupted or Withdrawn	0	0	0	0	0

Treatment Emergent Adverse Events – SAD Ocular

	SBI-100 Ophthalmic Emulsion SAD Ascending Dose (SAD)				
	SBI-100 0.5% (N=6)	SBI-100 1% (N=6)	SBI-100 2% (N=6)	SAD Placebo (N=6)	SAD Overall (N=24)
Total Number of TEAEs	6	7	10	7	30
Total Number of TESAEs	0	0	0	0	0
Number (%) Participants Reporting at Least One:					
TEAE	4 (66.7%)	6 (100.0%)	6 (100.0%)	6 (100.0%)	22 (91.7%)
TEAE by Severity					
Mild	4 (66.7%)	4 (66.7%)	6 (100.0%)	5 (83.3%)	19 (79.2%)
Moderate	0	0	0	1 (16.7%)	3 (12.5%)
Severe	0	0	0	0	0
TEAE Relationship to SBI-100					
Not Related	3 (50%)	1 (16.7%)	1 (16.7%)	2 (33.3%)	7 (29.2%)
Related	1 (16.7%)	5 (83.3%)	5 (83.3%)	4 (66.7%)	15 (62.5%)

Treatment Emergent Adverse Events – SAD Non-ocular

	SBI-100 Ophthalmic Emulsion SAD Ascending Dose (SAD)				
	SBI-100 0.5% (N=6)	SBI-100 1% (N=6)	SBI-100 2% (N=6)	SAD Placebo (N=6)	SAD Overall (N=24)
Total Number of TEAEs	1	2	4	1	8
Total Number of TESAEs	0	0	0	0	0
Number (%) Participants Reporting at Least One:					
TEAE	1 (16.7%)	2 (33.3%)	3 (50.0%)	1 (16.7%)	7 (29.2%)
TEAE by Severity					
Mild	1 (16.7%)	1 (16.7%)	3 (50.0%)	1 (16.7%)	6 (25.0%)
Moderate	0	1 (16.7%)	0	0	1 (4.2%)
Severe	0	0	0	0	0
TEAE Relationship to SBI-100					
Not Related	1 (16.7%)	1 (16.7%)	3 (50.0%)	1 (16.7%)	6 (25.0%)
Related	0	1 (16.7%)	0	0	1 (4.2%)

Treatment Emergent Adverse Events (TEAE) – MAD Overall

	SBI-100 Ophthalmic Emulsion MAD Ascending Dose (MAD)				
	SBI-100 0.5% (N=6)	SBI-100 1% (N=6)	SBI-100 2% (N=6)	MAD Placebo (N=6)	MAD Overall (N=24)
Total Number of TEAEs	28	53	68	19	168
Total Number of TESAEs	0	0	0	0	0
Number (%) Participants Reporting at Least One:					
TEAE	5 (83.3%)	6 (100.0%)	6 (100%)	5 (83.3%)	22 (91.7%)
TEAE by Severity					
Mild	5 (83.3%)	6 (100.0%)	2 (33.3%)	5 (83.3%)	18 (75%)
Moderate	0	0	3 (50.0%)	0	3 (12.5%)
Severe	0	0	1 (16.7%)	0	1 (4.2%)
TEAE Relationship to SBI-100					
Not Related	3 (50.0%)	5 (83.3%)	1 (16.7%)	2 (33.3%)	11 (45.8%)
Related	2 (33.3%)	1 (16.7%)	5 (83.3%)	3 (50.0%)	11 (45.8%)
TEAE Leading to Early Study Termination	0	1 (16.7%)	0	1 (16.7%)	2 (8.3%)
TEAE Where Drug Withdrawn	1 (16.7%)	1 (16.7%)	0	1 (16.7%)	3 (12.5%)
TEAE Where Drug Interrupted	0	0	0	0	0
TEAE Where Drug Interrupted or Withdrawn	1 (16.7%)	1 (16.7%)	0	1 (16.7%)	3 (12.5%)

Treatment Emergent Adverse Events – MAD Ocular

	SBI-100 Ophthalmic Emulsion MAD Ascending Dose (MAD)				
	SBI-100 0.5% (N=6)	SBI-100 1% (N=6)	SBI-100 2% (N=6)	MAD Placebo (N=6)	MAD Overall (N=24)
Total Number of TEAEs	24	41	65	16	146
Total Number of TESAEs	0	0	0	0	0
Number (%) Participants Reporting at Least One:					
TEAE	5 (83.3%)	6 (100.0%)	6 (100.0%)	5 (83.3%)	22 (91.7%)
TEAE by Severity					
Mild	5 (83.3%)	6 (100.0%)	2 (33.3%)	5 (83.3%)	18 (75.0%)
Moderate	0	0	3 (50.0%)	0	3 (12.5%)
Severe	0	0	1 (16.7%)	0	1 (4.2%)
TEAE Relationship to SBI-100					
Not Related	1 (16.7%)	1 (16.7%)	0	0	2 (8.3%)
Related	4 (66.7%)	5 (83.3%)	6 (100.0%)	5 (83.3%)	20 (83.3%)

Majority of events related to site instillation discomfort or pain

Treatment Emergent Adverse Events – MAD Non-Ocular

	SBI-100 Ophthalmic Emulsion MAD Ascending Dose (MAD)				
	SBI-100 0.5% (N=6)	SBI-100 1% (N=6)	SBI-100 2% (N=6)	MAD Placebo (N=6)	MAD Overall (N=24)
Total Number of TEAEs	4	12	3	3	22
Total Number of TESAEs	0	0	0	0	0
Number (%) Participants Reporting at Least One:					
TEAE	3 (50.0%)	5 (83.3%)	2 (33.3%)	2 (33.3%)	12 (50.0%)
TEAE by Severity					
Mild	3 (50.0%)	5 (83.3%)	2 (33.3%)	2 (33.3%)	12 (50.0%)
Moderate	0	0	0	0	0
Severe	0	0	0	0	0
TEAE Relationship to SBI-100					
Not Related	2 (33.3%)	5 (83.3%)	1 (16.7%)	2 (33.3%)	10 (41.7%)
Related	1 (16.7%)	0	1 (16.7%)	0	2 (8.3%)

Minimal related non-ocular adverse events, suggesting minimal systemic exposure to the active agent.

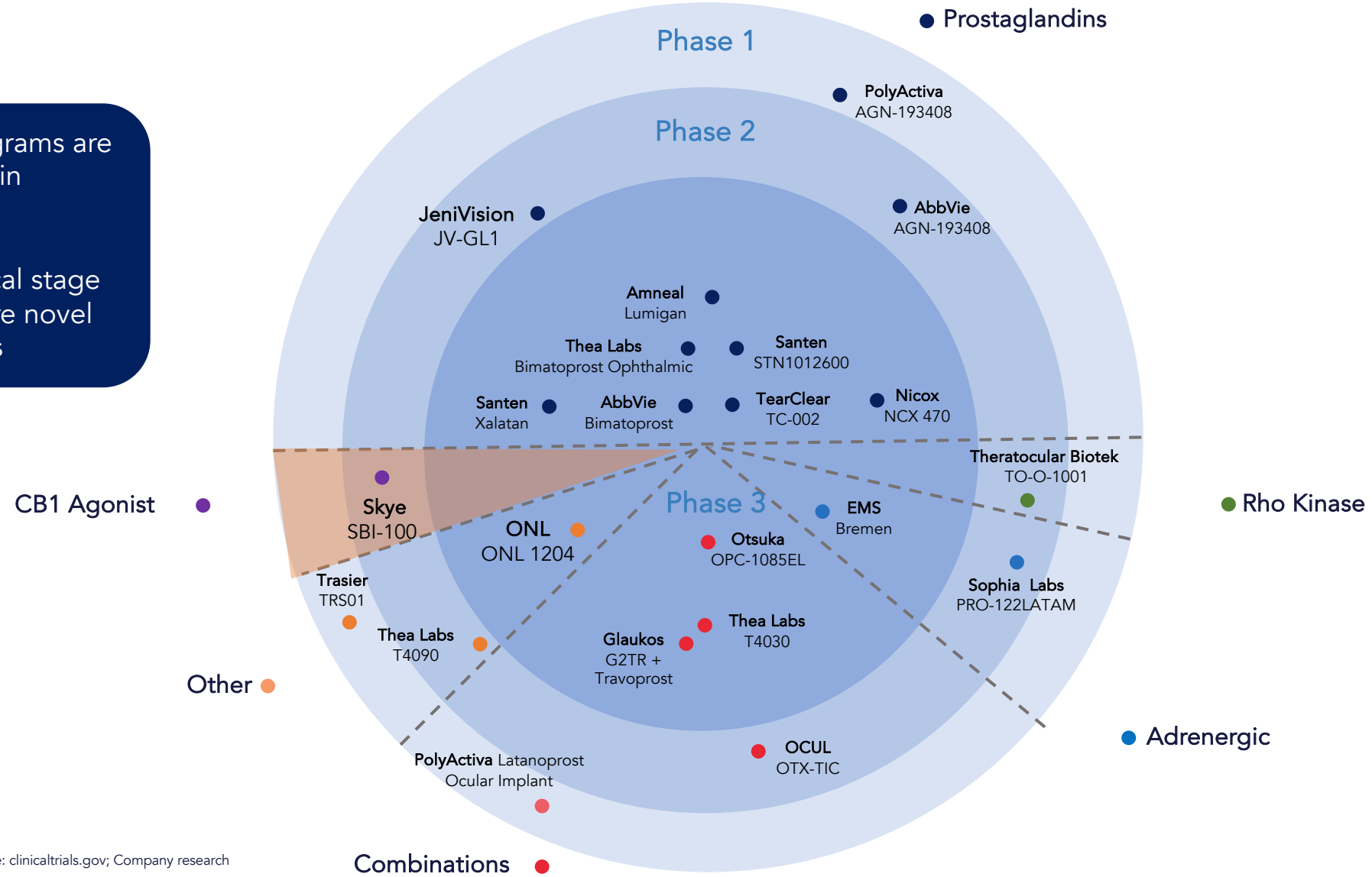
Most non-ocular events related to catheter site pain used for PK blood sampling.

Competitive Drug Pipeline

The clinical competitive pipeline is primarily made up of prostaglandin analogues and beta blockers

60% of programs are prostaglandin analogs

< 20% clinical stage programs are novel mechanisms



Source: clinicaltrials.gov; Company research