

Unlocking the Pharmaceutical Potential of the Endocannabinoid System

January 2024

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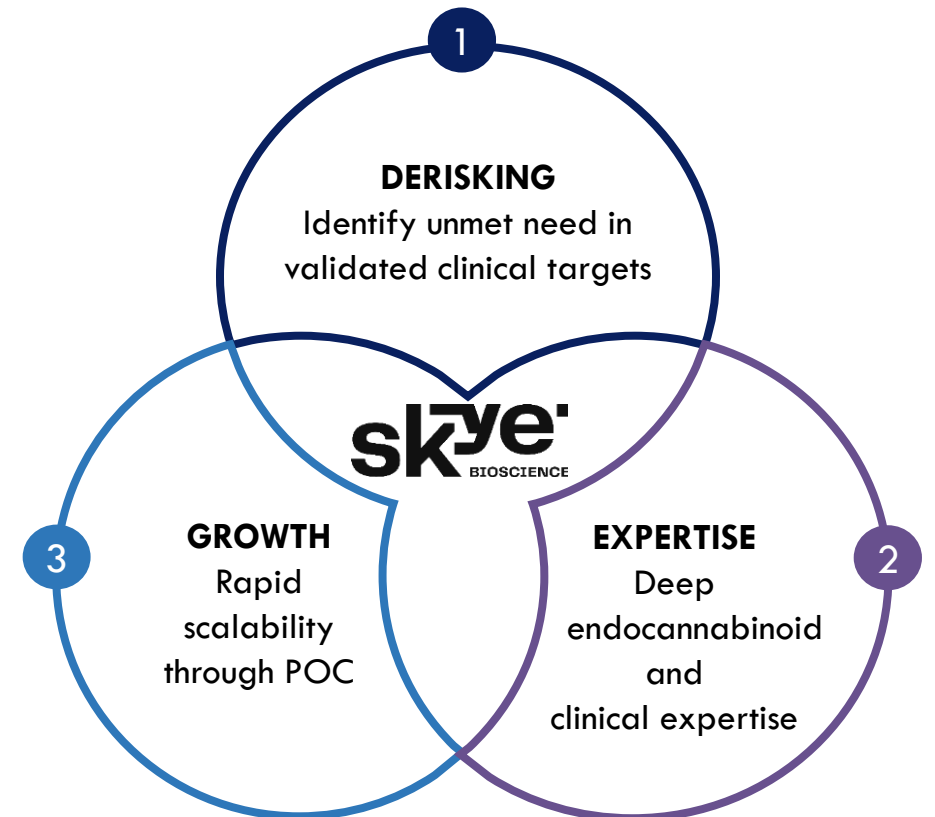
Skye is Building an Endocannabinoid Pharmaceutical Company

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.

Highly productive clinical development strategy optimized for speed, probability of success

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



Convergence of Right Space, Technology and Team

ENDOCANNABINOIDS

Endocannabinoid system is a renewed area of interest.

Two Phase 2 differentiated, endocannabinoid-system-targeting drugs in development.

TOP TIER INVESTORS

Supported by **5AM Ventures, Versant, GSK** other dedicated life science investors in Bird Rock Bio (acquired by Skye in August 2023).

ASSETS IN CLINIC

Nimacimab: *peripheral CB1 inhibitor*, targeting chronic kidney disease and obesity.

SBI-100 Ophthalmic Emulsion (“OE”): *CB1 agonist/activator* targeting glaucoma/ocular hypertension.

CLINICAL MILESTONES

Multiple clinical and development milestones across pipeline through 2024.

EXPERIENCED TEAM

Highly experienced group of experts, leaders, scientists and advisors **guiding clinical development strategy**.

INTELLECTUAL PROPERTY

Robust **intellectual property strategy**: composition of matter protection through 2037 (nimacimab) and 2029 (SBI-100).

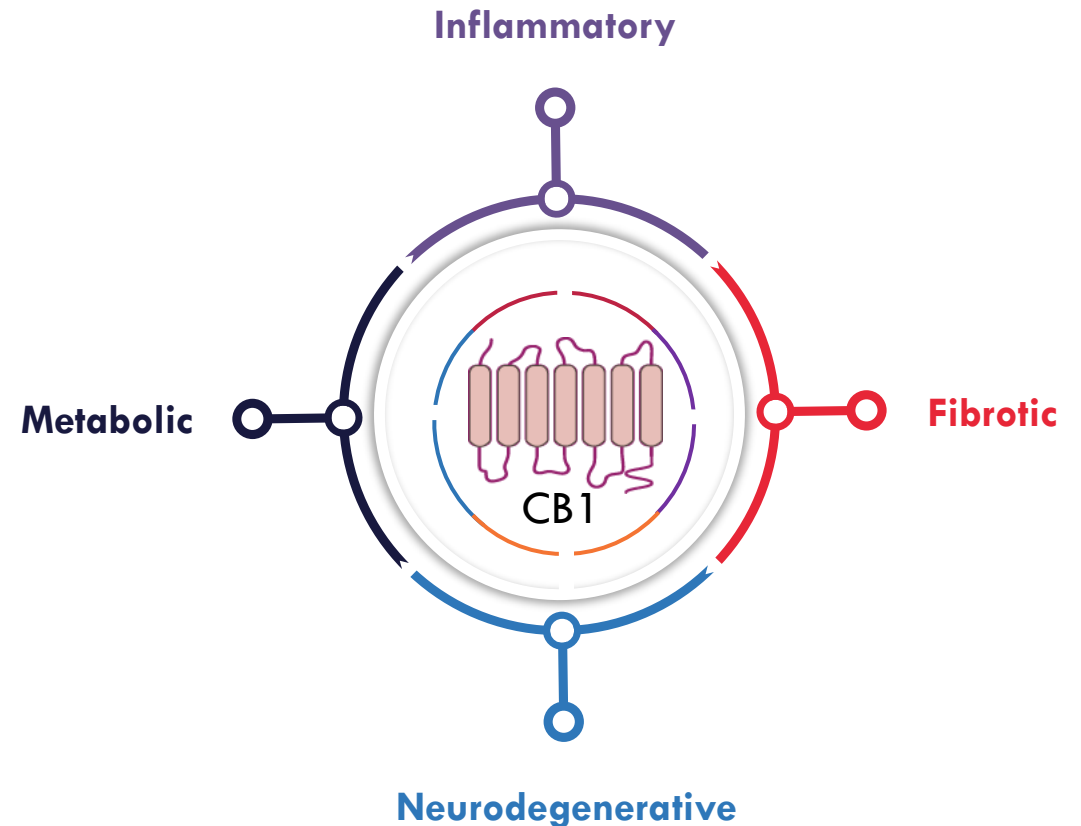
LARGE COMMERCIAL OPPORTUNITIES

Significant disease prevalence in targeted therapeutic areas, addressing multi-billion commercial opportunity.

CB1: High-potential Target for Physiological Regulation

CB1 is involved in many disease processes

- CB1 (cannabinoid receptor 1) is 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



Leadership

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

Executive Management

Board of Directors



Punit Dhillon
CEO & Chair of BOD



Tu Diep, MSc
Chief Development Officer



Andy Schwab
Managing Partner, 5AM Ventures



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



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



Chris Twitty, PhD
Chief Scientific Officer



Kaitlyn Arsenault, CPA
Chief Financial Officer



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









Praveen Tyle, PhD
Founder, Potens Pharma



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

Endocannabinoids: A Renewed Drug Development Frontier

ECS (endocannabinoid system) receptors help modulate and maintain homeostasis of physiological functions. Over- or under-activation of these receptors is involved in an array of diseases

Notable ECS Transactions					
Company	Acquirer	Deal Value	Lead Asset//Indication	Healthcare Investors	Year
		Up to \$1.1B	INV-202 CB1 inverse agonist// Cardiometabolic	NEA, Forbion, Deerfield and Farallon	Aug 2023
		\$7.2B	Epidiolex natural CBD// Epileptic indications	Orbimed, Deerfield, Adage, Venrock, Farallon	May 2021
		\$20M Aug 2023	Nimacimab CB1 inhibitor// Cardiometabolic	5AM Ventures, Versant Ventures	Aug 2023

Nimacimab

Novel CB1-targeting mAb therapeutic for cardiometabolic conditions: peripheral CB1 inhibitor



MOA	Disease	R&D	Phase 1	Phase 2
CB1 Receptor Inhibitor <i>Sub-cutaneous</i>	Obesity & Chronic Kidney Disease			

Best-in-class Monoclonal Antibody

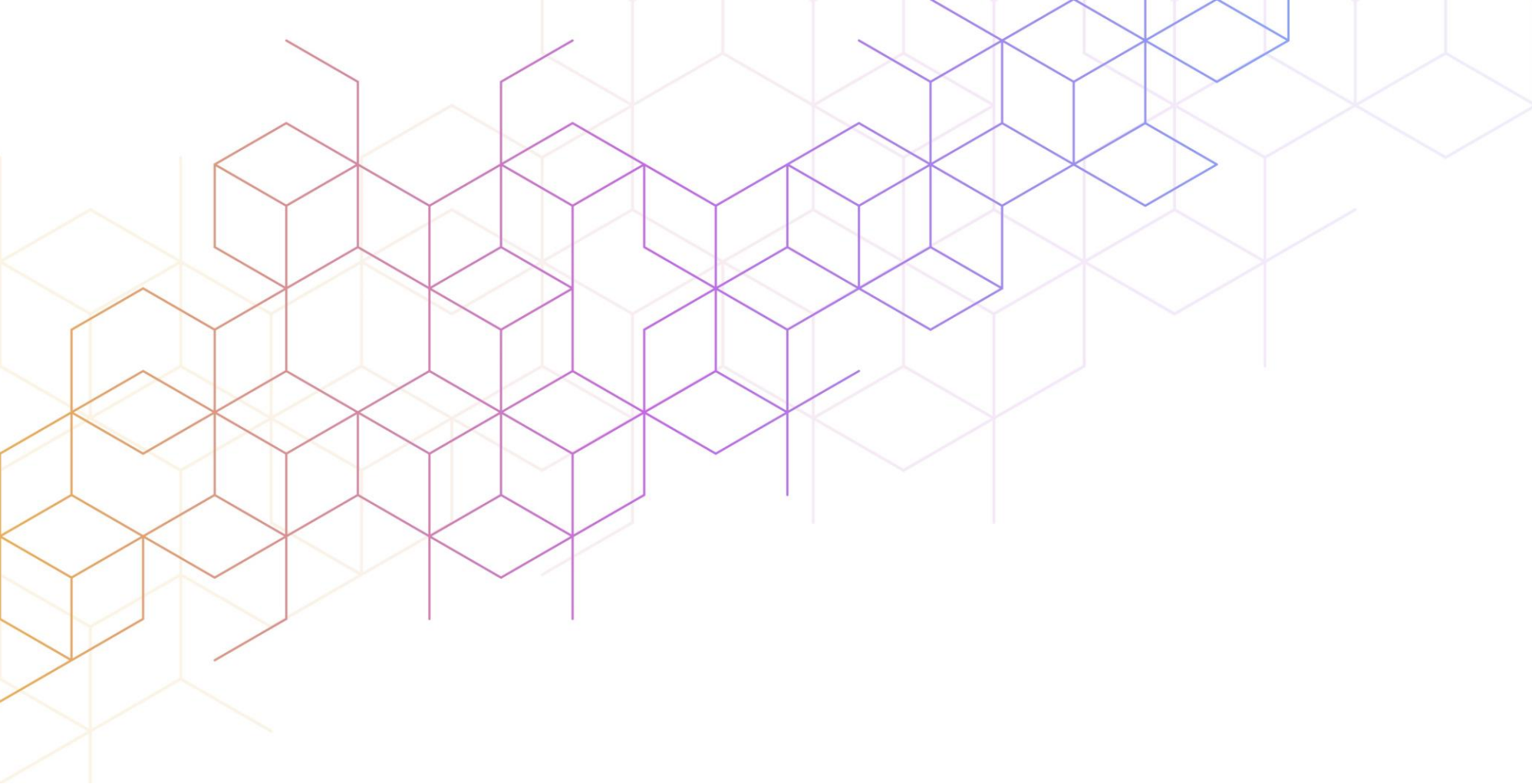
Phase 2-ready molecule with open IND for obesity/weight loss.
Only CB1 negative allosteric modulating humanized monoclonal antibody (**mAb**) **in clinic**.
A highly selective inhibitor of CB1, with no detectable binding to CB2 or other GPCRs. Mechanism of action has therapeutic potential in fibrotic, inflammatory and metabolic diseases.

Past Comp 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

Evolved drug design.
Very limited brain penetration. Encouraging safety and tolerability identified through preclinical and Phase 1 data, with no CNS issues identified.

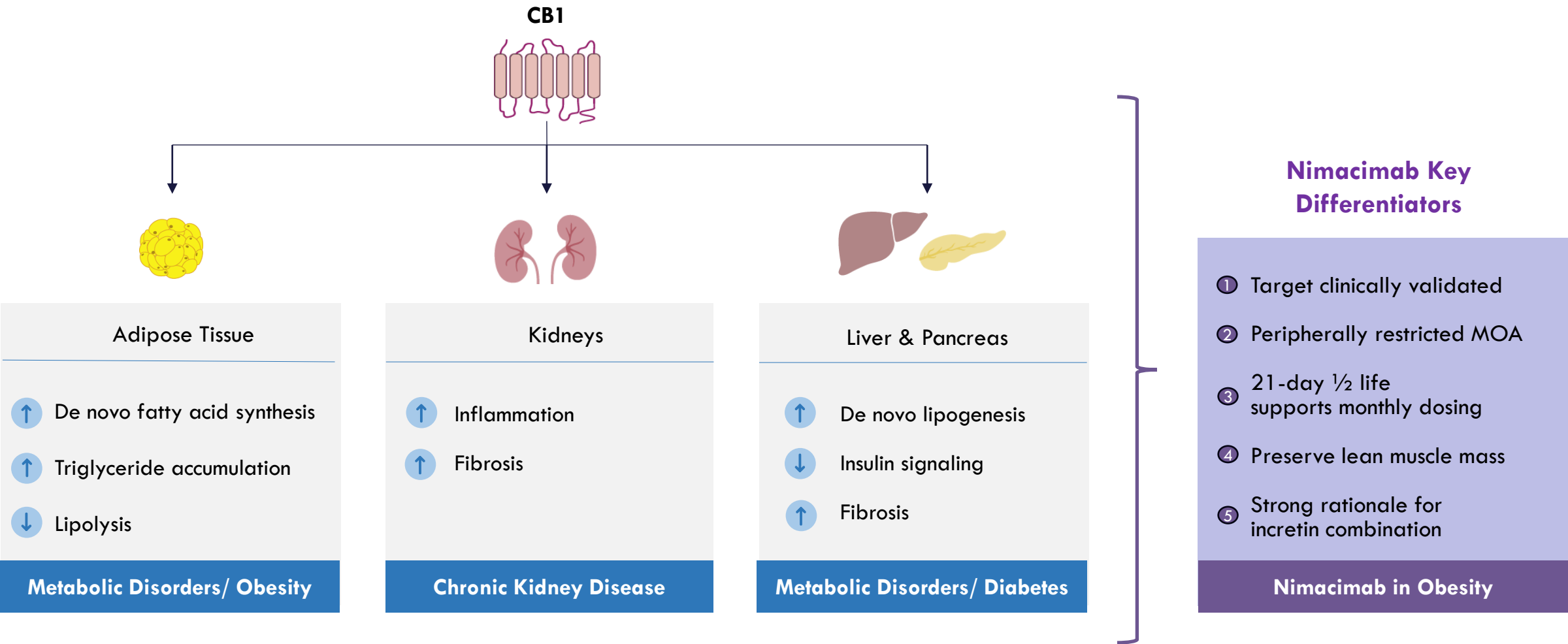


Nimacimab

Broad Metabolic Potential With Clinically Validated Mechanism of Action

Nimacimab: Differentiated Therapeutic in Obesity

Upregulation of CB1 signaling is involved in multiple inflammatory, fibrotic and metabolic diseases in various organs with significant prevalence and unmet needs



The Promise of CB1 Inhibition

Clinically validated MOA

sanofi

Rimonabant (Accomplia) developed by Sanofi and approved for weight loss in 2006 in EU

Demonstrated up to 10% weight loss over 1 year

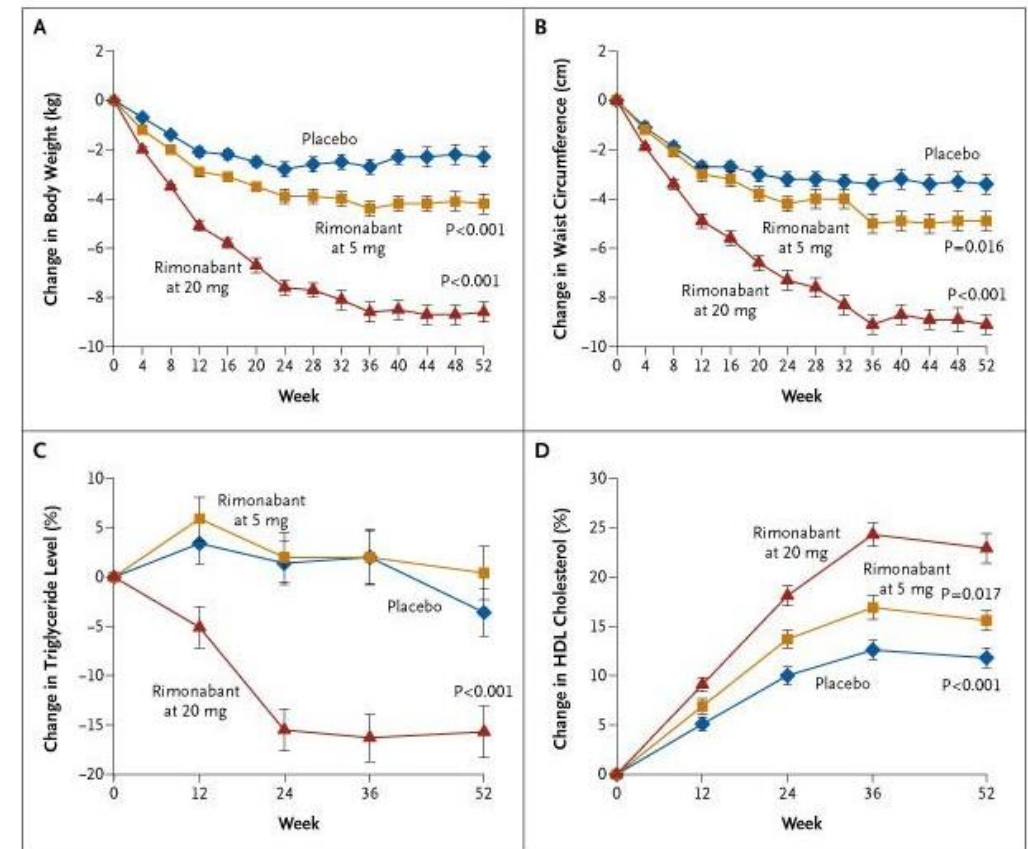
Improvements in metabolic outcomes as well

Removed from market due to CNS liabilities: depression and suicidal ideation

Resulted in multiple pharma's dropping CB1 inverse agonist programs.

Rimonabant

RIO-lipids Phase 3 study placebo (n=342); 5 mg rimonabant (n=345);
20 mg rimonabant (n=346)



Rimonabant in the Periphery: Metabolic Benefits Beyond Caloric Restriction

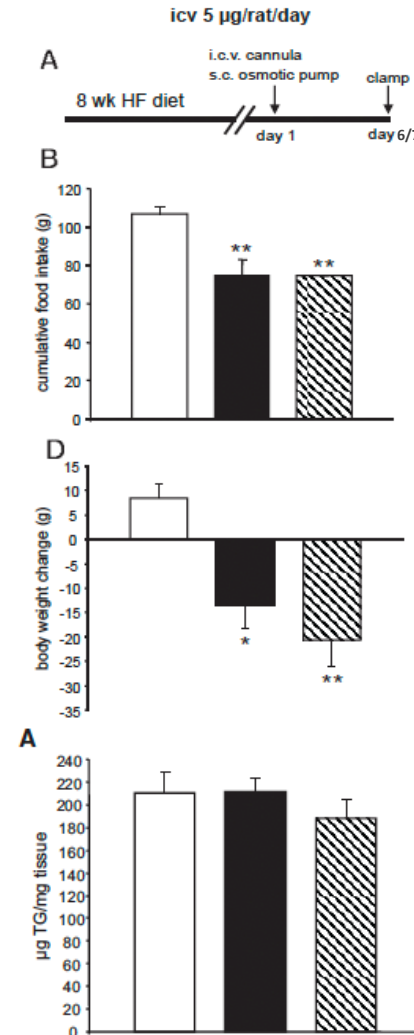
Study highlights impact of peripheral CB1 inhibition

Using a DIO model with a specific vehicle arm to control for the anorexic effect (hashed bars = vehicle-pf) by matching the caloric intake of CB1 blockade

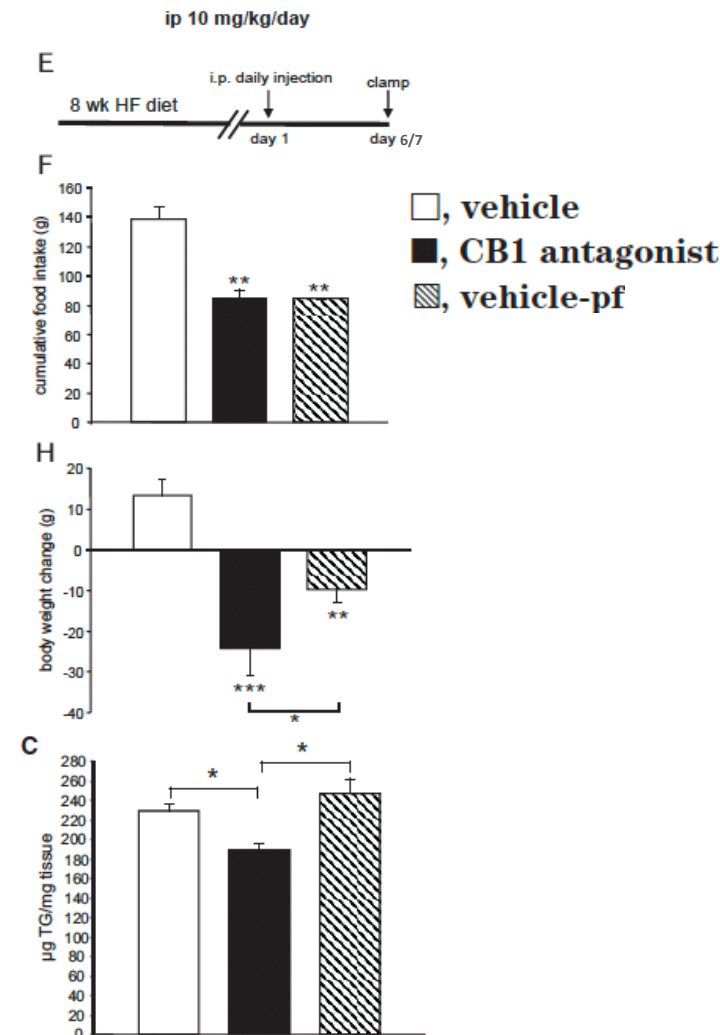
Blockade of peripheral, but not central, CB1 is a key driver of metabolic changes

- Body weight loss beyond caloric restriction highlights mechanisms beyond central anorexic effects
- Data is consistent with peripheral CB1 blockade decreasing body fat relative to mean mass

Central Inhibition Only



Global Inhibition

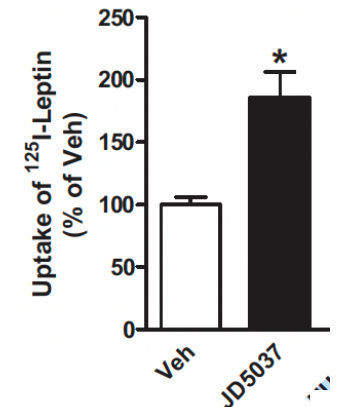
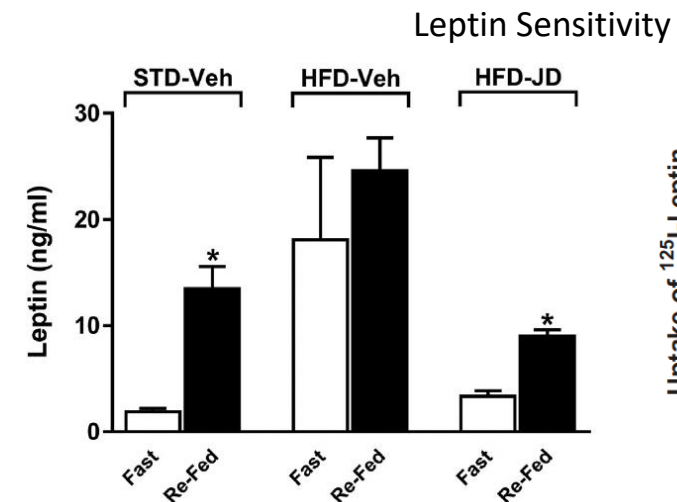
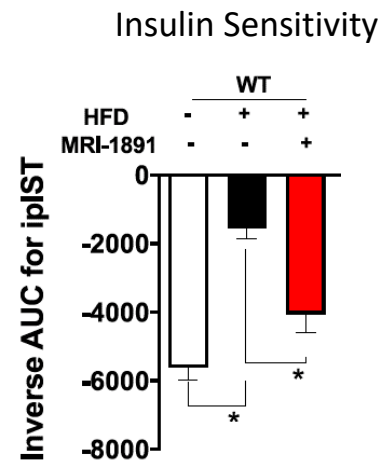
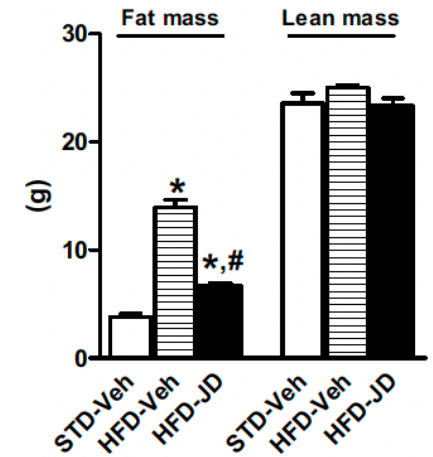
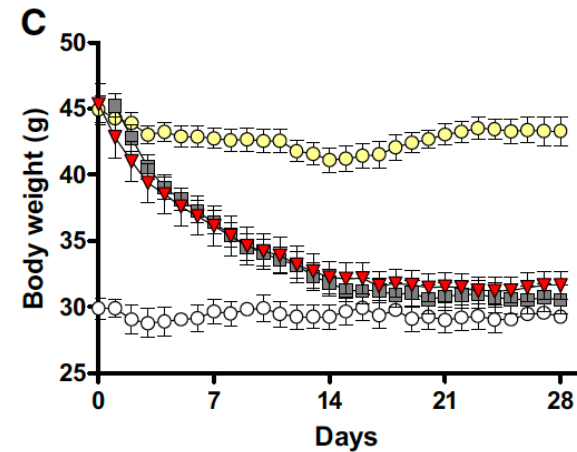
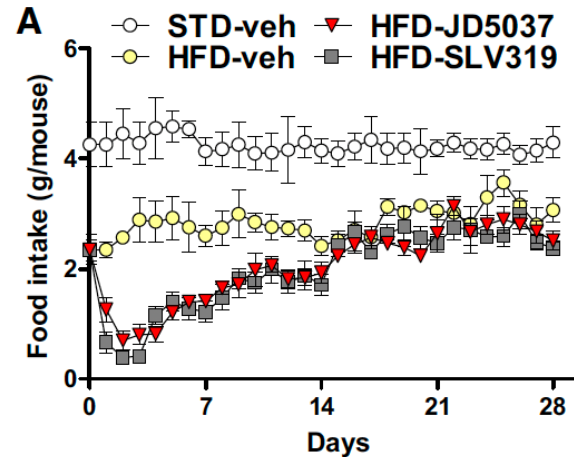


2nd Generation Peripherally Restricted CB1 Inhibitors Remain Efficacious

Peripherally restricted CB1 inhibitors reduce food intake and body weight (DIO model) comparable to non-restricted CB1 inhibitors

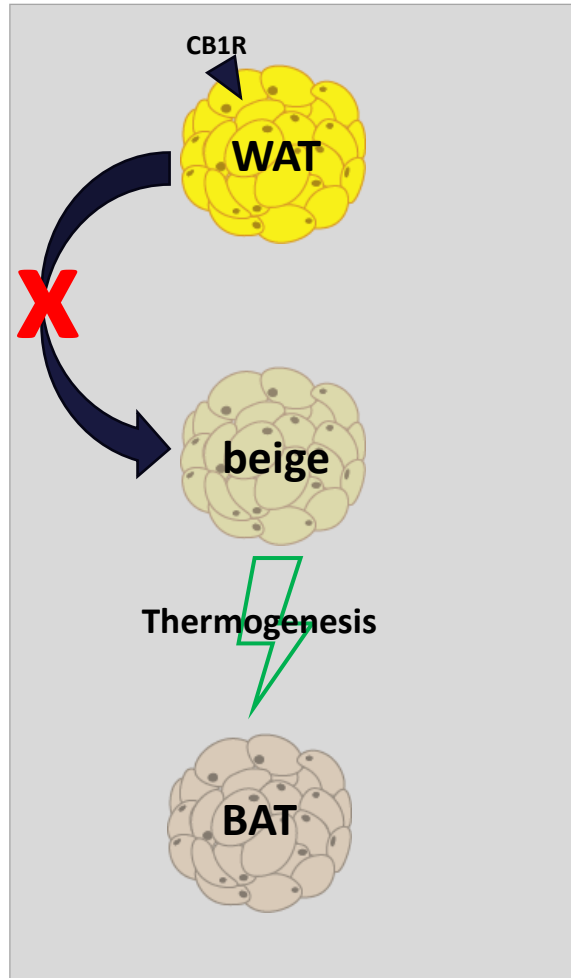
Peripheral CB1 inhibitors mediate reduction in fat mass but not lean mass

Blockade of peripheral CB1 can drive anorexigenic effects with additional metabolic gains (lean mass: body fat ratios, increased insulin/leptin sensitivity)



Peripheral CB1 Receptors and Fat Metabolism

Blocking CB1 potentially triggers metabolic reprogramming in adipose tissues, mediating conversion of white adipose tissue to beige adipose tissue



- The ECS is deeply involved in controlling energy metabolism.
- CB1 is highly expressed in adipose tissue and increases with obesity.
- Data suggests that blockade of CB1 could induce the trans-differentiation of white adipose tissue (WAT) towards thermogenic brown adipose tissue (BAT).
- Increase in UCP-1 expression correlated with upregulation in endocannabinoid expression.

Targeting Obesity Comes in Different Flavors

CB1 impacts key metabolic pathways that complement existing products & strategies

Key Targets Characteristics	KEY TARGETS / MECHANISMS			
	GLP-1	GIP	Glucagon	CB1
Decreases Appetite / Increases Satiety	✓	? (limited)	✗	✓
Delays Gastric Emptying	✓	✗	✓ (limited)	✗
Stimulates Insulin Secretion	✓	✓	✓	✓ (limited)
Insulin/Leptin Sensitivity	✗	✗	✗	✓
Lean Mass Preservation	✗	✗	✗	✓
Tolerability	✗	✗	✗	✓
Key Safety Concerns	Nausea, vomiting, diarrhea	Nausea, vomiting, diarrhea	Increased heart rate, LFT, glucose	Neuro- psychiatric symptoms
Other Notable Considerations	Reduces glucagon secretion	Perceived synergistic in CNS w/ GLP1	Metabolic benefits/mimics exercise	Complements incretin backbone

Opportunities for Nimacimab

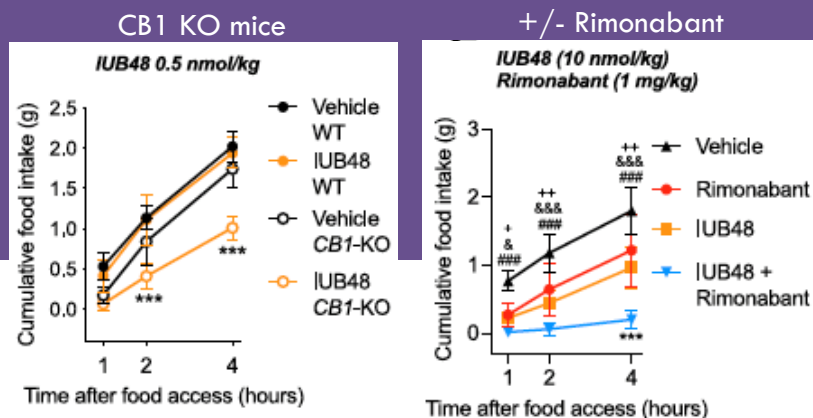
- ✓ Magnitude and sustainability of weight loss
- ✓ Safety/tolerability profile (e.g. GI side effects)
- ✓ Frequency of drug administration
- ✓ Need for dose titration (PK/PD)
- ✓ Maintenance dose / setting
- ✓ Combinability with other mechanisms / agents

Prescribers/patients/payors will consider multiple different product attributes based on individual needs

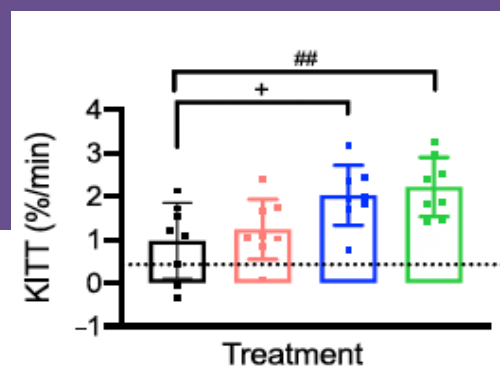
Preclinical Rationale for Combination of CB1 and GLP-1

Complementary pathways may provide additive therapeutic effects for GLP-1 agonists

CB1 and GLP-1-dependent caloric restriction

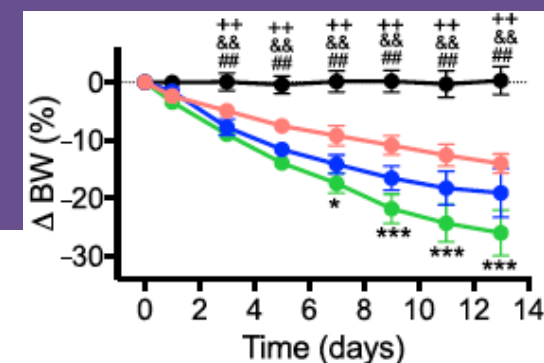


Increased insulin sensitivity with CB1 inhibition



● Vehicle ● Semaglutide ● JD-5037 ● Semaglutide + JD-5037

Significant weight loss with combination



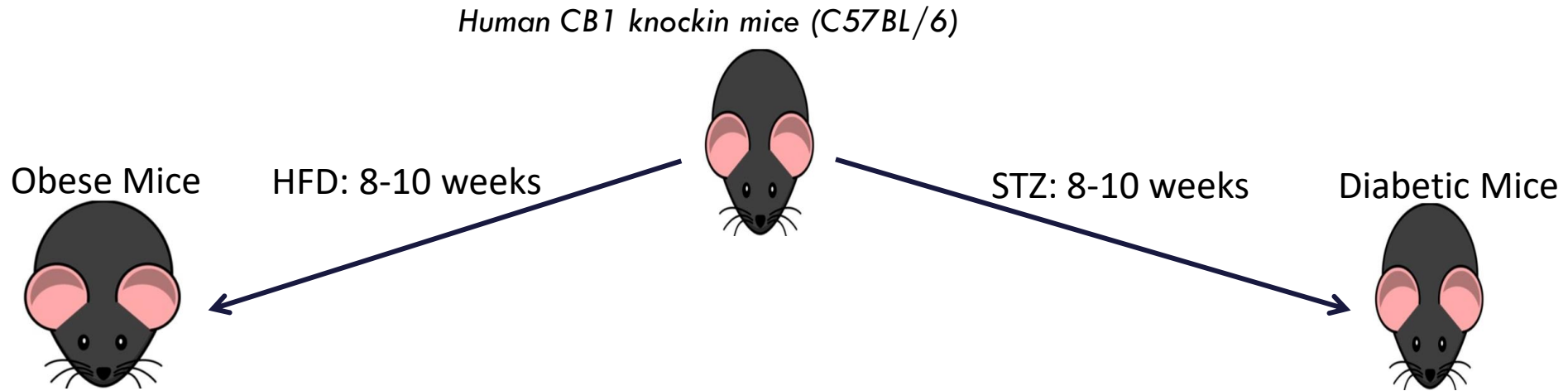
- Knockout mice and small molecule blockade both suggest that CB1 may augment anorexigenic effect of GLP-1
- Consistent with clinical data that associates CB1 signaling with reduced incretin secretion²

- CB1 blockade may drive key orthogonal metabolic pathways
- In addition to leptin sensitivity, insulin sensitivity may further augment more durable metabolic gains

- Both semaglutide and CB1 inhibitor drive weight loss
- Combination data suggest that effects may be driven by non-overlapping MOA

Preclinical Strategy to Evaluate Key Opportunities

Skye's human CB1 transgenic mouse: critical tool to model obesity and nephropathy



Q: Can peripheral CB1 blockade mediate weight loss comparable to rimonabant or GLP1-RA? Mechanistic rationale to combine with GLP1-RA?

- Measure lean mass and body fat (vs control and pair-fed)
- Metabolic gains beyond anorexigenic
- Insulin (+ sensitivity), leptin, CCK, ghrelin levels
- Reduced liver fat deposits

Q: Can peripheral CB1 blockade reduce progression of diabetic nephropathy? Comparable to ACEi/ARB? Mechanistic rationale to combine?

- Measure progression of albuminuria/GFR
- Reduction of nephrin/podocin, inflammation, and markers of fibrosis
- Dietary induced obesity can additionally be used to model CKD with renal-focused endpoints

Nimacimab: Development Plan for Obesity and Chronic Kidney Disease

Phase 1 Clinical Data and Phase 2 Update

Nimacimab Biodistribution

Little to no accumulation in the brain

Cyno	Day 1 (post 1 st dose)	Day 8 (post 2 nd dose)	Day 15 (post 3 rd dose)
CSF/Serum 3 mg/kg IV q1w	BLQ	<0.02%	<0.02%

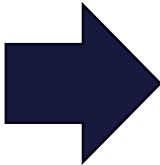
Cyno	9 hours
CSF/Serum 40 mg/kg IV	0.01%

Level in CSF determined using quantitative ELISA at the time points studied.

Rhesus	48 hours
CSF/Plasma	0.05%
Prefrontal Cortex/Plasma	0.83%
Cerebellum/Plasma	0.84%
Liver/Plasma	16.44%

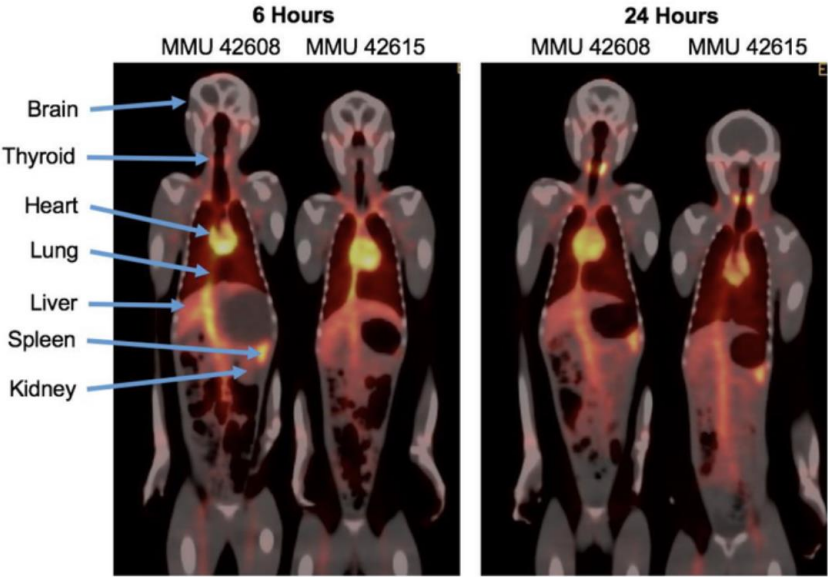
- Tissues harvested without perfusion
- Tissue to plasma assuming 1 mL = 1 g

Uptake of I241-nimacimab labeled antibody in tissues at the timepoints studied. PET imaging also confirmed no accumulation in brain



Little to no nimacimab found in the brain

High levels of nimacimab found in the plasma at 24 hours



Nimacimab Toxicology – NOAEL > 75 mg/kg

Safe with significant safety window established

- **IND-enabling toxicology study completed with up to 75 mg/kg nimacimab administered weekly IV for 4 weeks.**
 - No nimacimab-related observations in toxicology assessments performed including neurological observations.
- **Three-week and 26-week toxicology studies completed with up to 75 mg/kg nimacimab administered bi-weekly SubQ.**
 - No nimacimab-related clinical signs or changes in ophthalmology, electrocardiography, blood pressure, blood chemistry, hematology and histopathology.
 - NOAEL of > 75 mg/kg.
 - Long half-life of ~21 days and high exposure at the end of the study.

Nimacimab Phase 1 Data

Demonstrated encouraging tolerability, pharmacokinetics and encouraging evidence of efficacy

Phase 1 SAD in Healthy Volunteers and MAD in NAFLD (diabetic/pre-diabetic)

- SAD
 - 24 patients enrolled (18 patients used as PK population)
 - 0.6 mg/kg, 1.2 mg/kg and 2.5 mg/kg administered IV over 30 minutes
- MAD
 - 82 patients enrolled
 - 0.6 mg/kg, 1.2 mg/kg and 2.5 mg/kg administered IV over 30 minutes on weeks 0, 1, 2 and 3
- PK: 18-22 days
- ADA < 10% of subjects dosed
- Biomarkers
 - Trends in reduction of ALT, AST, alkaline phosphatase, GGTP, and ELF score (non-dose dependent) with significant reduction in hyaluronic acid; suggests potential anti-inflammatory and anti-fibrotic effect of nimacimab
 - Dose-dependent reduction in LDL-c observed

SKYE has received FDA clearance of its IND for a Phase 2 clinical trial for nimacimab in obesity and chronic kidney disease

Nimacimab Bioavailability Study

Intravenous versus subcutaneous dosing

Study Design

- Single 100 mg SC dose vs. single 100 mg IV dose of nimacimab
- 10 subjects dosed SC vs. 10 subjects with IV

Conclusions

- Absolute bioavailability approximately 60% after a single dose
- No new trends in safety parameters
- As expected, slower absorption for SC than IV dosing
- SC dosing in Phase 2 enabled
- Similar ADA effect on PK (10%-20%) of subjects in IV and SC groups

Chronic Kidney Disease in Obesity

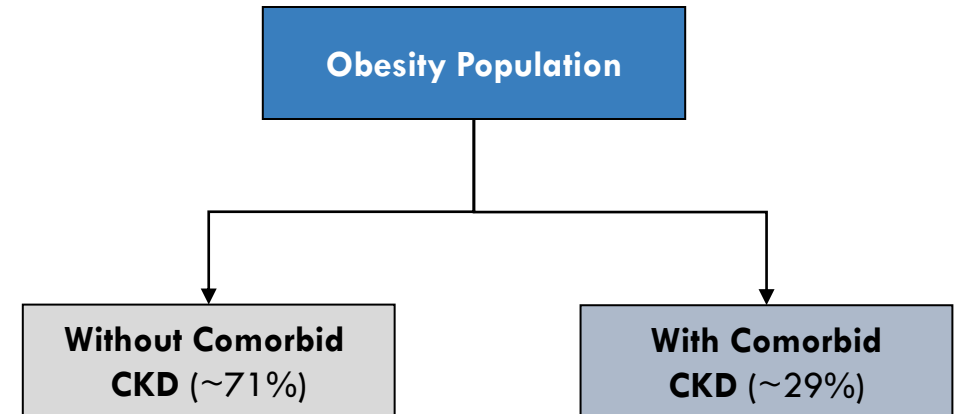
~30% of obese patients have CKD; >80% of CKD patients are overweight/obese

Chronic Kidney Disease (CKD) in Obesity



More than 1 in 7 US adults have CKD; obesity is one of leading causes

- Patients who develop CKD are at risk of build-up of toxic waste and fluid accumulation, leading to **high blood pressure, heart disease, stroke, and early death**
- Studies have demonstrated a strong correlation between **obesity and development and progression of CKD**, as well as development of ESRD
- Obesity is intimately linked to hypertension and diabetes—the **two biggest contributors** to the development of kidney disease—but has also been shown to **predispose patients to CKD independent** of these two other related conditions
- Studies estimate that **~24-33% of obese patients have comorbid CKD** (for an average of ~28.5%), while **>80% of CKD patients are overweight or obese**
- As prevalence of obesity has risen over decades, so has that of CKD



While the **exact mechanistic association between obesity and CKD remains unclear**, researchers acknowledge that a combination of hemodynamic/metabolic changes and lipid nephrotoxicity (excessive lipid deposition) likely **cause and/or aggravate CKD in obese individuals**

Proposed Phase 2 Clinical Trial Design: Obesity and Diabetic Kidney Disease

Key Inclusion Criteria

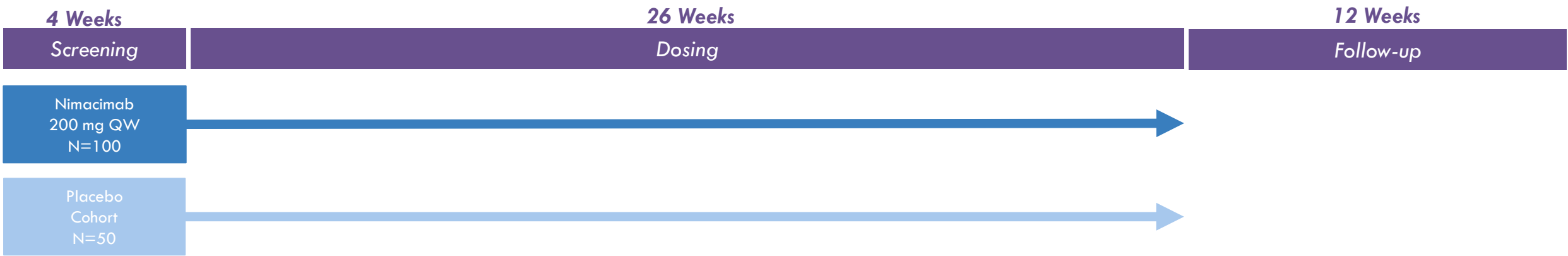
- Obese: BMI ≥ 30 kg/m²
- Overweight: BMI ≥ 27 and < 30 kg/m²
- UACR ≥ 200 mg/g
- eGFR 20 – 60 ml/min

Primary Endpoint

- Change in weight from baseline

Secondary Endpoint

- Change in UACR, UPCR and eGFR from baseline
- Exploratory biomarkers



“Multiple Shots on Goal”: Multiple Metabolic-Related Data Points from Phase 2 Design

Obesity

- Changes in weight loss
- Changes in muscle wasting
- Changes in triglycerides and cholesterol
- Changes in HbA1C

Chronic Kidney Disease

- Changes in eGFR
- Changes in UACR and UPCR
- Renal biomarkers
 - Glomerular (BTP, B2M)
 - Endothelial (ADMA, fetuin-A)
 - Tubular injury (KIM-1, NGAL)

Other Biomarkers of Metabolic Disorder

- Markers of inflammation
- Markers of fibrosis
- Appetite hormones

Metabolic Diseases Indications and Usage By Drug Class

Potential for targeting obesity and diabetic kidney disease as an indication

	ACEi	ARB	SGLT2			MRA	GLP-1		CB1
	Lotensin	Avapro	Jardiance	Farxiga	Invokana	Kerendia	Ozempic / Wegovy	Mounjaro	INV-202
CKD	✗	✓*	✓	✓	✓*	✓* / Phase 3	Phase 3	Phase 3	Phase 2*
Obesity	✗	✗	✗	✗	✗	✗	✓	Filed	Phase 2**
T2D	✗	✗	✓	✓	✓	✗	✓	✓	Phase 2**
CVD	✓	✓	✓	✓	✓†	Phase 3	✗	Phase 3	Phase 2**
NASH	✗	✗	✗	✗	✗	✗	Phase 3	Phase 2	Phase 2**

Drug classes are indicated or being trialed across metabolic disorders

Table Legend

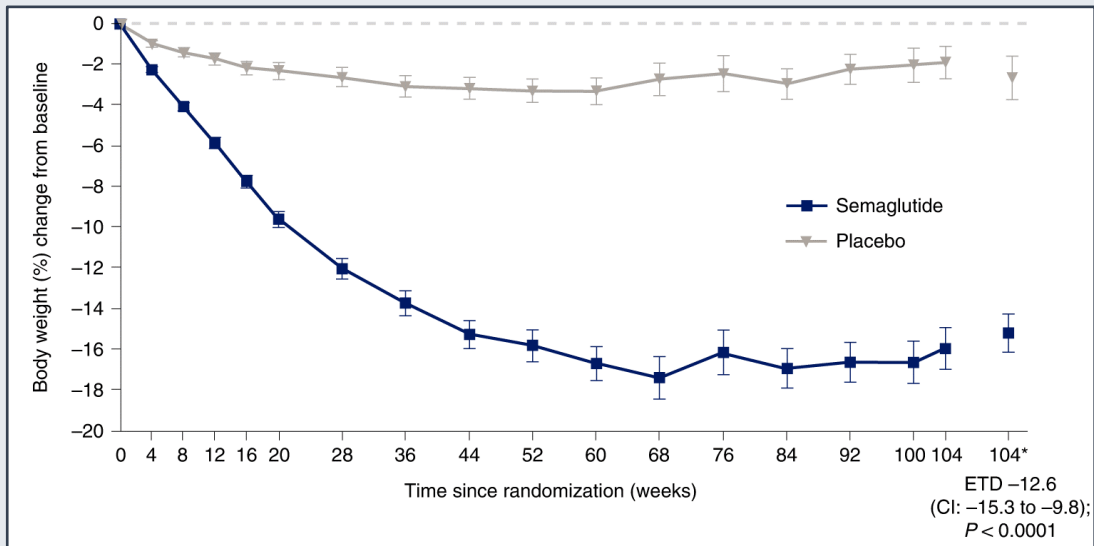
✓	Approved for indication	*	Approved/in-development for diabetic kidney disease only
✗	Not approved for indication	**	Under investigation in metabolic syndromes which includes obesity, T2D, CVD and NASH
Phase	In-development for indication	†	Approved for CVD only in patients with T2DM

Challenges Associated with Long-Term Use of GLP-1 RA Treatment

Plateau and rebound effect

Considerations of Long-term Treatment with GLP-1 Receptor Agonists

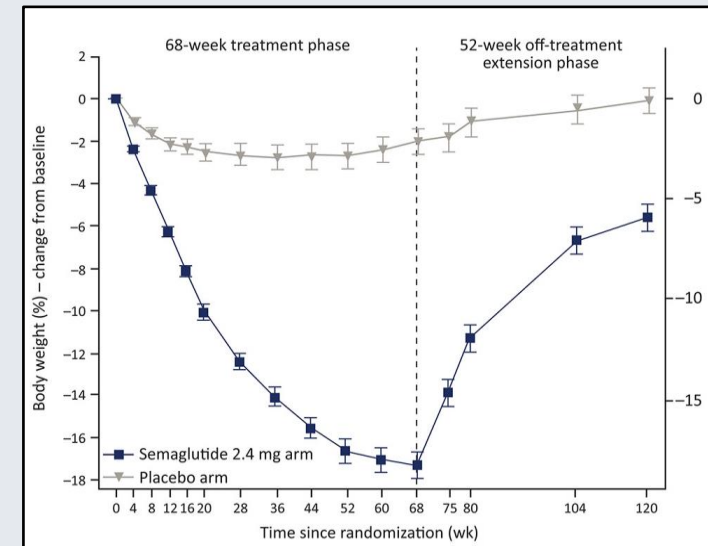
STEP 5: Durability of Weight-loss Over 2 Years



Garvey et al., Nat Med. 2022

- The STEP-5 trial demonstrated patients treated with semaglutide were able to achieve significant weight loss over first 68 weeks
- After 68 weeks of treatment, additional treatment with semaglutide did not result in additional weight loss as weight plateaued

STEP 1 Trial Extension: Withdrawal of Semaglutide



Wilding et al., Diabetes Obes Metab. 2022

- Results from STEP 1 trial extension showed withdrawal of semaglutide was associated with weight gain
- Approximately 1 year after treatment withdrawal, most patients had regained ~66% of weight initially lost on treatment

GLP-1 RA Effects on Muscle Wasting

Opportunities for improvement

Clinical Data

- As the FDA has not required body composition as a primary endpoint in weight loss studies, **data surrounding GLP-1's effect on lean body mass and skeletal muscle is lacking**
- **Lean loss is inevitable with significant weight reduction**; ~25% lean body weight loss is typical
- From sub-studies of 178 and 140 semaglutide-treated patients in SUSTAIN and STEP trials, **lean mass accounted for ~40% of total weight loss**
- As the FDA suggests only a minority of trial participants should receive body composition measurements, the **muscle atrophy effect is unlikely to prevent products from reaching market**
- **Despite the incomplete data, muscle atrophy is highly publicized and frequently cited as a danger of GLP-1 treatment**

PETER ATTIA
MD

Lean mass loss on GLP-1 receptor agonists: a downside of the “miracle drugs”

General sentiment from health commentators

Ongoing Collaborations

- **Lilly and Bioage Labs announced a collaboration** (Oct 2023) to conduct a Phase II trial to assess weight loss for patients treated with Mounjaro (tirzepatide) in combination with BGE-105 (azelaprag)
- BioAge previously presented clinical data showing that azelaprag **prevented muscle atrophy in older healthy volunteers** who were placed on 10 days of strict bed rest
- In preclinical mice models, **administration of tirzepatide + azelaprag was linked to healthier weight loss than tirzepatide alone**
- **Lilly also recently acquired Versanis** which is testing their product in combination with semaglutide for its ability to preserve muscle mass during weight loss

Nimacimab Clinical Development Summary

Broad metabolic potential

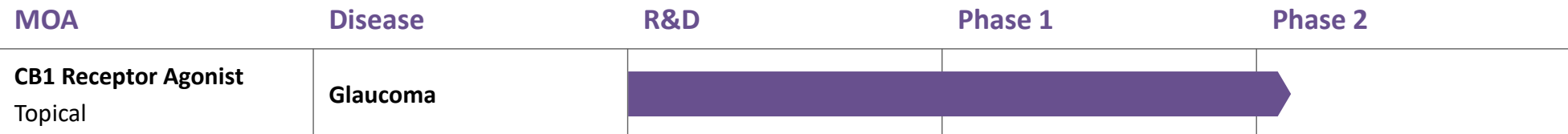
- **Nimacimab has significantly improved peripheral restriction than INV-202.**
 - Potentially better safety.
- **Nimacimab has potential to treatment multiple metabolic indications**
 - Rimonabant has demonstrated clinical efficacy in obesity.
 - Preclinical data demonstrate peripheral CB1 inhibition independent of central control in metabolic benefits.
 - Multiple clinical/preclinical data demonstrating CB1 expression and relevance in inflammatory and fibrotic mechanisms of disease.
- **Phase 2 clinical trial design targets patient population that will allow for multiple metabolic data points and potential approvable indication (i.e. obese patients with CKD).**
 - Phase 2 design provides signal detection across multiple metabolic-related indications.
 - Obese patients with CKD is a potential unclaimed indication by any current or future drug.
- **Obesity market is nascent and constantly changing with better understanding of impacts on long-term use of GLP-1 receptor agonists**
 - Combination opportunities
 - Post-GLP-1 RA failure opportunities

SBI-100 OE

Significant Unmet Needs in Glaucoma with Opportunity for New Class of Medicine

SBI-100 Ophthalmic Emulsion

Improving CB1-targeting drug design for glaucoma



Best-in-class Molecule

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.

Clinical Development History of Class

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.

New Drug Design/Improvements

New 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.

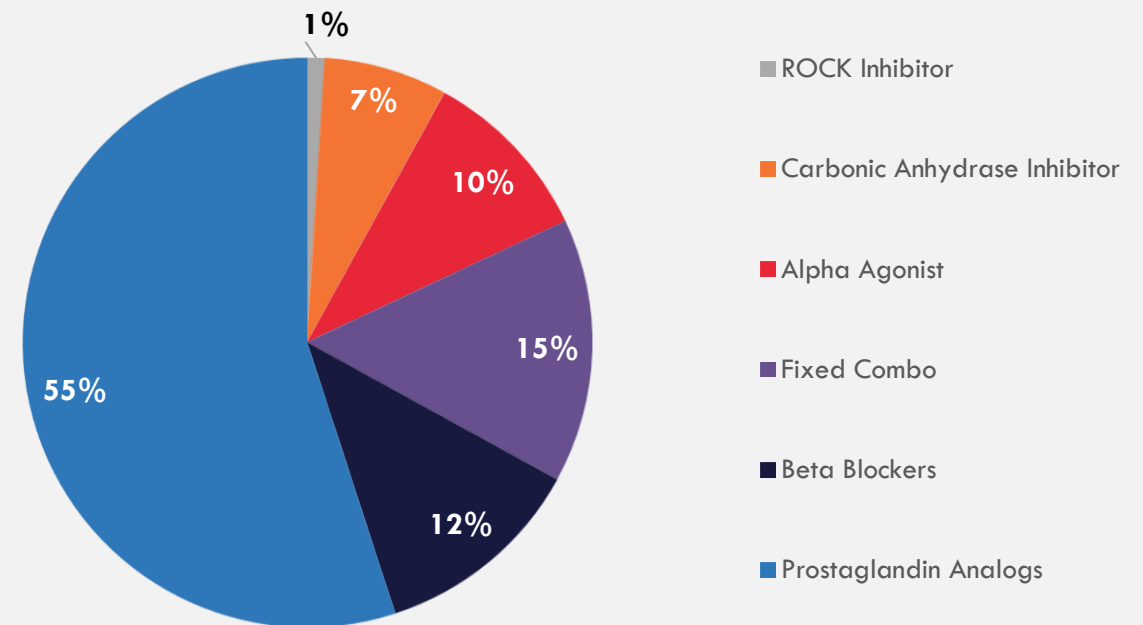
All drugs are investigational and subject to regulatory approval. For investor audiences only.
1: Hepler RS, Frank IR. Marijuana smoking and intraocular pressure. JAMA. 1971 Sep 6;217(10):1392. PMID: 5109652.
2: Hepler R.S., Petrus R.J. Experiences with administration of marijuana to glaucoma patients. In: Cohen M., editor. *The Therapeutic Potential of Marijuana*. Springer; New York, NY, USA: 1976. pp. 63–75
3: Hepler R.S., Frank I.M., Petrus R. Ocular effects of marijuana smoking. In: Braude M.C., Szara S., editors. *The Pharmacology of Marijuana*. 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.

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 1 st 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.



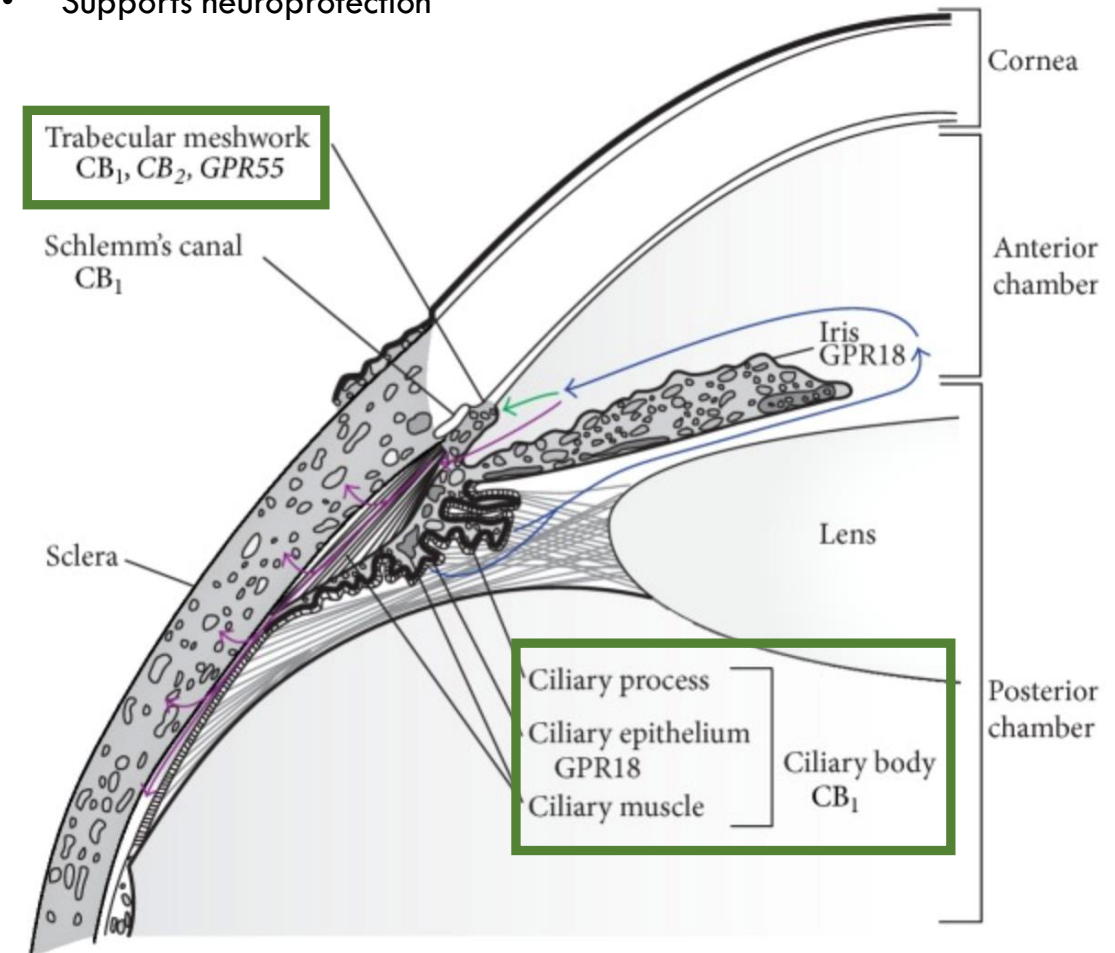
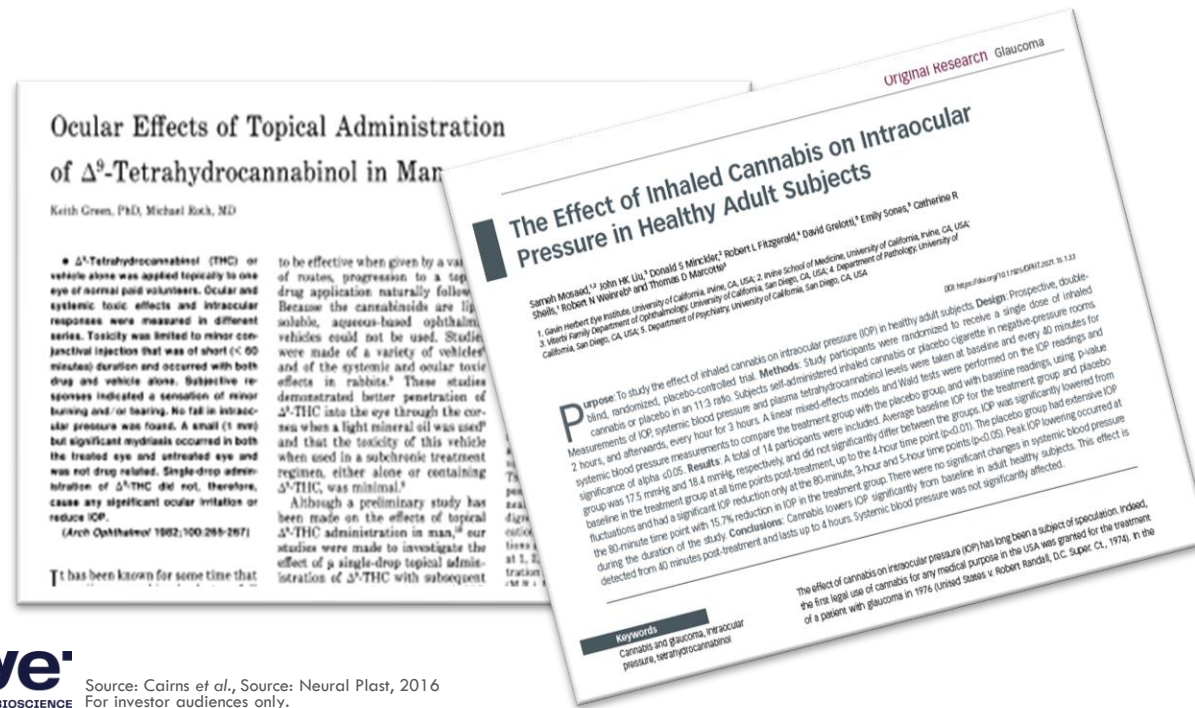
CB1 Agonism as New Therapeutic Class to Treat Glaucoma

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

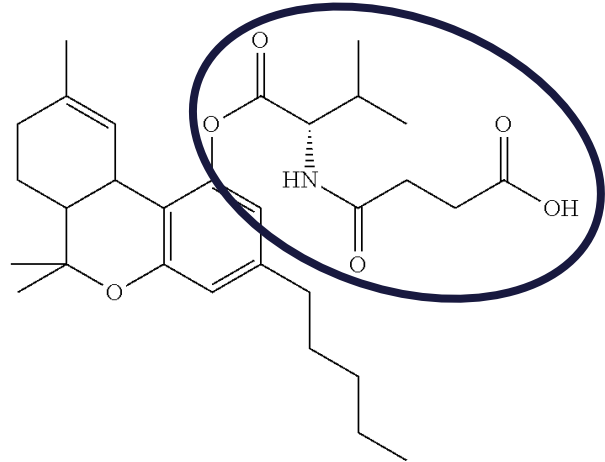
CB1 is expressed in key ocular tissues and its engagement¹:

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



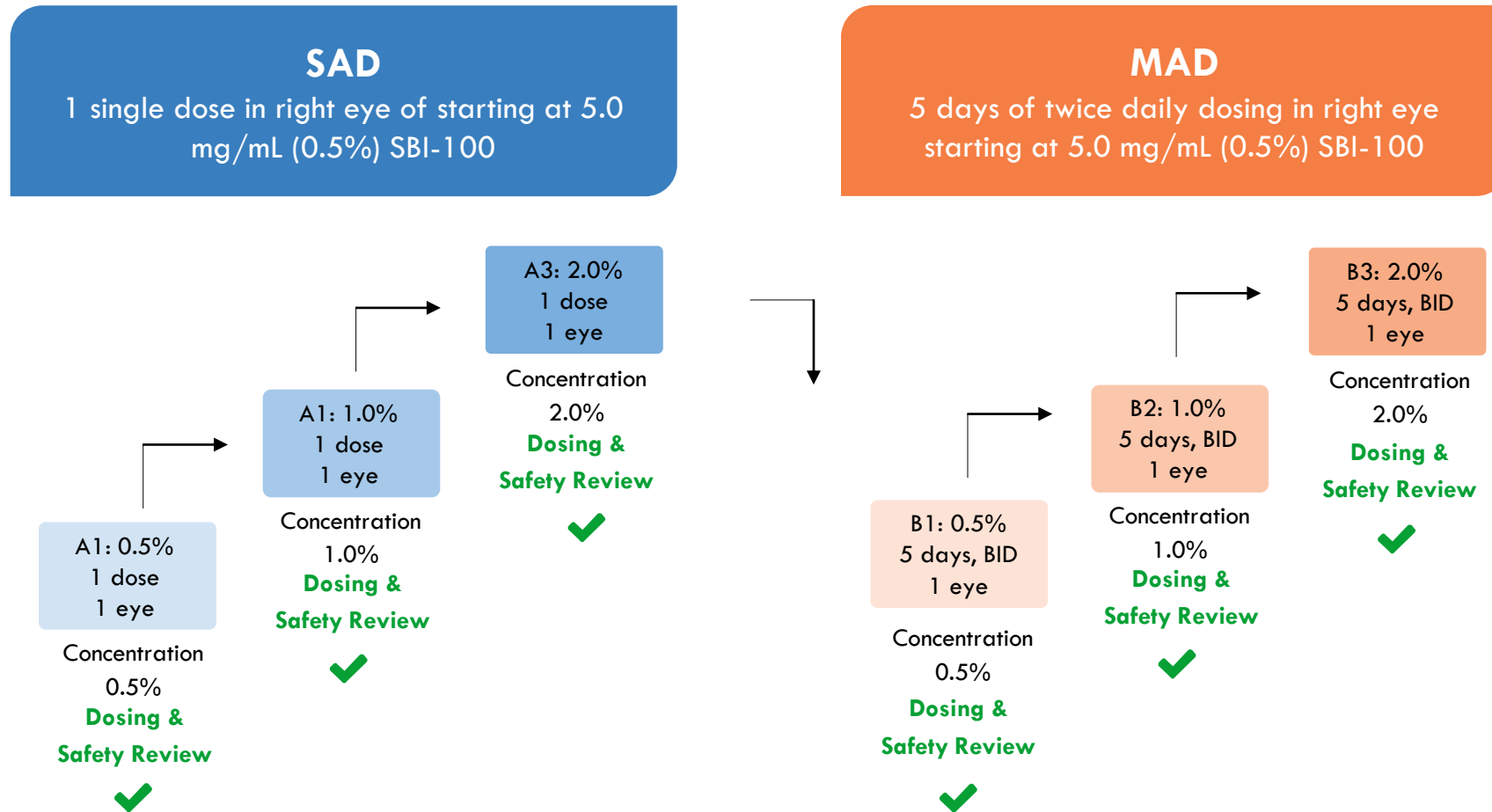
SBI-100 Ophthalmic Emulsion: Synthetic THC-based Prodrug

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

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



Pharmacokinetics – Little to no Exposure of THC in Plasma

MAD PK population

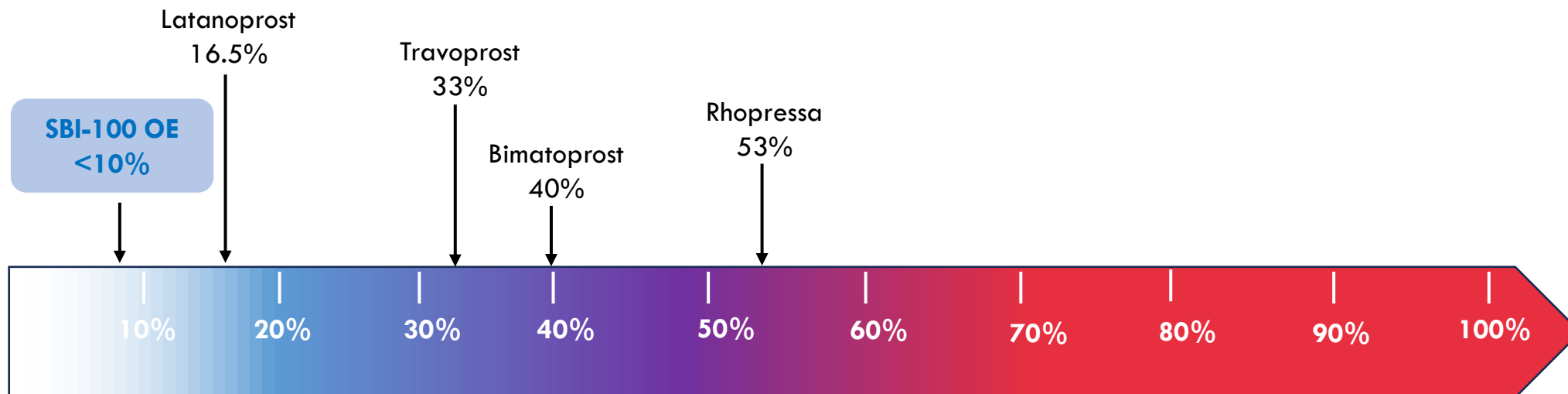
	0.5% SBI-100 N=6	1.0% SBI-100 N=6	2.0% SBI-100 N=6
Day 1 PK Parameters, Mean (SD)			
AUC (h*ng/mL) SBI-100	0.9184 (0.4252)	0.8252 (0.2533)	2.131 (1.139)
Cmax (ng/mL) SBI-100	0.2742 (0.07336)	0.2973 (0.1103)	0.7202 (0.3403)
Day 5 PK Parameters, Mean (SD)			
AUC (h*ng/mL) SBI-100	3.003 (1.014)	1.948 (0.6637)	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.

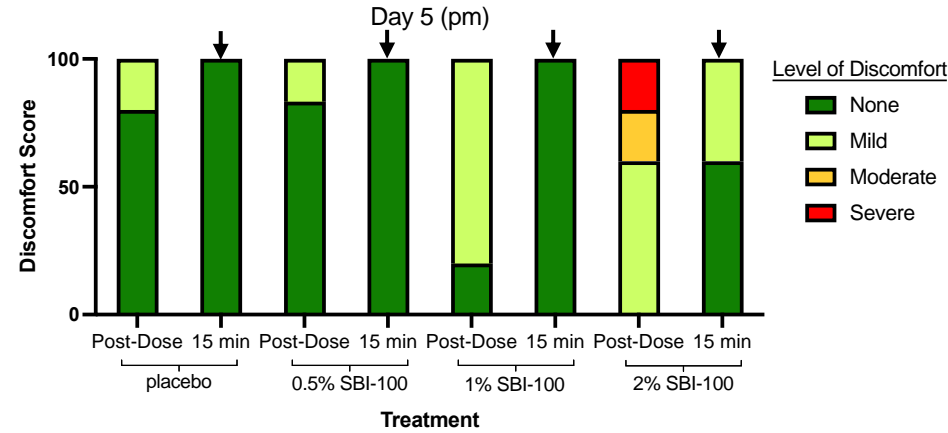
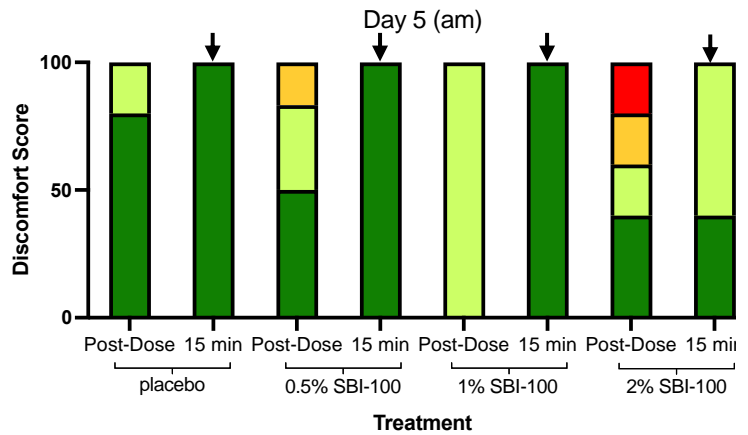
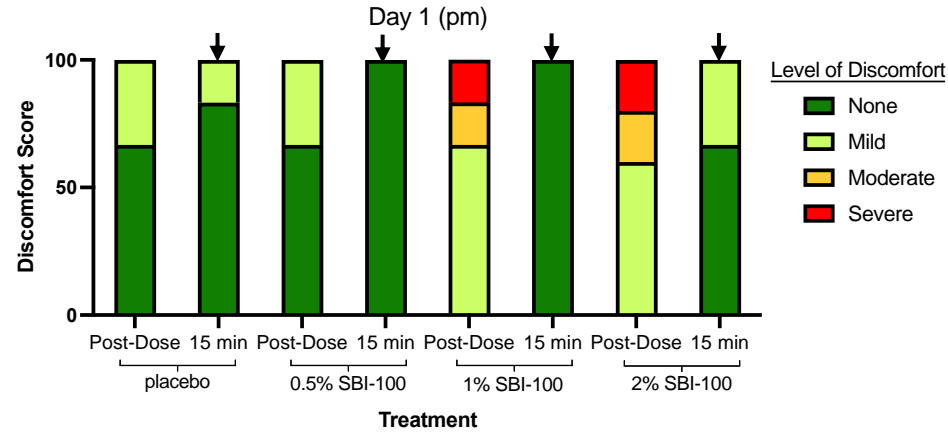
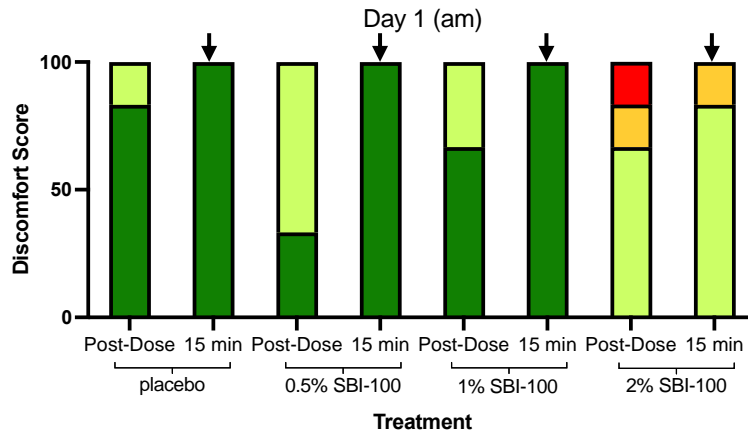
SBI-100 OE Demonstrates Significantly Less Hyperaemia Compared to Other Therapies

Hyperaemia has notable impact on patient adherence to drug regimen

Incidence of hyperaemia in currently approved drugs vs. SBI-100 OE



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.

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 Analysis¹ – “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

SBI-100 OE Phase 1 Safety Profile/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 2 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

4 Weeks

14 Days

Screening

Dosing

Safety Follow-up

Cohort 1
0.5 % BID
N=18



Cohort 2
1.0 % BID
N=18



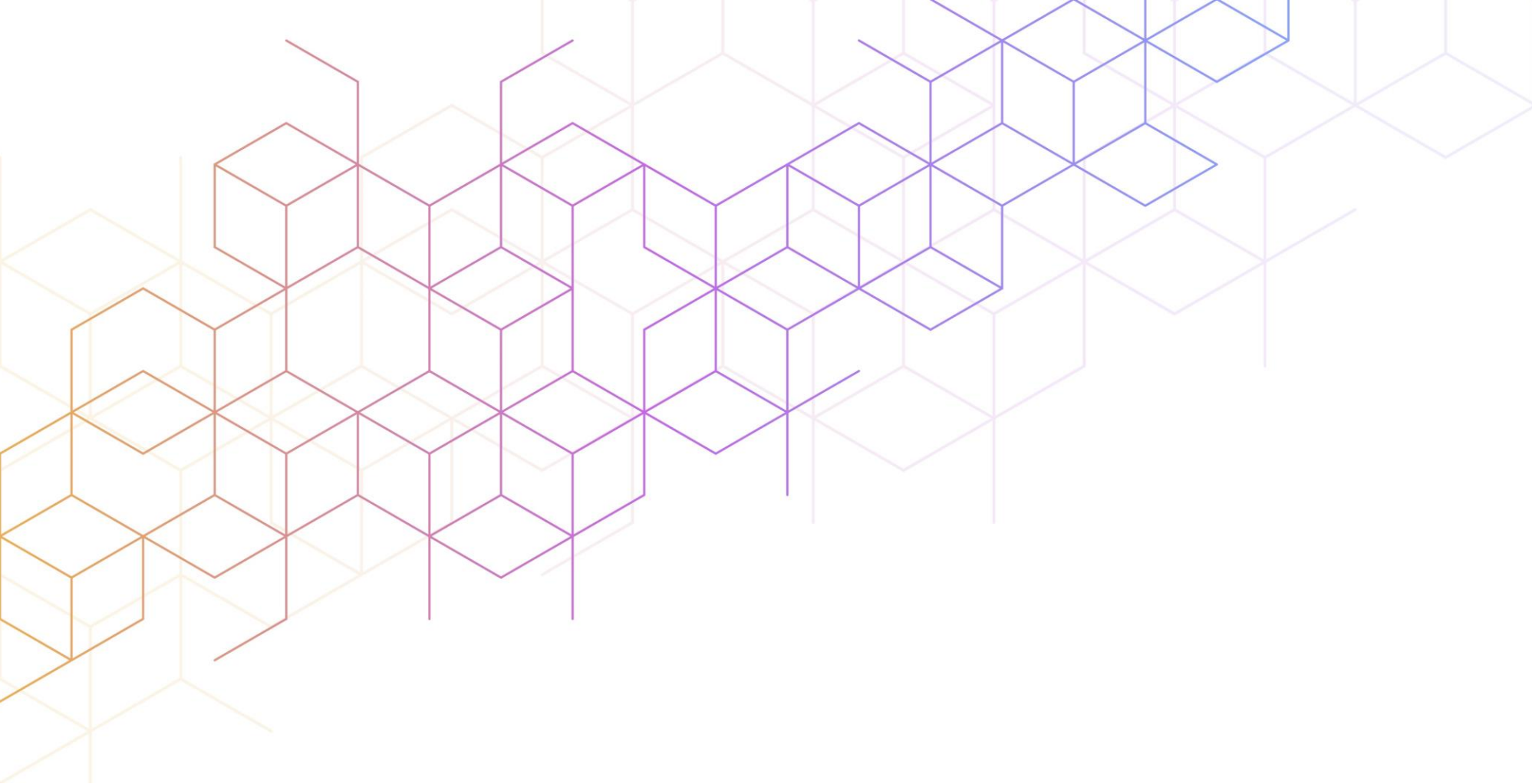
Placebo
Cohort
N=18



**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



Summary

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

- ✓ SBI-100 OE Phase 1 study data in healthy volunteers – Q4
- ✓ SBI-100 OE Phase 2a glaucoma clinical trial Initiation – Q4
- ✓ Nimacimab IND submission for weight loss/CKD – Q4
(clearance announced January 9th 2024)
- ✓ Continued in vivo studies, biomarker development, next-generation efforts

2024

Nimacimab Phase 2 obesity/CKD clinical trial initiation – mid-'24

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 study initiation – Q4

Capitalization

Cap Table¹

Common shares o/s	12.3 M
Options and RSUs	0.5 M
Warrants	3.3 M
Convertible note (as-converted basis)	1.0 M
Common shares f/d	17.1 M
Float ²	3.2 M
Cash & Cash Equivalents *	\$5.1 M

Ticker: SKYE (OTCQB)

Avg. daily volume (YTD)	8.3 K
Market cap ³	\$32.1 M

Top Holders⁴

5 AM Ventures	37%
Versant Ventures	16%
GSK	6%
Apposite Healthcare Fund LP	6%
Other Inst./Corp.	9%
Total	74%

¹ Per Q3 10Q filing

² Bulk of new investment locked up for 12 months to August 2024

³ 01/9/24

⁴ 08/21/23

*Excludes \$9.1 million restricted cash posted as appellate bond

Thank you

Learn more, please contact:

ir@skyebioscience.com, +1 (858) 410-0266

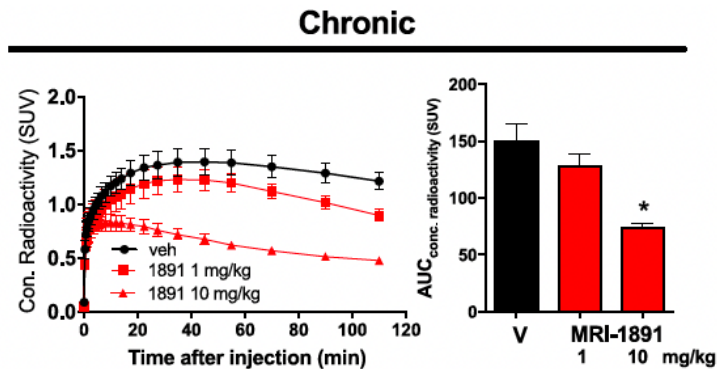
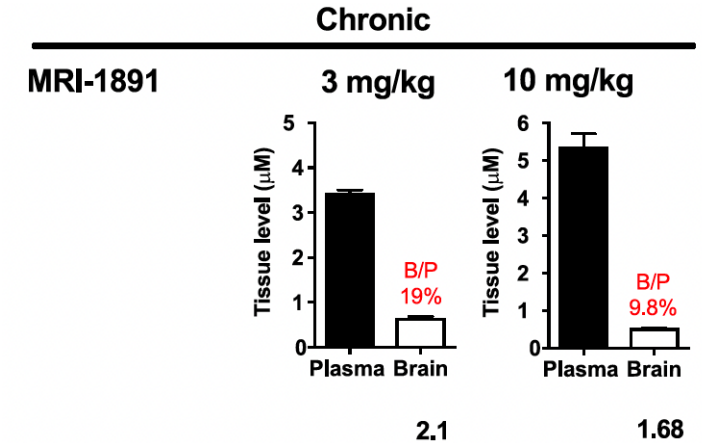
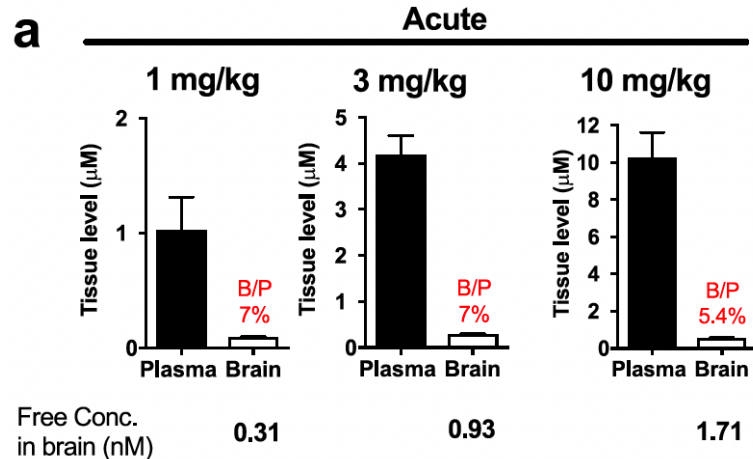
Appendix – Nimacimab Supplemental Slides

Some CNS Exposure with Small Molecule 2nd Generation CB1 Inhibitors

Since the demise of rimonabant, multiple groups have tried to develop new CB1 inhibitors that are peripherally restricted

Most are small molecules and also inverse agonists similar to rimonabant

However, even current lead 2nd generation CB1 inhibitor, INV-202, still has significant CNS penetration and cause for concern related to CNS liabilities in humans

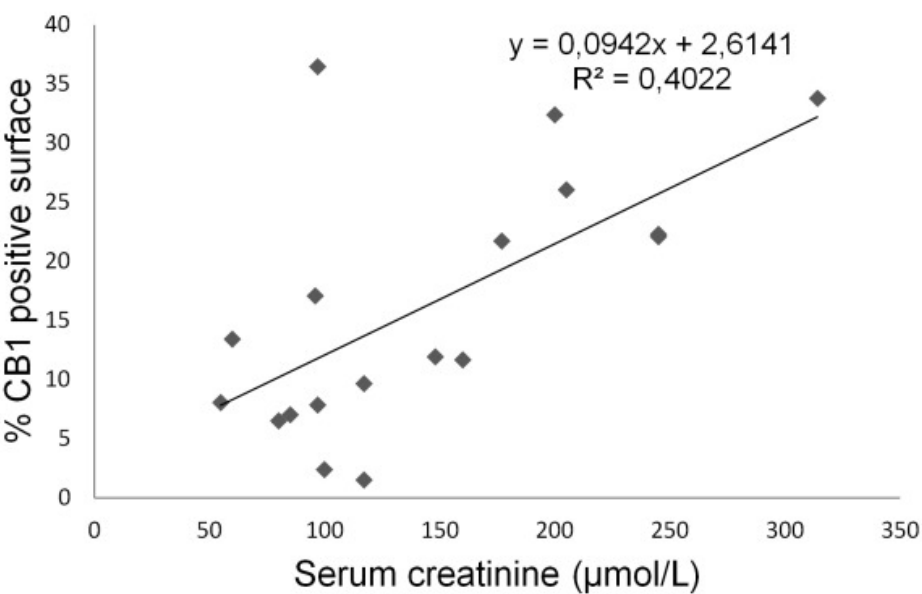
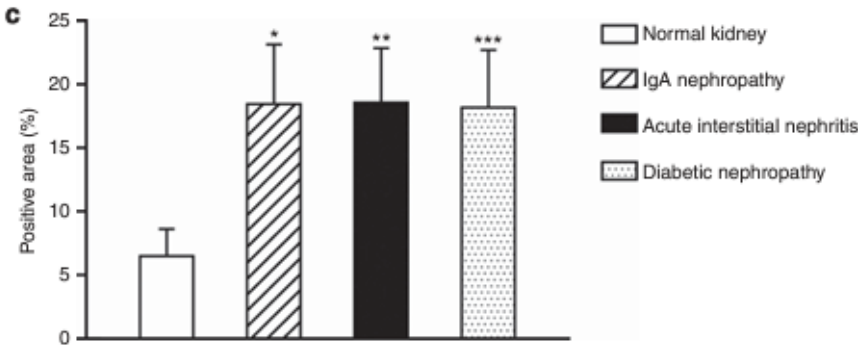


Significant receptor occupancy with chronic dosing at 10mg/mL

CB1 Up-regulation is Associated with Human Kidney Disease

Patient biopsies in IgAN, nephritis and diabetic nephropathy demonstrate increased CB1

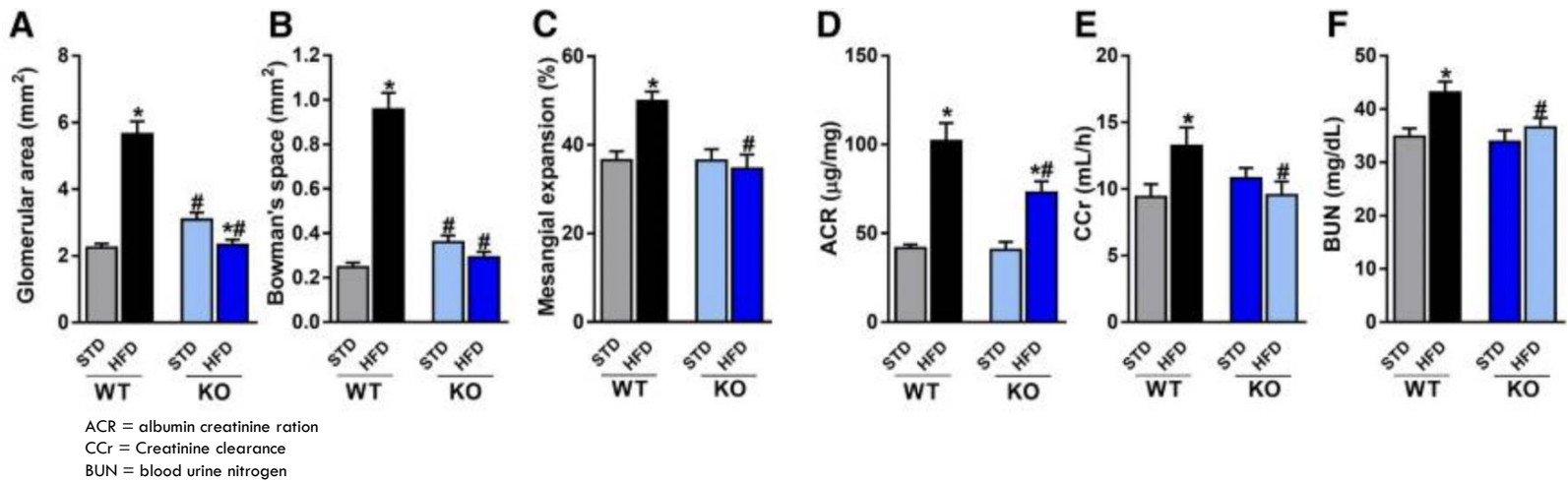
	Normal kidney	IgA nephropathy	Acute interstitial nephritis	Diabetic nephropathy
Tubules	+/-	++	++	++
Interstitial	0	+	+	+
Glomeruli	+/-	++	+	++



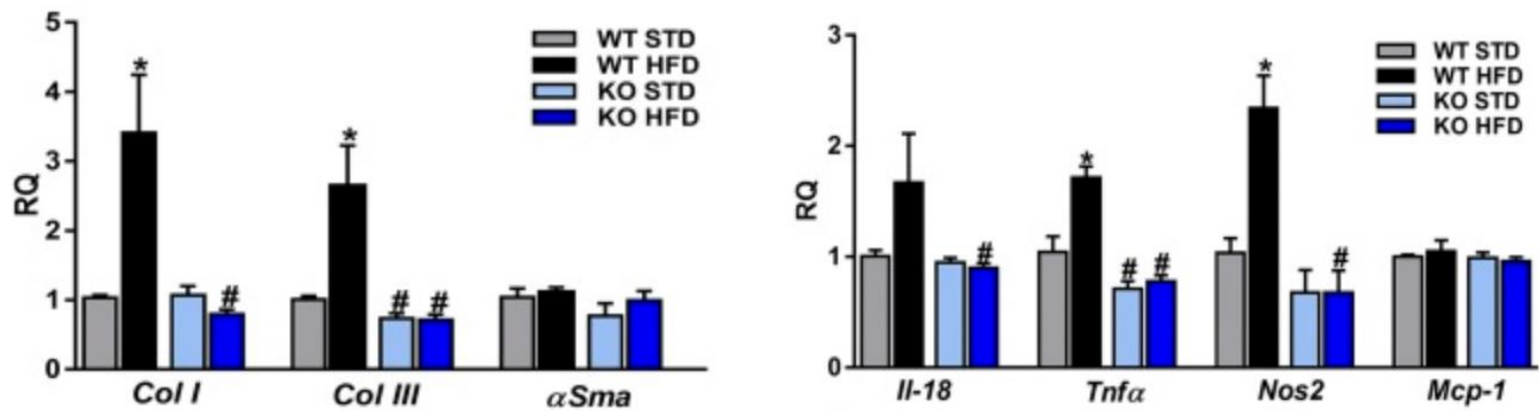
- Elevated CB1 expression was found in tubules, interstitial cells and podocytes in diabetic patients
- Elevated CB1 expression was found in mesangial cells in IgAN patients
- High CB1 expression appears to correlate with poor kidney function as measured by serum creatinine

CB1 Contributes to Obesity-induced Kidney Disease

CB1 knockout mice protected from renal dysfunction, fibrosis and inflammation



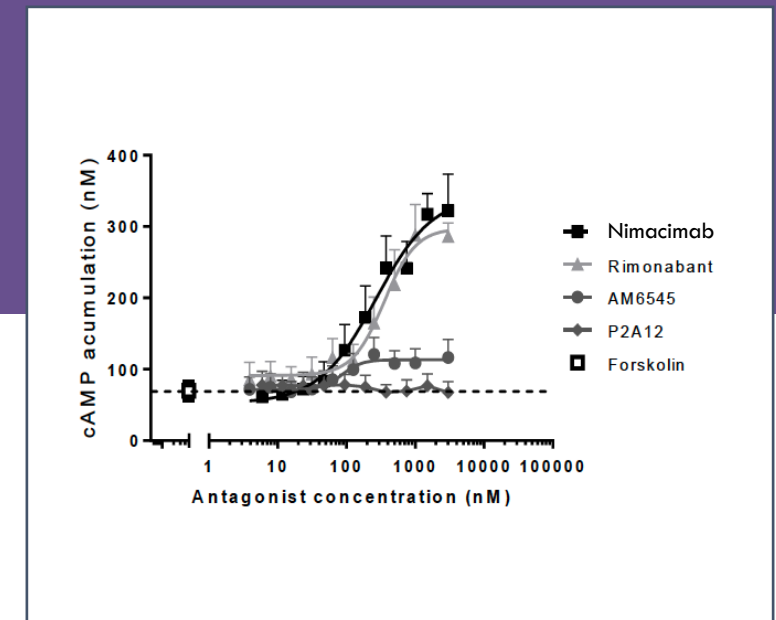
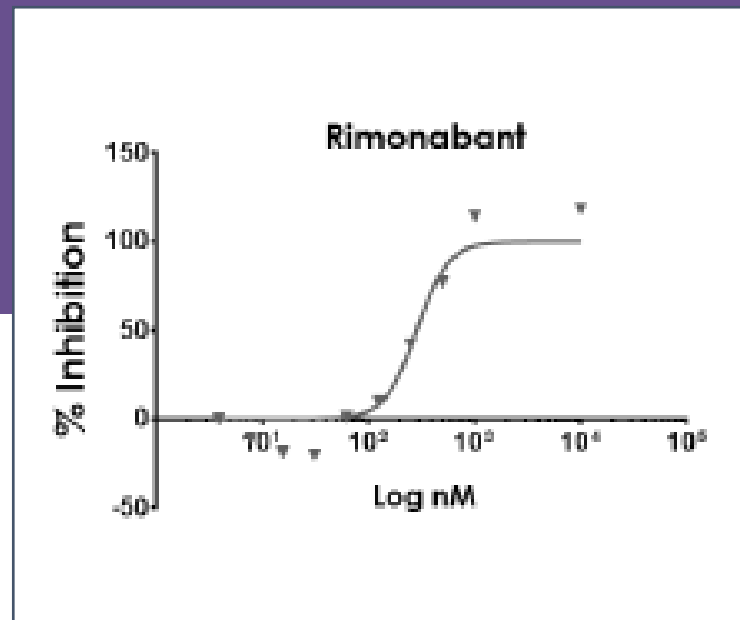
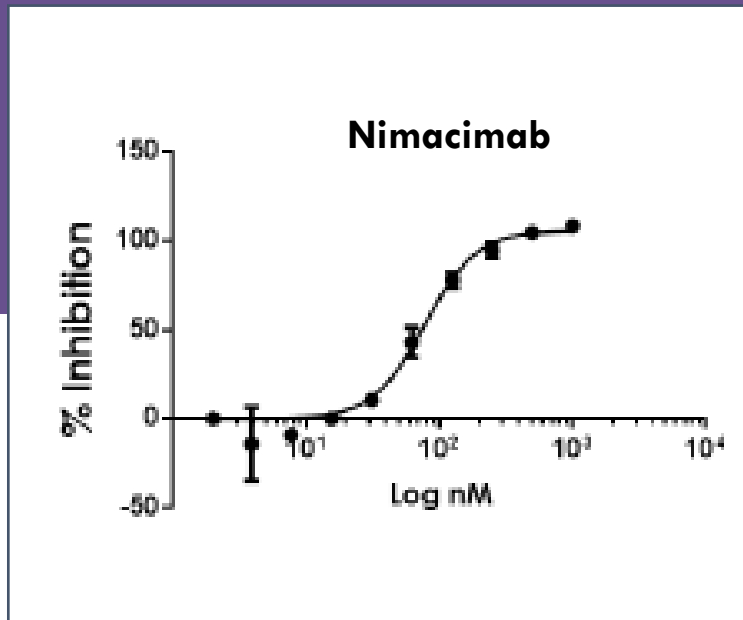
Fibrotic and Inflammation Markers



- Obesity-related structural and functional changes in the kidney develop early in the course of obesity and occur independently of hypertension, diabetes, and dyslipidemia.
- Activating renal CB1 induces nephropathy, whereas CB1 blockade improves kidney function.
- CB1 contributes to the pathogenesis of obesity-induced renal lipotoxicity and nephropathy

Nimacimab: Powerful Negative Allosteric Modulating Antibody for CB1

Nimacimab is effective at inhibiting CB1 signaling; similar antagonist activity to rimonabant



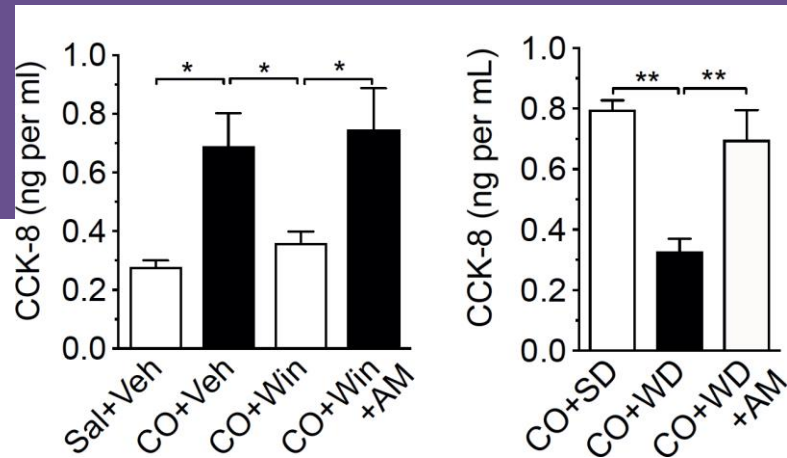
Cisbio's competitive cAMP assay was used to quantify nimacimab's antagonist activity

Nimacimab compares favorably to neutral agonists (AM6545) and equivalent to rimonabant

Peripheral CB1 Receptors and Appetite Hormones

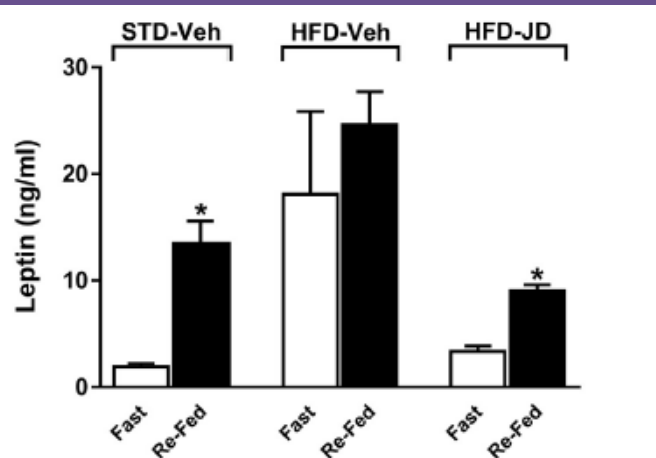
CB1 modulates the activity of key appetite-regulating hormones leptin, ghrelin, and CCK

Increases release of cholecystikin (CCK)



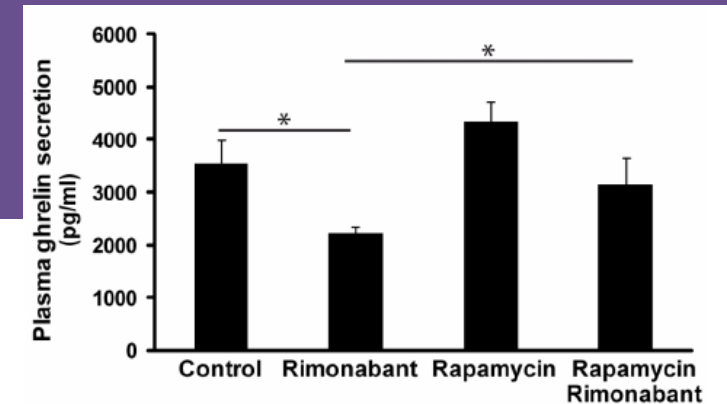
- CCK release inhibited by CB1 activation (WIN-55), which is normalized by CB1 blockade (AM6545)
- Mediated through small intestine epithelium and gut-brain axis

Increases sensitivity of leptin in the brain



- Obesity is associated with hyperleptinemia and resistance to leptin
- CB1 blockade appears to reverse leptin resistance in DIO mice.

Reduces ghrelin secretion from the stomach



- Blockade of CB1 in the stomach significantly reduces gastric ghrelin secretion.
- CB1 blockade/gastric secretion appears to be mediated by mTOR pathway.

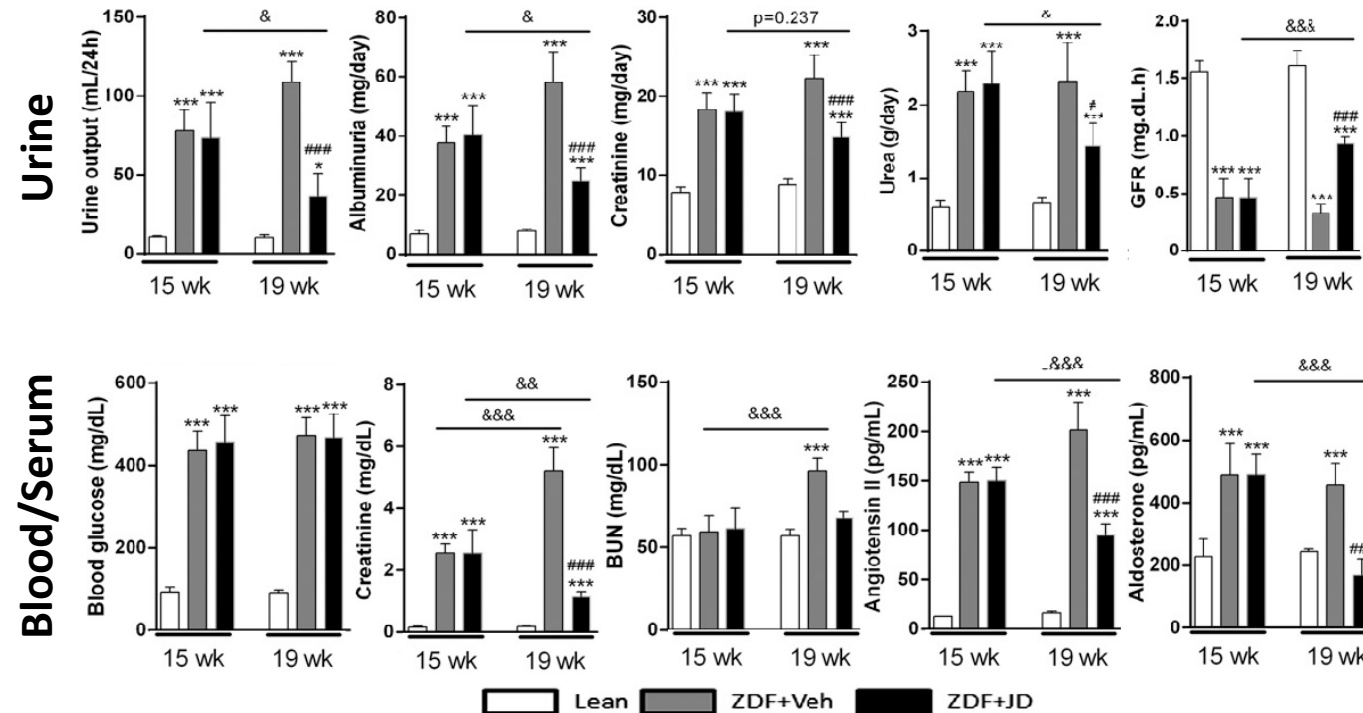
Comparison of Key Mechanism with CB1 and GLP-1 Therapeutics

Overlapping as well as unique mechanisms provide a rationale for differentiation

GLP-1R Agonist	CB1 Inhibitor
<ul style="list-style-type: none">• Incretin released by L cells in the small intestine following food ingestion and is rapidly degraded by DPP-4; ~15% of secreted GLP-1 reaches systemic circulation• DPP-4 resistant GLP-1RAs have a longer half-life than endogenous GLP-1• In the pancreatic β cells, GLP-1 RA binds to GLP1R, which activates the cAMP-PKA pathway and promotes exogenous insulin secretion• GLP-1 RA also suppresses glucagon secretion at blood glucose levels above fasted levels• Other physiological effects of GLP-1 RAs: hypophagia (brain), decreased hypertension (heart), and decreased glucose production (liver)	<ul style="list-style-type: none">• In the pancreatic β cells, CB1 signaling increases cAMP and promotes exogenous insulin secretion• Increased leptin and insulin sensitivity• Decrease in fat preference/dyslipidemia/conversion of WAT>BAT• Decrease in Inflammation and fibrosis• Hypophagia (brain), via peripheral modulation of appetite-regulating hormones (increased CCK /decreased ghrelin and leptin)• Promotes secretion of incretins from the pancreas

Peripheral CB1 Antagonism Reverses Fully Developed Diabetic Nephropathy

- Zucker diabetic fatty (ZDF) rats were treated daily with 3 mg/kg JD5037 (CB1 inhibitor) or vehicle P.O. for 4 weeks
- Polyuria, albuminuria, uricosuria, increased plasma and urinary creatinine, and increased plasma levels of angiotensin II and aldosterone were decreased by peripheral CB1 blockade and GFR was increased significantly beyond pretreatment levels.



Preclinical and Clinical Data Demonstrate CB1 Affects Metabolic, Inflammatory and Fibrotic Pathways Important in the Development of Diabetic Nephropathy

Compelling evidence for CB1 blockade in diabetic nephropathy

Parameter	CB1 Effect
Expression in human disease	Increased in diabetic nephropathy patient samples Increased in podocytes exposed to high glucose or angiotensin
Genetic linkage	Polymorphism associated with increased risk of diabetic nephropathy in humans
Clinical data	Blockade improves hyperglycemia
In vitro data supporting effect on mesangial expansion, thickening of the glomerular basement membrane, and glomerular sclerosis	Inhibition in podocytes maintains perm-selectivity and decreases inflammatory and fibrotic factors, in proximal tubular cells prevents hypertrophy and in mesangial cells reduces inflammatory and fibrotic factors
Transgenic mice data	Develop glomerular inflammation and fibrosis
Animal models of diabetic nephropathy	Increased expression; blockade improves microalbuminuria, metabolic parameters, inflammation and fibrosis in multiple animal models with multiple antagonists

Competitive Landscape – 2nd Gen CB1 Inhibitors

Nimacimab sets itself apart from other CB1 peripherally-targeted agents

	GOLDFINCH	CORBUS	INVERSAGO	SKYE
	GFB-024	CRB-913	INV-202	NIMACIMAB
Molecule Type	Antibody	Small Molecule	Small Molecule	Antibody
Allosteric Modulator	N/A	N/A	N/A	✓
Inverse Agonist	✓	✓	✓	N/A
Favorable Safety Phase 1 data	✓	N/A	✓	✓
No CNS Accumulation Preclinical data	✓	○	○	✓
Low Immunogenicity	○	N/A	N/A	✓

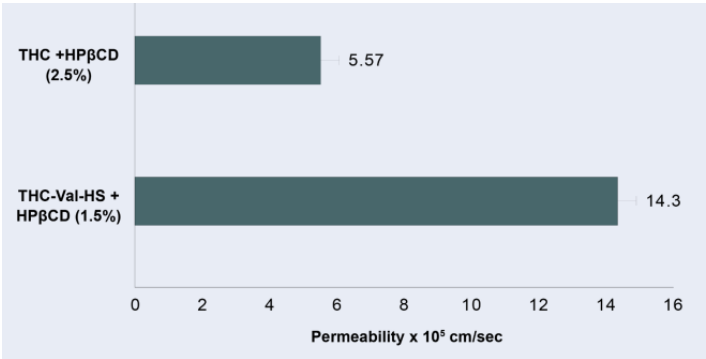
Not currently in development

Appendix – SBI-100 Supplemental Slides

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

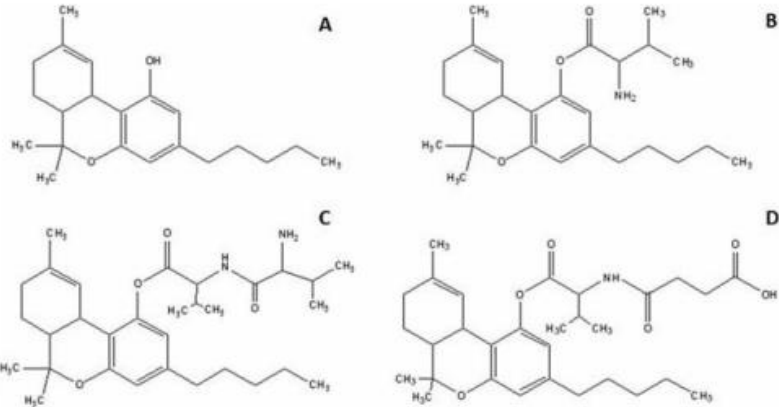


FIGURE 1. Chemical structures of (A) (THC), (B) THC-Val, (C) THC-Val-Val, and (D) THC-Val-HS.

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

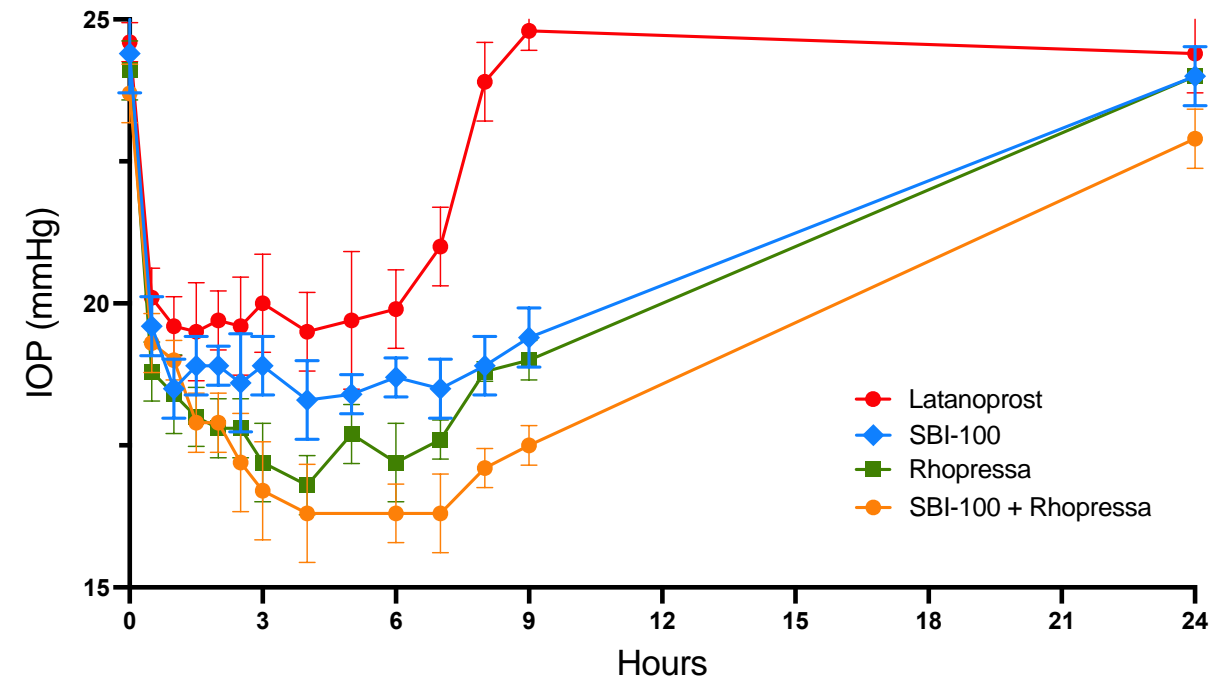
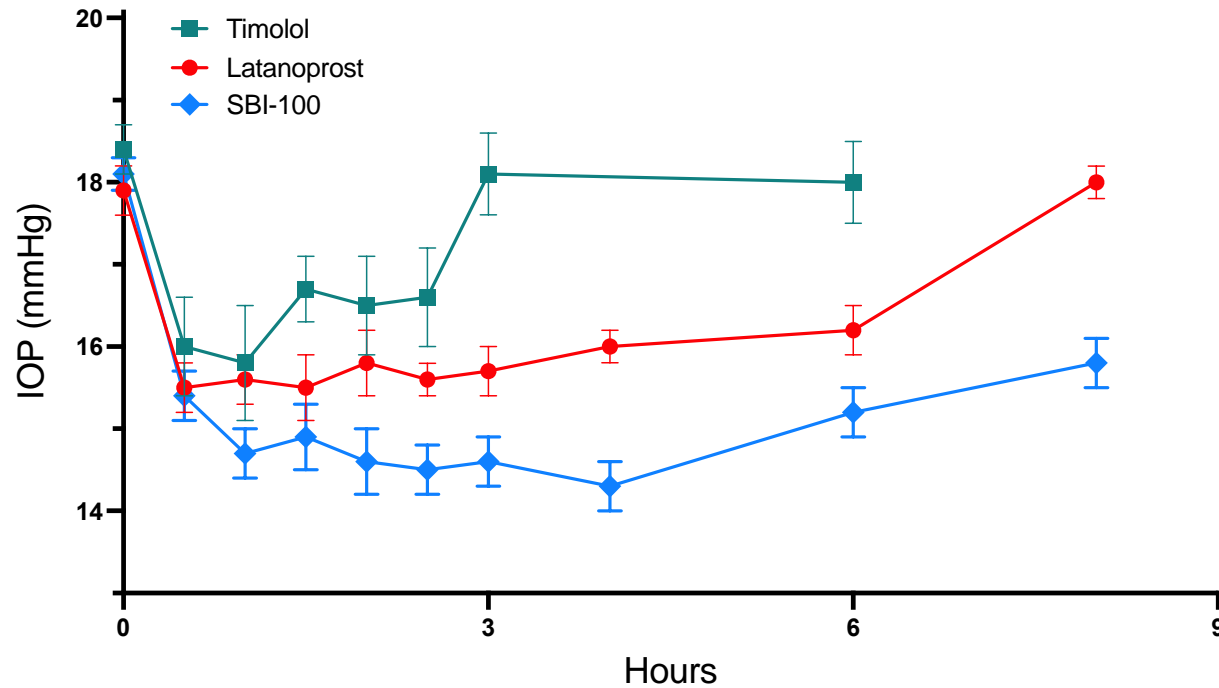
Tissue	THC			THC Val-HS		
	Light Mineral Oil	Emulsion	Micellar Solution 1	Cyclodextrin Solution	Micellar Solution 1	
	1 Hour	1 Hour	1 Hour	1 Hour	3 Hours	1 Hour
Drug concentration in terms of THC, % w/v	0.1	0.37	0.125	0.26		0.25
Dose, µg	50	185	62.5	130		125
Cornea, ng/50 mg tissue	68.8 (14.5)	300.6 (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

Tissue	Molecule			
	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 head-to-head 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

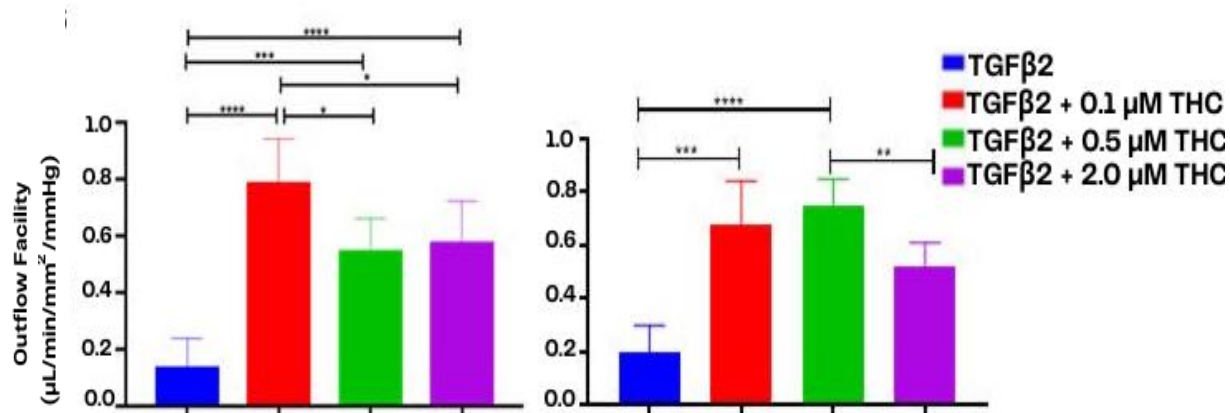
In **combination**, SBI-100 + Rhopressa demonstrated enhanced efficacy, suggesting the potential for clinical combinations

Day 5 multidose study with normotensive New Zealand rabbits

Human Trabecular Meshwork Model Highlights Key Mechanism of Action

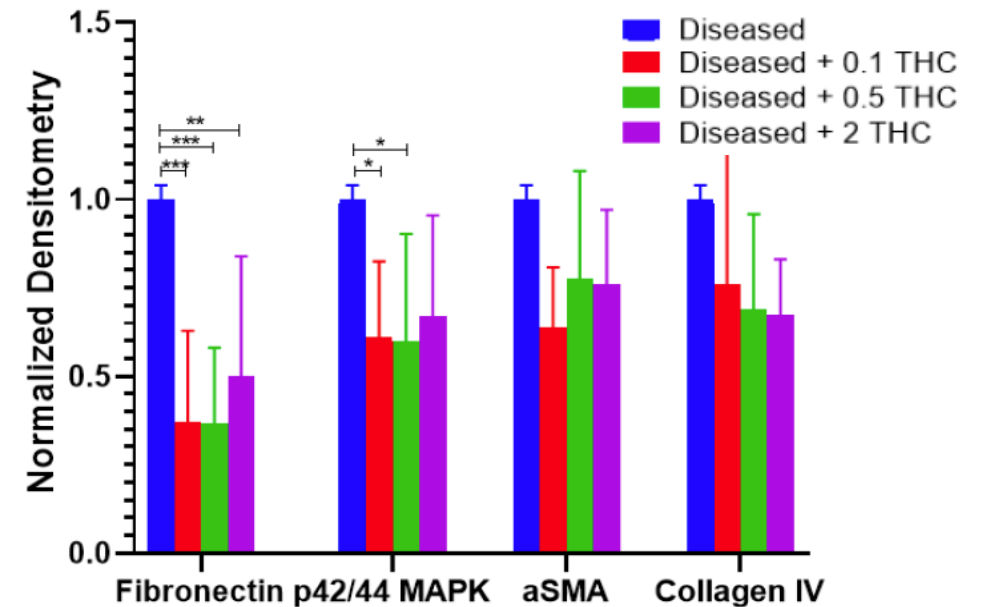
Measuring outflow facility via trabecular meshwork

- 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



Potential Neuroprotective Benefits with SBI-100 OE

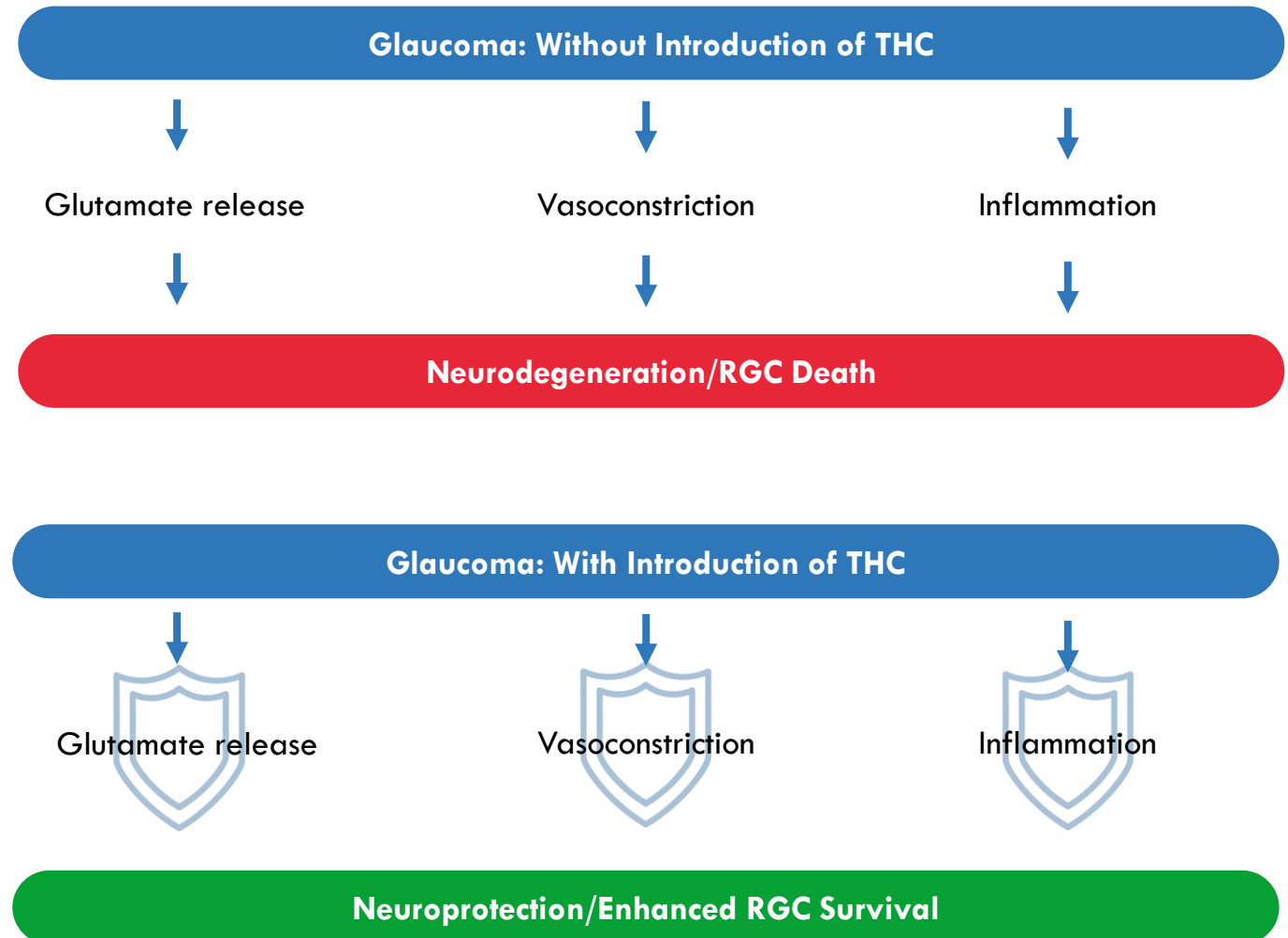
Additional complementary therapeutic mechanism to potentially address associated neuropathy

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 release¹
- Vasoconstriction of optic nerve²
- Inflammation³



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- α fodrin, 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

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.

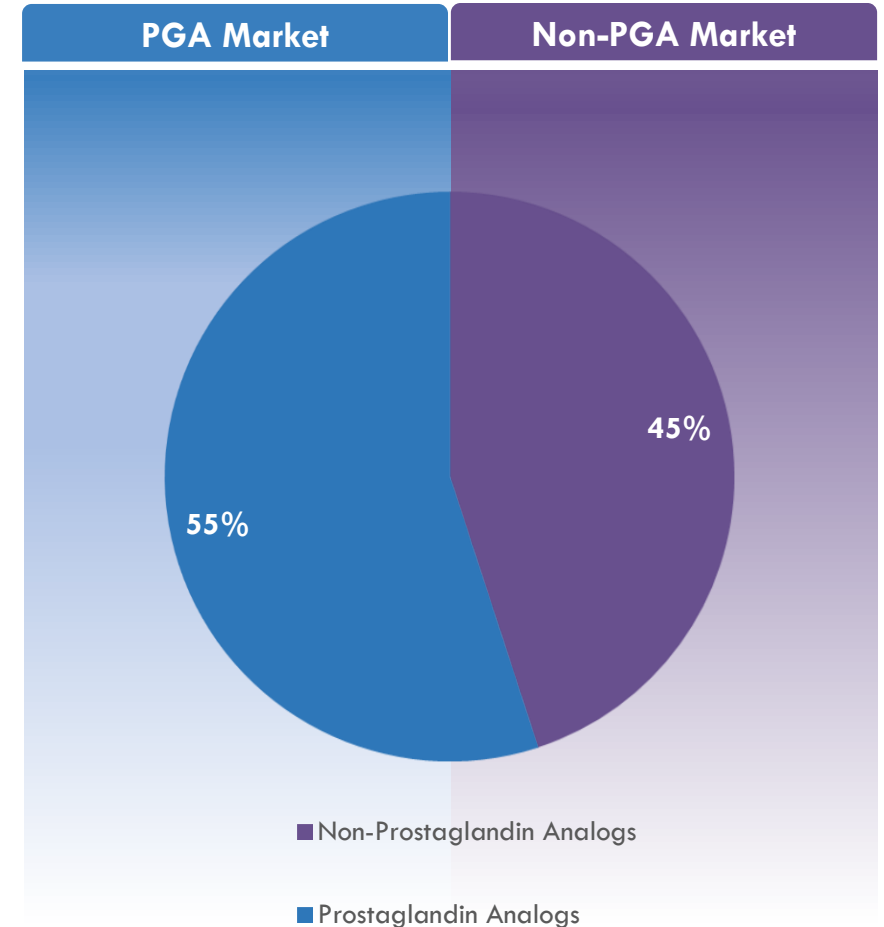
Challenges & Unmet Needs in Treating Patients with Glaucoma

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

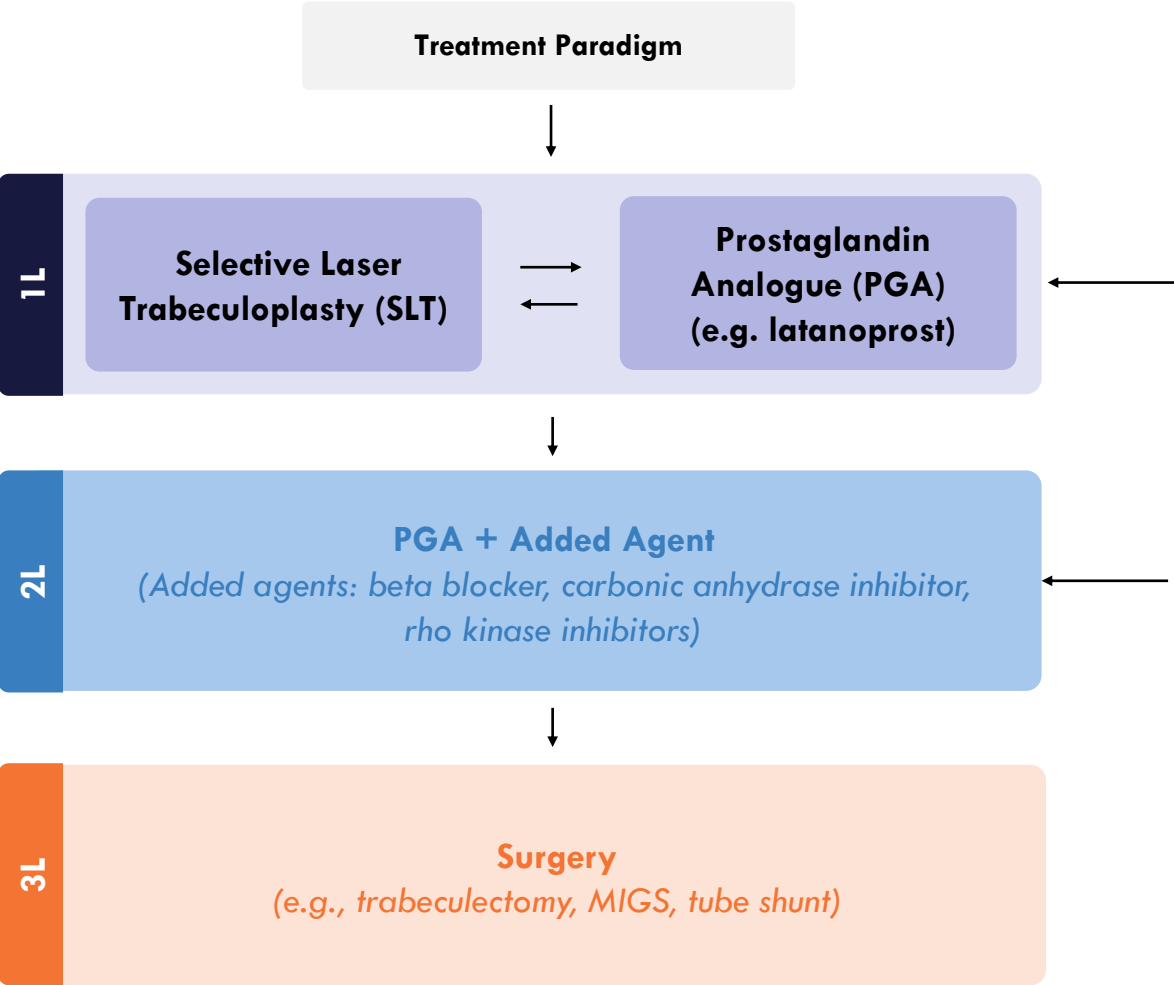
- Magnitude of IOP reduction is often titrated by disease severity and benefit/risk of desired treatment.
- The more severe the disease the more aggressive and riskier the lowering of IOP becomes.
- Current maximal medical therapy may not provide the IOP lowering required to protect from further nerve 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.

Key Opportunities for SBI-100 OE

- **Targets the tissue of disease**
 - Current medications either:
 - Inhibit aqueous production from the ciliary body: beta-blockers and carbonic anhydrase inhibitors
 - Increase uveoscleral outflow (secondary physiological outflow): prostaglandin analogs
 - Increase trabecular outflow (primary physiological outflow pathway): rho-kinase inhibitors
- **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
- **Safe and more tolerable agent that can be combined with available therapies**



Current Treatment Paradigm



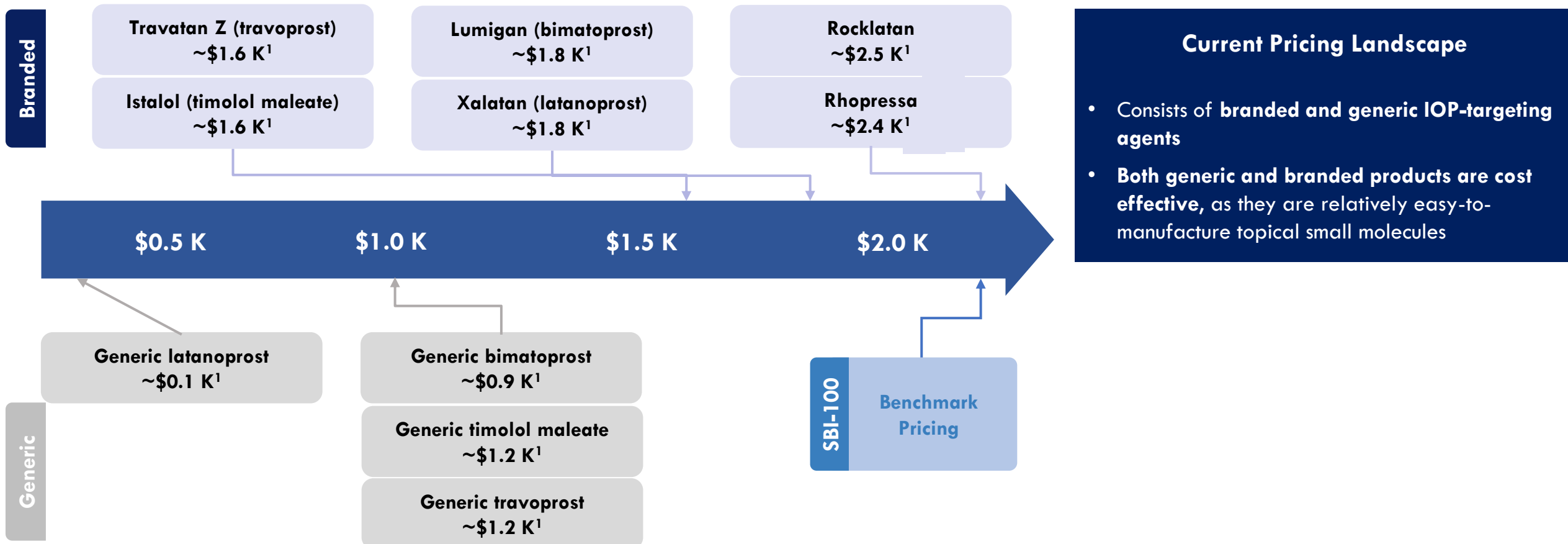
Depending on data SBI-100 OE could potentially be 1L therapy

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

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



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

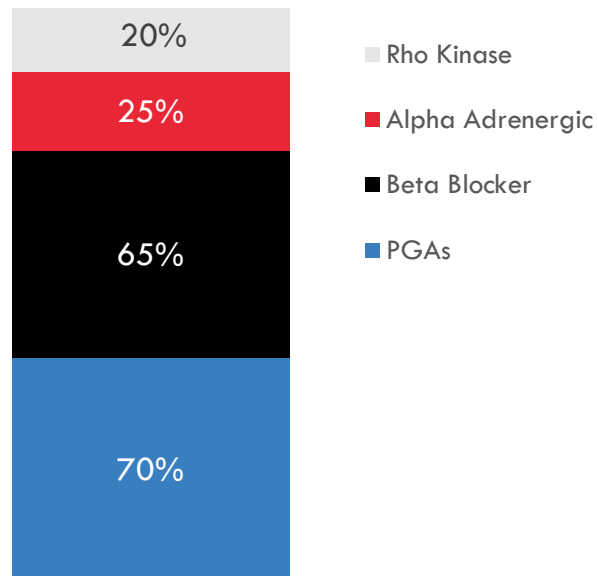
* Prices reflect January 2022 WAC price – Assumes 1 drop per day in each eye, ~90 drops per bottle, 1 bottle per 45 days, 8.1 bottles per year (Queen. Am J Ophthalmol. 2016 Mar; 163: 70–74.e1); Cost of therapy assumes a full 365 days of treatment

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



POAG & OH

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

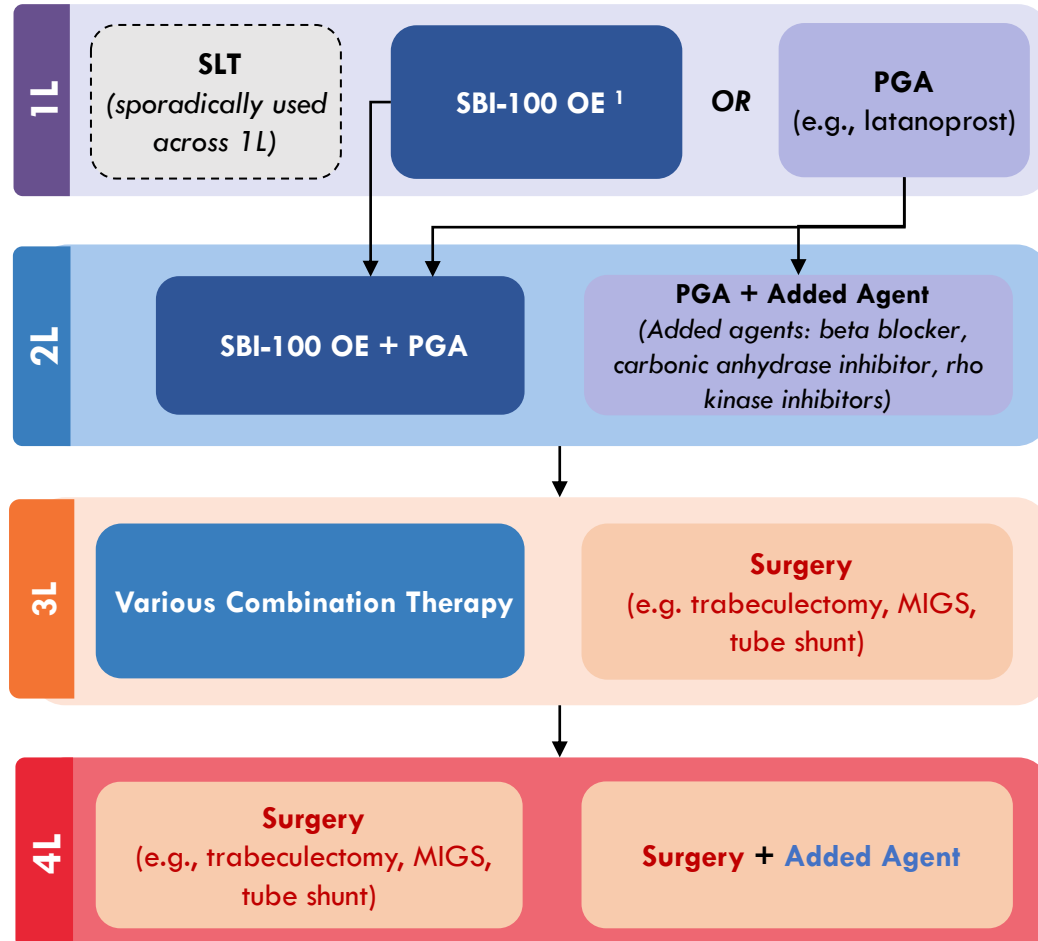
2L+ Treatment Paradigm

KOL-mentioned Payor Dynamics

- The likelihood of progressing past 1L is directly correlated with increasing severity; **moderate-severe patients, as indicative of the $\geq 50\%$ 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
- 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

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

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