



NO LIMITS.

Investor Hour

October 12, 2021

AGENDA

Introduction, Vision, Overview & Evolution

*Punit Dhillon
CEO & Chair*

Glaucoma Clinical Development Strategy & Program Overview

*Tu Diep, MSc
SVP, Development*

SBI-100 Effectiveness & Glaucoma Therapeutic Landscape

*Miguel González-Andrades, MD, PhD
Clinical Advisor*

*Assistant Professor, Department of Ophthalmology, University of Cordoba
Consultant Ophthalmologist, Reina Sofía University Hospital
Research Scientist, Maimónides Biomedical Research Institute of Córdoba (IMIBIC)
Adjunct Scientist, Department of Ophthalmology, MEEI-Harvard Medical School
Chair, YO Section, European Society of Ophthalmology*

Regulatory Strategy Overview

*Rhea Williams, MPH
Head of Regulatory Affairs & Quality Assurance*

Intellectual Property & New Invention Opportunities

*Tom Kim, LLB
General Counsel & Director of IP*

Cannabinoid Research & Innovation

*Eduardo Muñoz, MD, PhD
Scientific Advisor*

*Professor of Immunology, Department of Cell Biology, Physiology & Immunology of the University of Córdoba (Spain)
Director, Inflammation & Cancer Research Group, Institute Maimonides for Biomedical Research of Córdoba*

Closing Remarks

Punit Dhillon

Q&A

Moderator:
Punit Dhillon

Speakers:

*Tu Diep, MSc
Rhea Williams, MPH
Tom Kim, LLB*

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INTRODUCTION
VISION, OVERVIEW & EVOLUTION

PUNIT DHILLON

CEO & CHAIR

SAN DIEGO, CA

**Cannabinoid
pharmaceuticals
have the
potential to
disrupt many
therapeutic
unmet needs.**

Broad Therapeutic Potential

- Ability to tackle **complex therapeutic pathways**
- Ability to **combine with other novel, synthetically-derived molecules that enable precise modulation**

Platform Potential

- **Ability to affect multiple targets**
- New platform for medicine, with the **potential to demonstrate safety and efficacy** for a range of therapeutic applications

Flexible Manufacturing

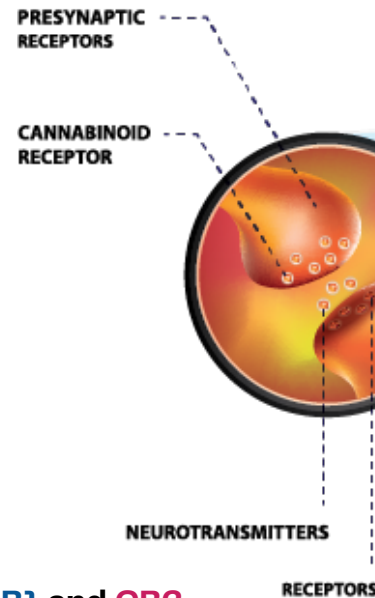
- **No need for large-scale farming or complex process for API** – ability to develop proprietary, synthetic molecules to novel cannabinoid therapeutics using the same process
- **Plant-free, scalable manufacturing process**

Large opportunity for first-in-class therapeutic portfolio.

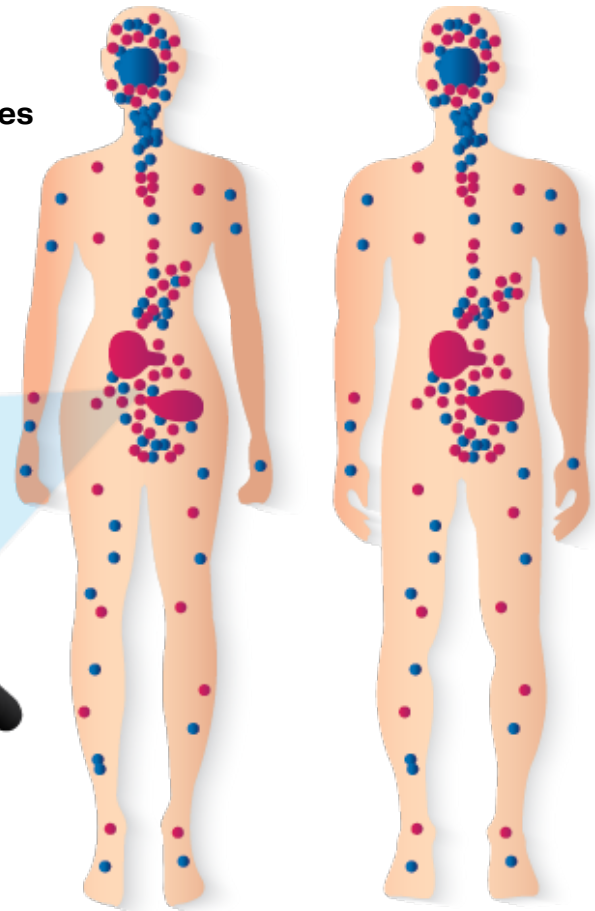
- ✓ **GO BIG** product opportunity
- ✓ Key existing data provides for higher probability of success – **OPTIMAL DEVELOPMENT**
- ✓ Accelerated R&D timelines – **GO FAST**
- ✓ Greater capital efficiency – we develop the opportunities that have the optimal development path for best-in-class therapeutics – **BE BETTER**

Cannabinoid pharmaceuticals as a potential new class of medicines will have a significant impact on human health.

Cannabinoids and cannabinoid-derivatives can be specifically designed to modify the ECS to positively impact multiple diseases



CB1 and CB2 receptors are the most characterized and validated drug targets of the ECS



ECS impacts almost all physiological processes in the body

GLAUCOMA DEVELOPMENT
STRATEGY & PROGRAM OVERVIEW



TU DIEP, MSc

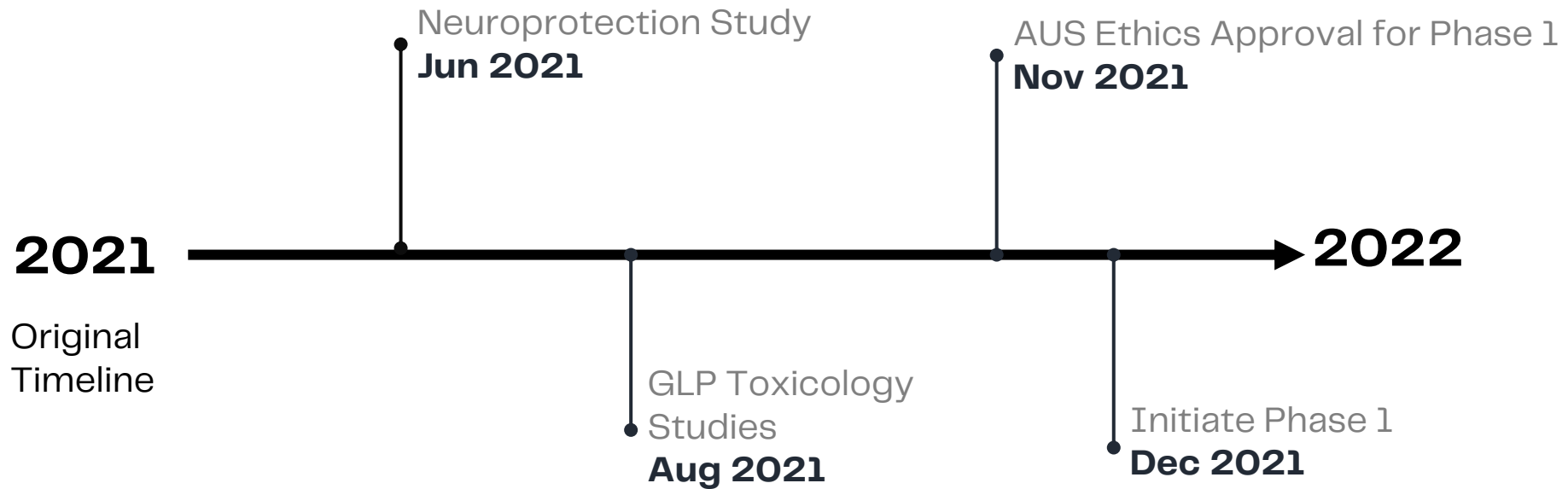
SVP, DEVELOPMENT

SAN DIEGO, CA

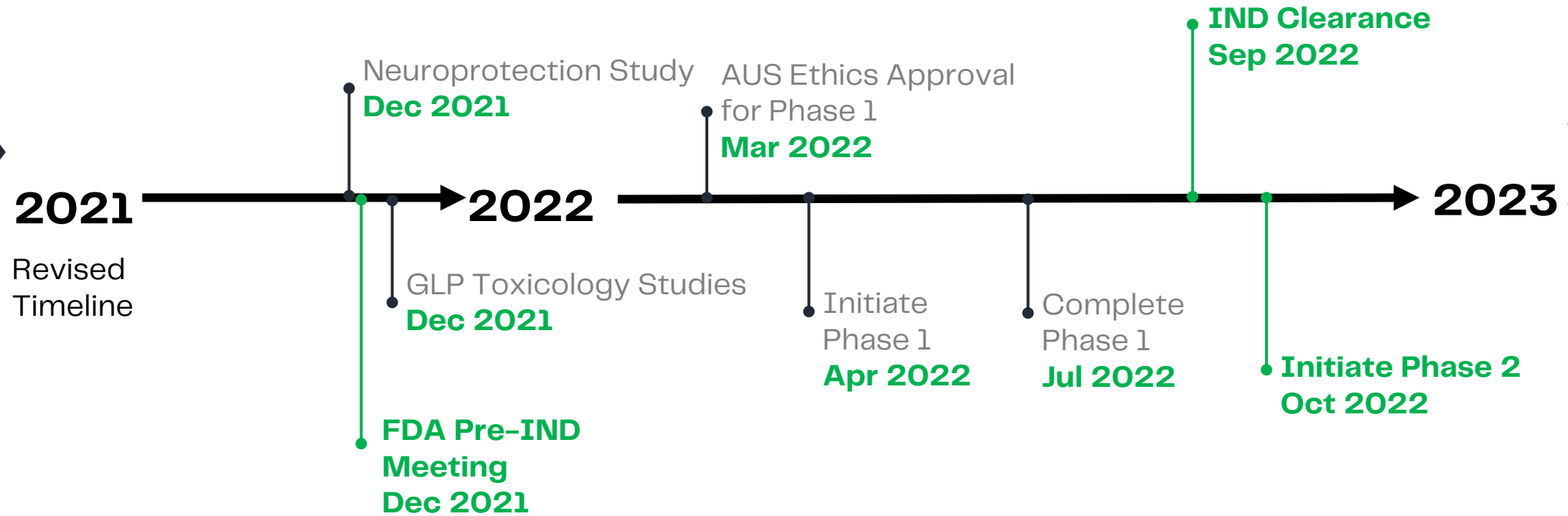
2021 CLINICAL ACHIEVEMENTS

- ✓ Manufactured first batch of SBI-100 using a proprietary nanoemulsion formulation
- ✓ Acceptance of two late-breaking abstracts related to the formulation of SBI-100 and its combination with currently approved therapies
- ✓ Completed EpiOcular irritation study which demonstrated little to no irritation of eye drop formulation in a cell-based assay
- ✓ Completed GLP genotoxicity studies confirming THCVHS causes little to no damage to DNA or chromosomes
- ✓ Received DEA approval to conduct GLP nonclinical toxicology studies and recently initiated GLP toxicology studies with Calvert Labs

AN IMPROVED DEVELOPMENT STRATEGY



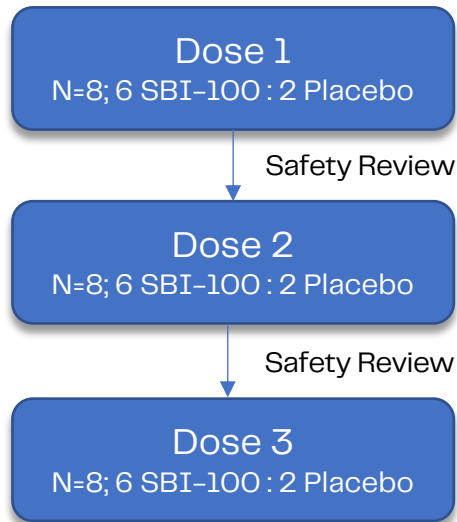
OPPORTUNITY TO GENERATE MEANINGFUL DATA



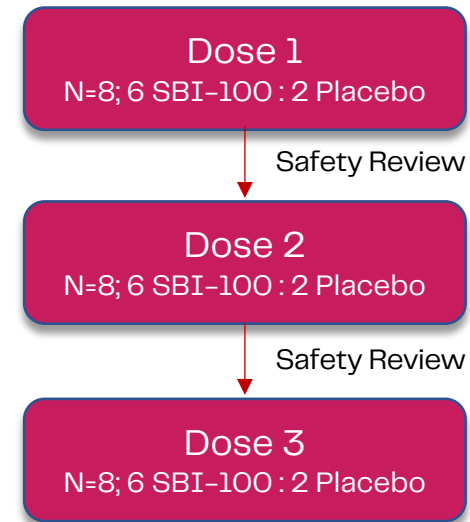
PHASE 1 SAD/MAD DESIGN FOR SBI-100

Study Objectives: A randomized, double-masked study to evaluate safety, tolerability, pharmacokinetics, and intraocular pressure (IOP)-reducing effects of SBI-100 in 48 healthy subjects following single and multiple ascending doses of SBI-100.

Part A: Single Ascending Dose
in Healthy Subjects
(single dose, single eye)



Part B: Multiple Ascending Dose in
Healthy Subjects
(5-day dose, twice-a-day, both eyes)



Safety Review

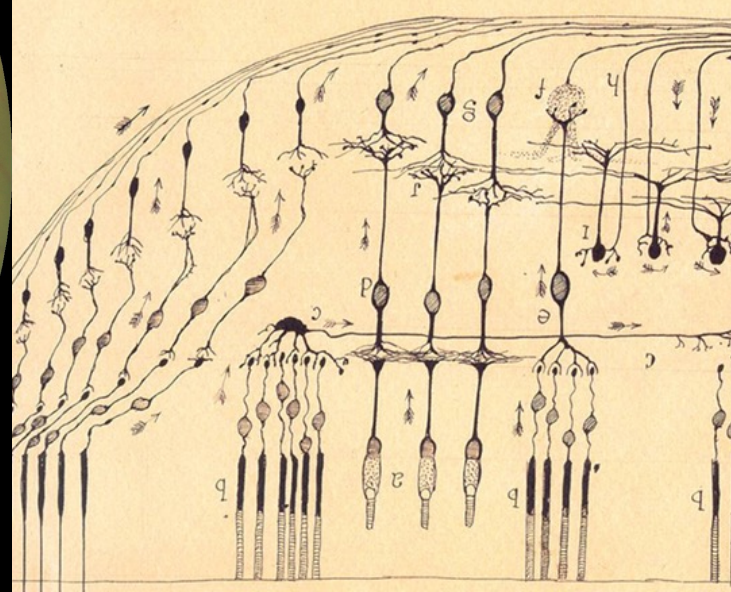
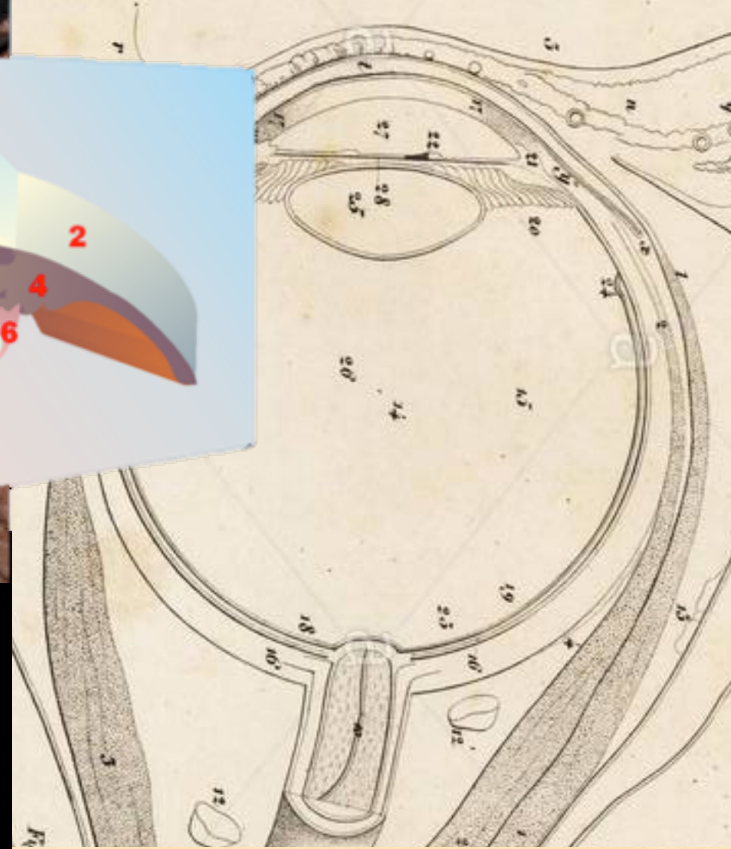
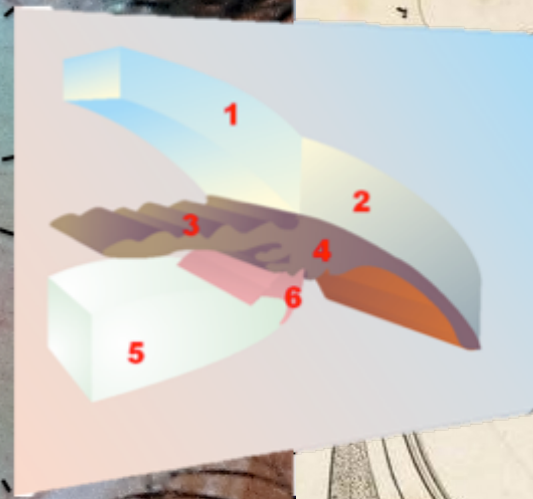
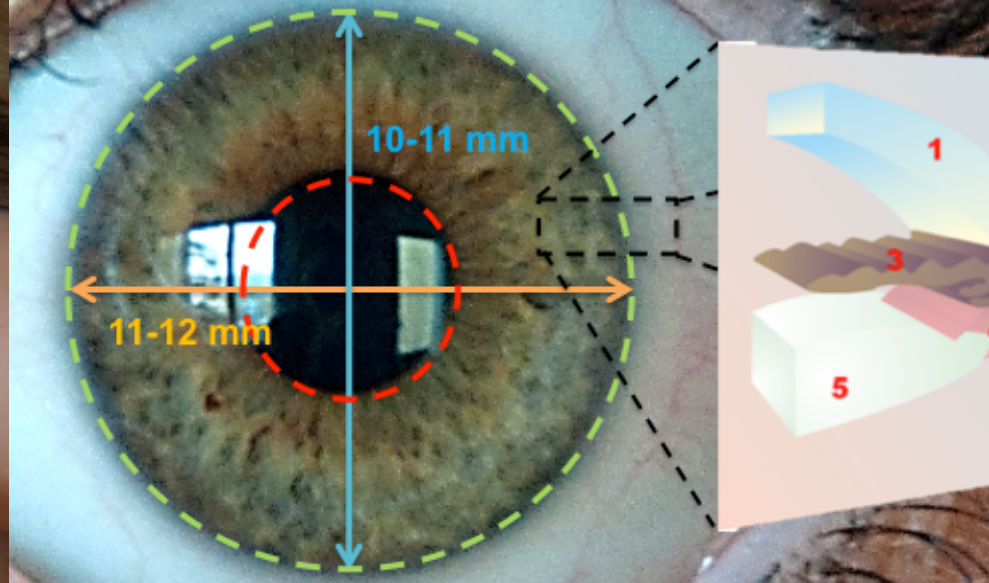
SBI-100 EFFECTIVENESS & GLAUCOMA
THERAPEUTIC LANDSCAPE

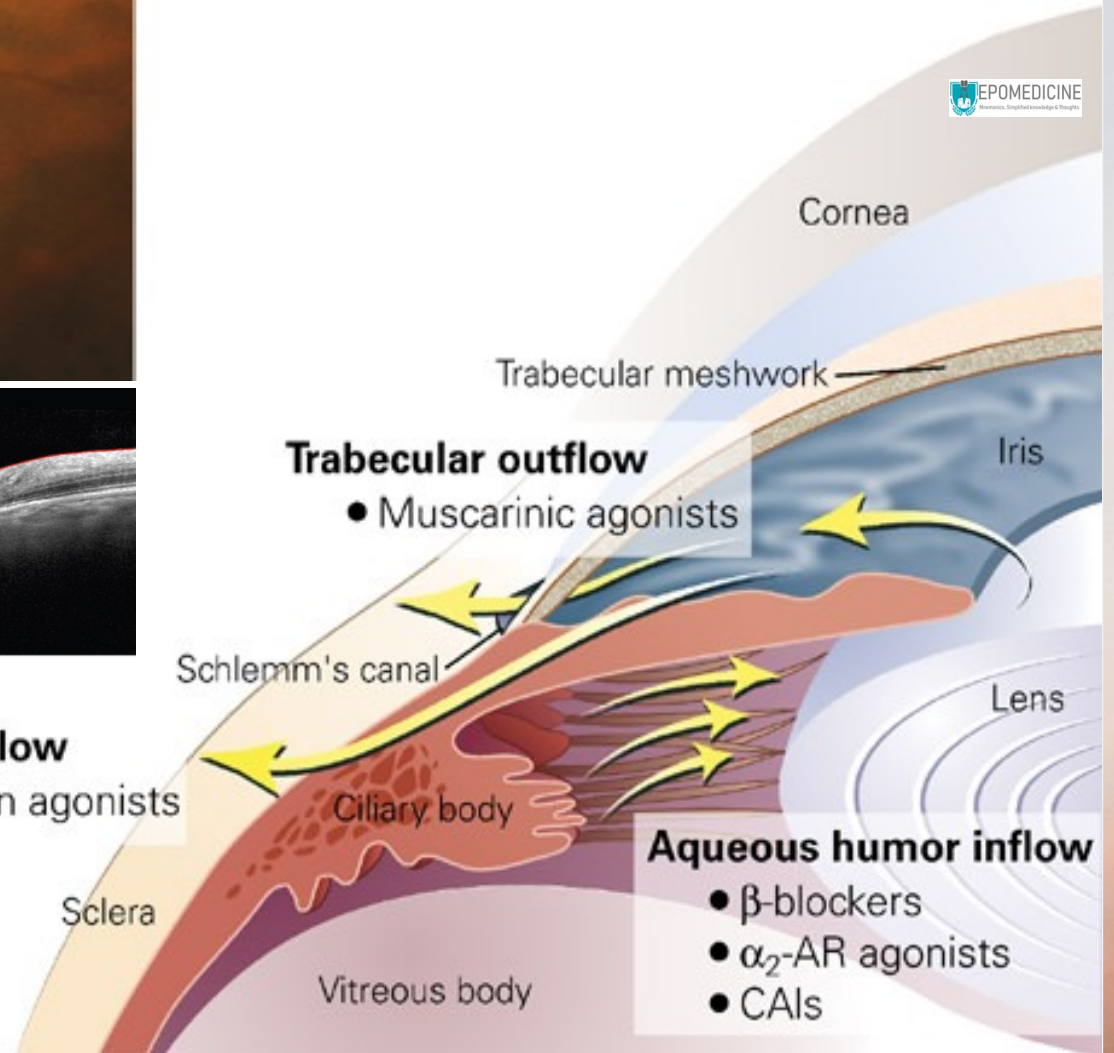
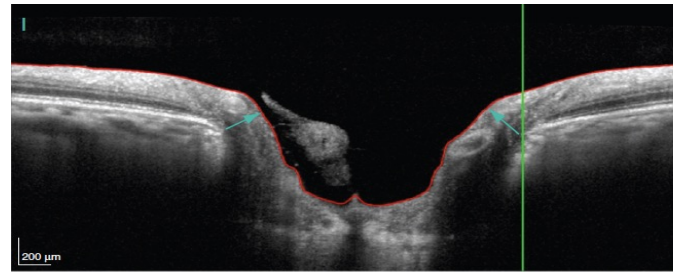
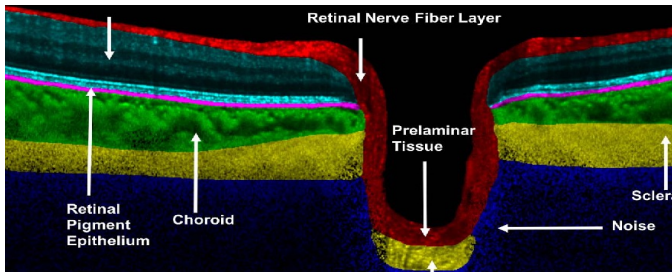
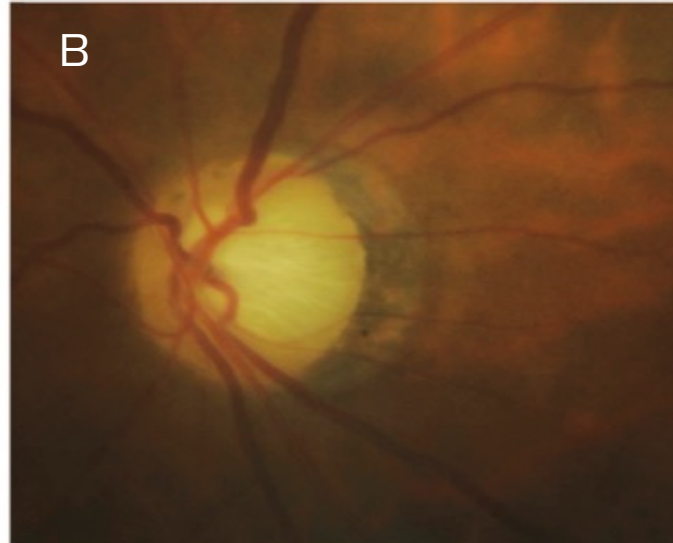
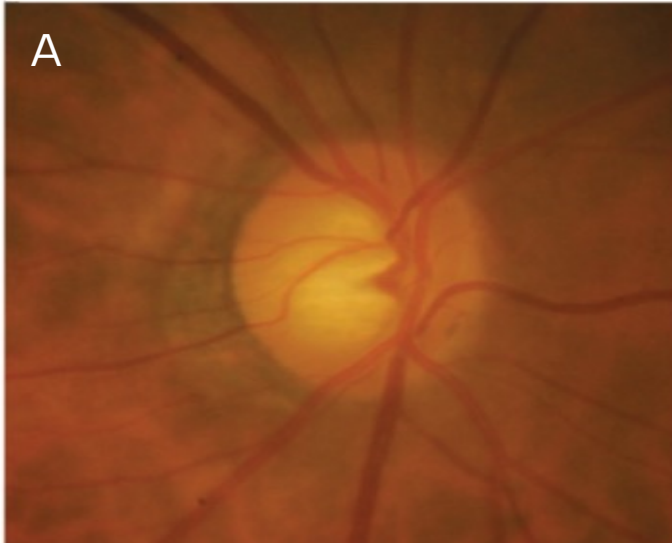


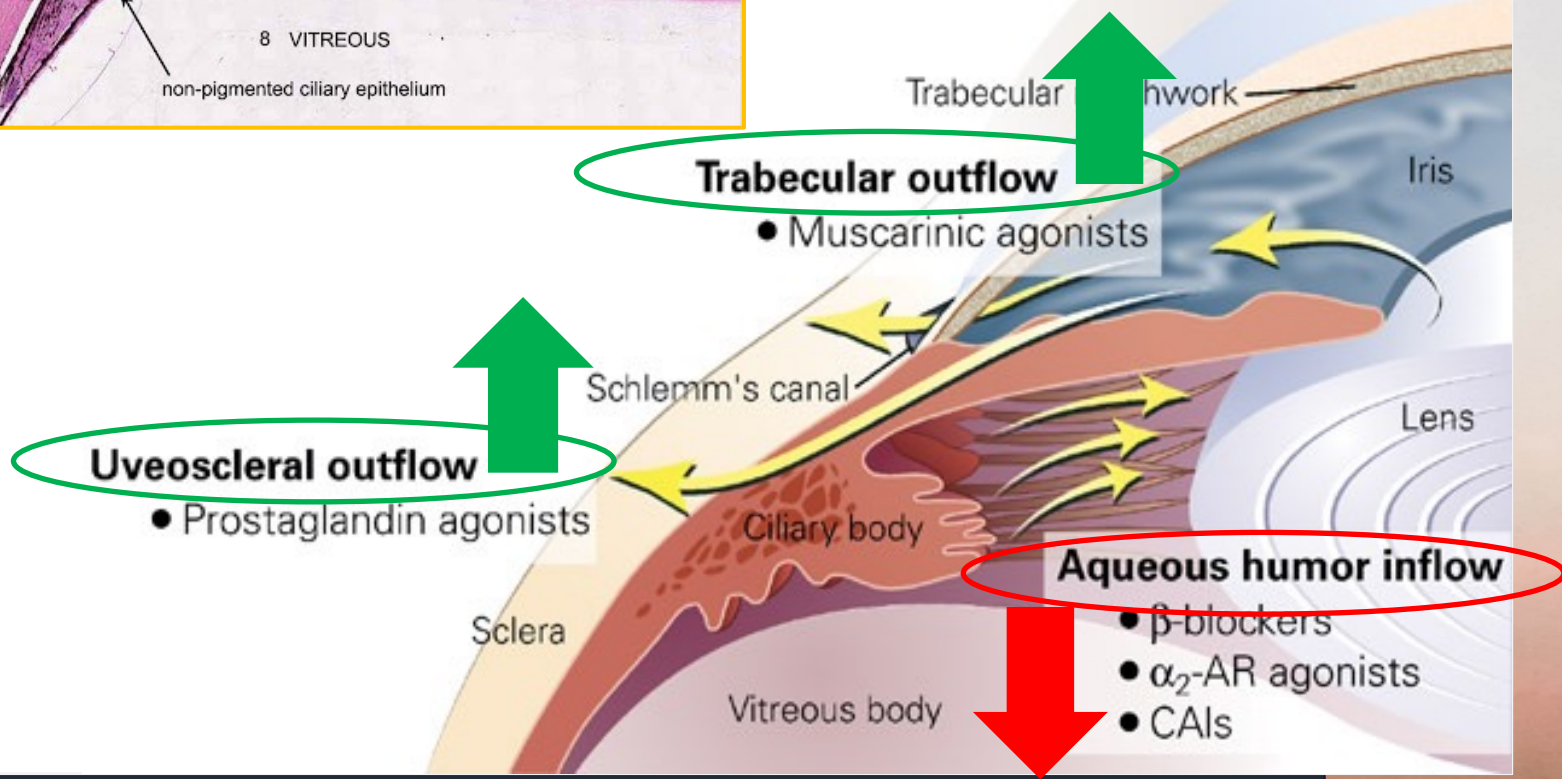
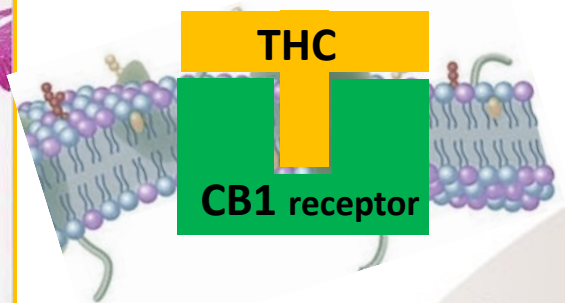
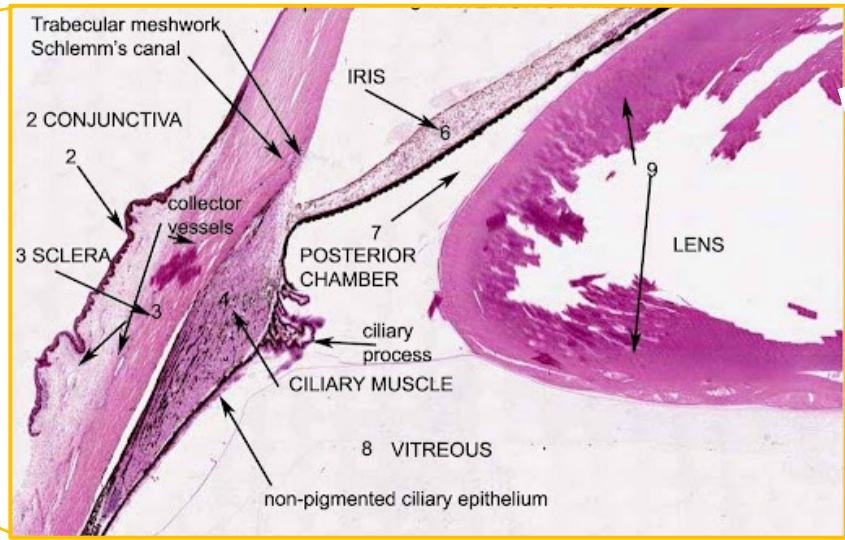
**MIGUEL
GONZALEZ-
ANDRADES,
MD, PhD**

CLINICAL ADVISOR

CORDOBA, SPAIN

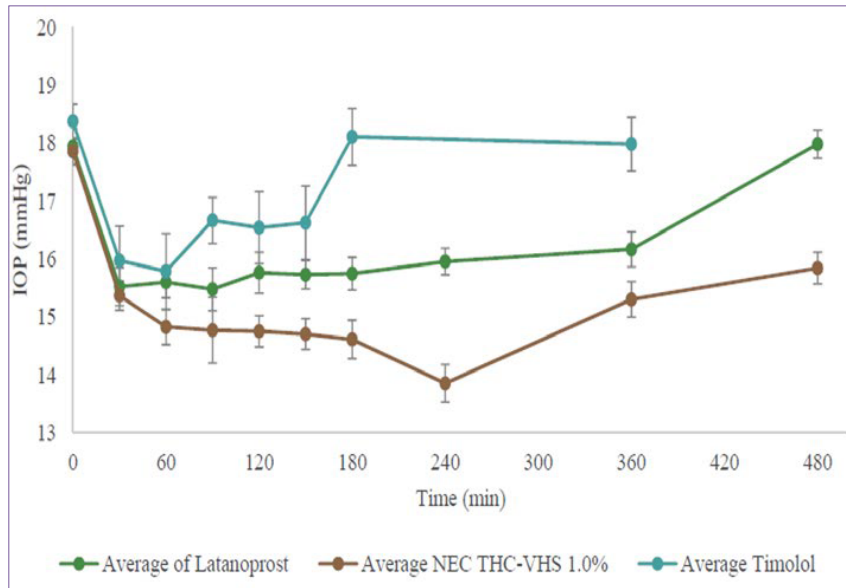




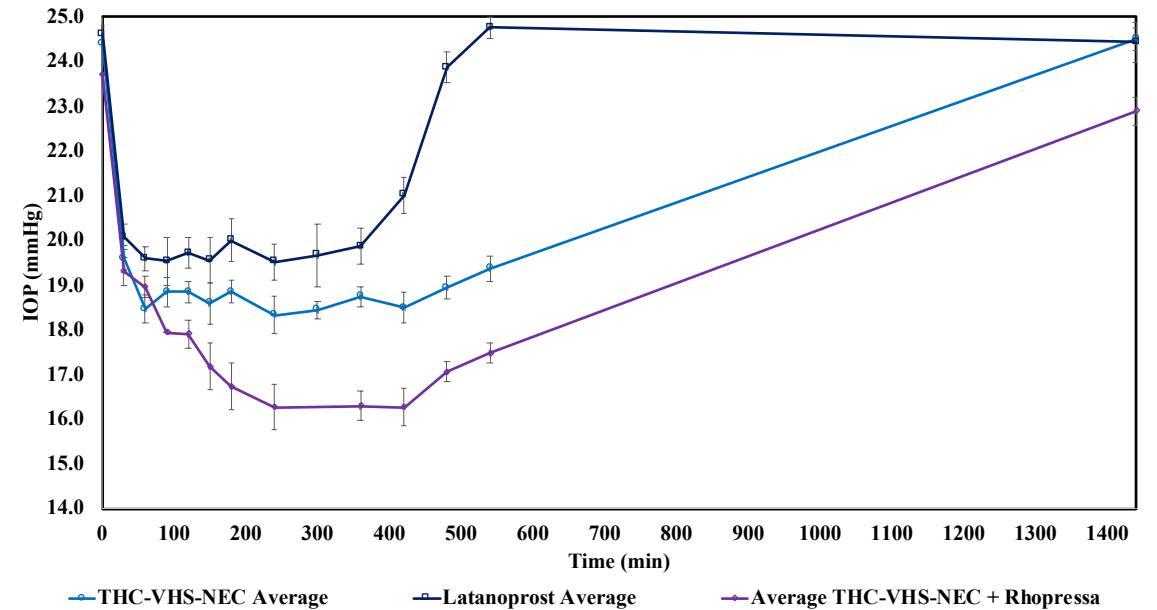


H2H PHARMACOLOGY STUDY (NON-GLP) IN RABBITS

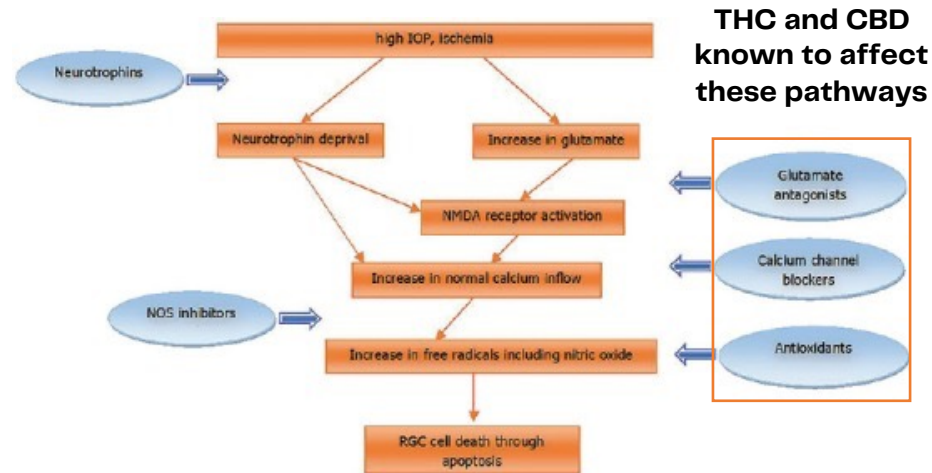
Average IOP vs Time profile of Latanoprost (0.005%) vs
THCVHS (1.0%) vs Timolol (0.25%)



Average IOP vs Time profile of Latanoprost vs THCVHS vs THCVHS + Rhopressa (Netarsudil)

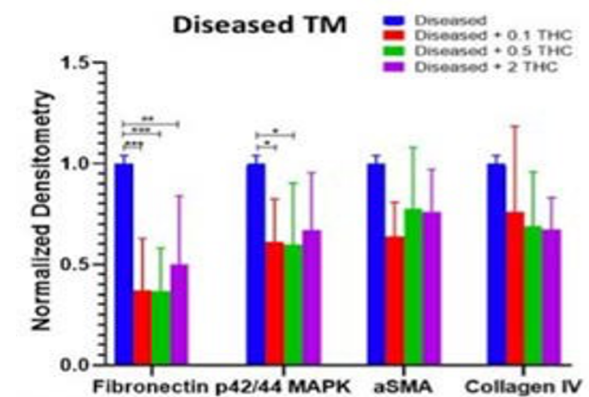
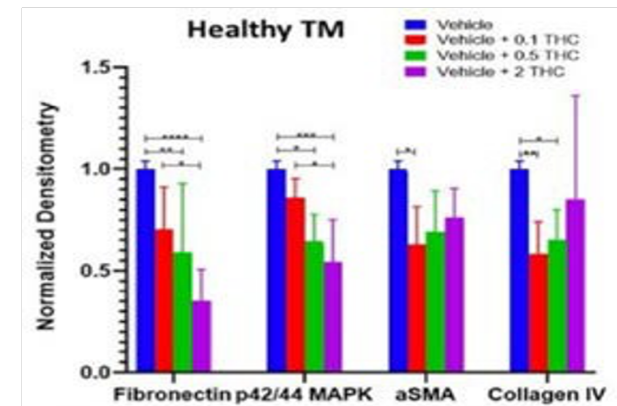


NEUROPROTECTION AND ANTI-INFLAMMATORY EFFECTS



Cannabinoid	Receptor	Cell/tissue/serum	Effect	Ref.
THC	ND	Macrophage cell line (RAW264.7)	Decreases TNF- α	[40]
THC	ND	Peritoneal macrophages	Increases IL-1 α and IL-1 β	[41]
THC	ND	Human cell lines	Decreases TNF- α , GM-CSF and IFN- γ , IL-10 Increases IL-8	[26]
THC	CB1 and CB2 independent	Rat microglial cells	Decreases TNF- α , IL-1 α , IL-1 β and IL-6	[28]
<i>In vivo</i> WIN55,212-2 and HU-210	CB1 dependent	Serum	Decreases TNF- α , IL-12 Increases IL-10	[29]
Ajulemic acid	ND	Human synovial monocyte-derived macrophage	Decreases IL-6 and IL-1 β	[32]
HU-308	CB2 dependent	Serum and liver homogenates	Decreases TNF- α , MIP-1 α and MIP-2	[33]
CP55,940 WIN55,212-2	CB1 and CB2 independent	Rheumatoid fibroblast-like synoviocytes	IL-6 and IL-8	[34]
2-AG	CB2 dependent	Promyelocytic leukemia cell line (HL-60)	Increases IL-8, CXCL8 and CCL2	[37]

Anti-fibrosis



Doozandeh and Yazdani, *J Oph Vis Res* 2016



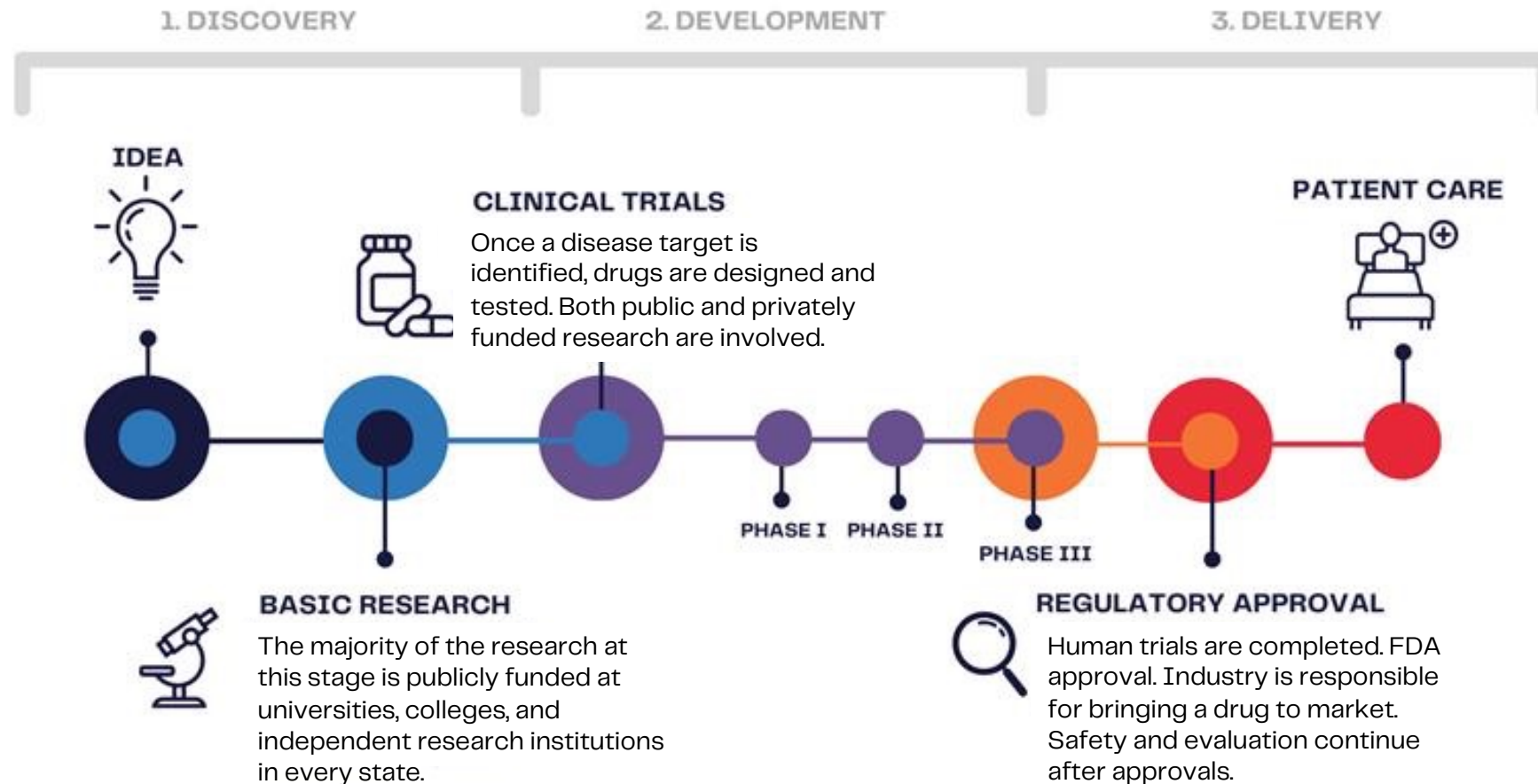
REGULATORY STRATEGY OVERVIEW

RHEA WILLIAMS, MPH

HEAD OF REGULATORY AFFAIRS
& QUALITY ASSURANCE

SAN DIEGO, CA

THE DRUG DEVELOPMENT PROCESS



INTELLECTUAL PROPERTY &
NEW INVENTION OPPORTUNITIES



TOM KIM, LLB

GENERAL COUNSEL &
DIRECTOR OF IP

SAN DIEGO, CA

OUR EXISTING PATENT PORTFOLIO LANDSCAPE

SBI-100: Amino Acid Ester Prodrugs of Delta-9-Tetrahydrocannabinol

- 2 US granted: 8,809,261; 9,630,941
- 16 EU countries validated: EP 2,352,497
- Canada, Australia, Hong Kong, and Japan patent grants

SBI-200: Biologically Active Cannabidiol Analogs

- 1 US granted: 10,709,681
- 5 US divisional patents filed
- Australia, Japan, South Korea, South Africa, and New Zealand patents granted
- Pending applications in Europe, Brazil, Canada, Columbia, Peru, Mexico, Israel, India, and Hong Kong



CANNABINOID RESEARCH
& INNOVATION



**EDUARDO
MUÑOZ, MD, PhD**

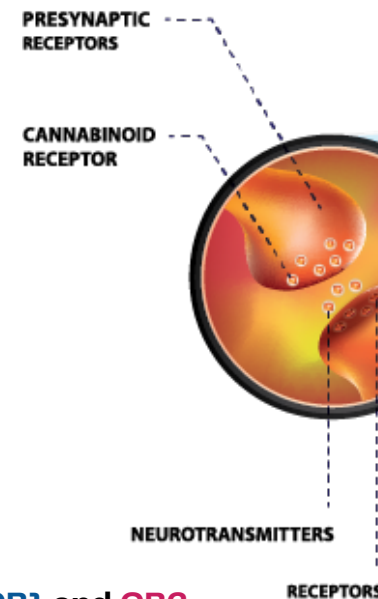
SCIENTIFIC ADVISOR

CORDOBA, SPAIN

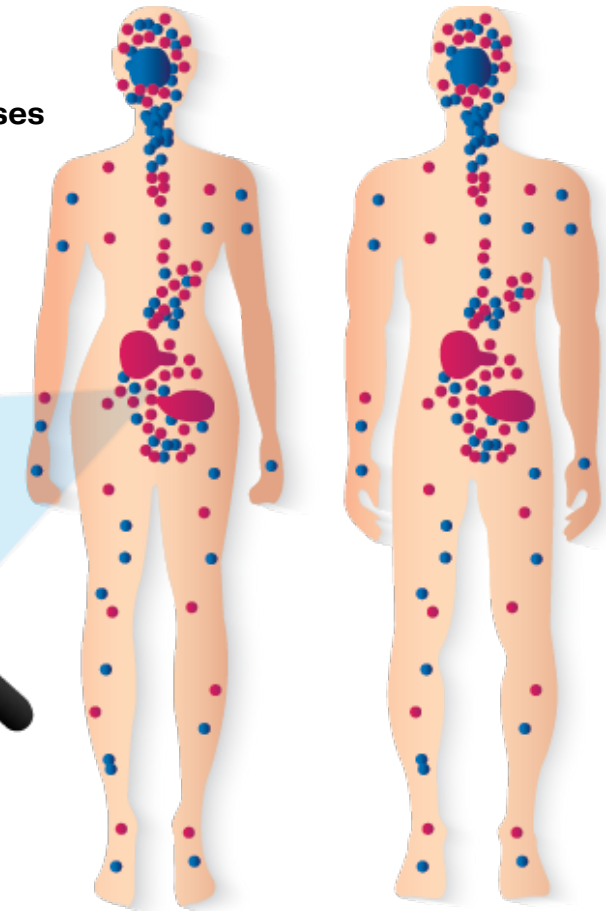
THE ENDOCANNABINOID SYSTEM

Modulating ECS activity at different levels holds therapeutic promise for a broad range of diseases.

Cannabinoids and cannabinoid-derivatives can be specifically designed to modify the ECS to positively impact multiple diseases

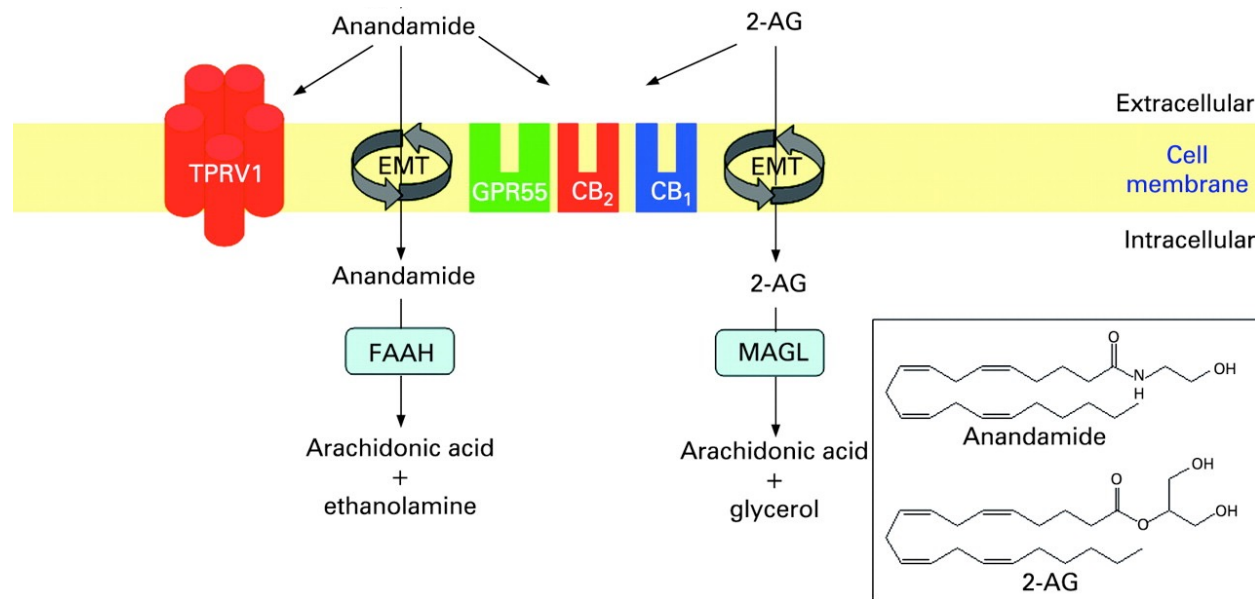


CB1 and **CB2** receptors are the most characterized and validated drug targets of the ECS

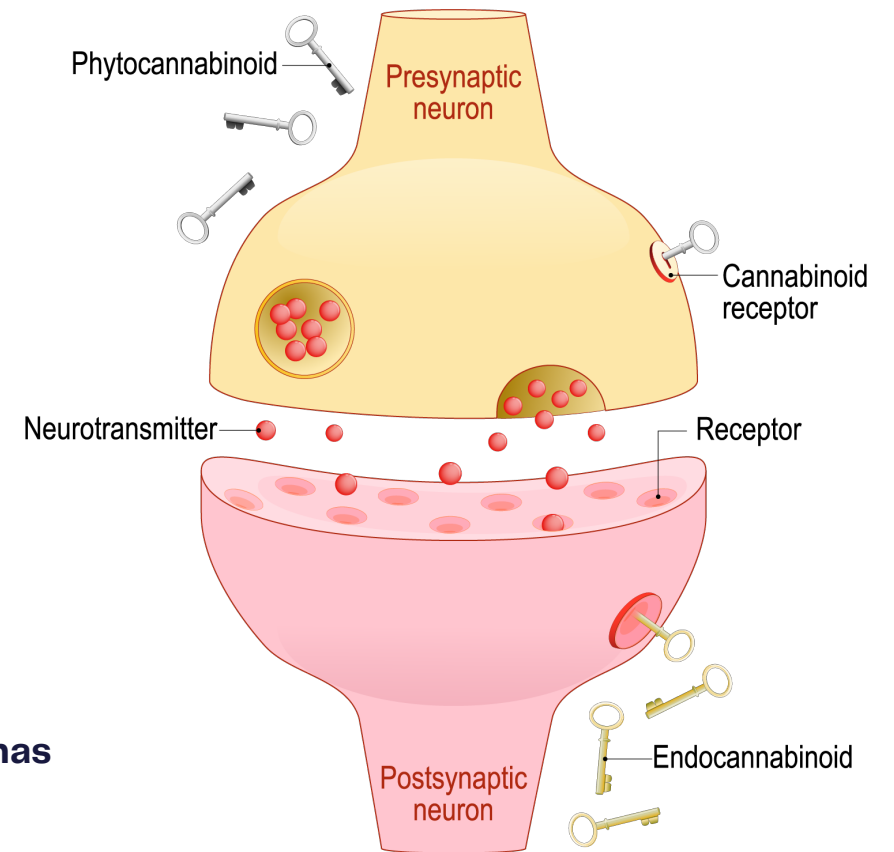


ECS impacts almost all physiological processes in the body

CANNABINOID RESEARCH & THE ENDOCANNABINOID SYSTEM

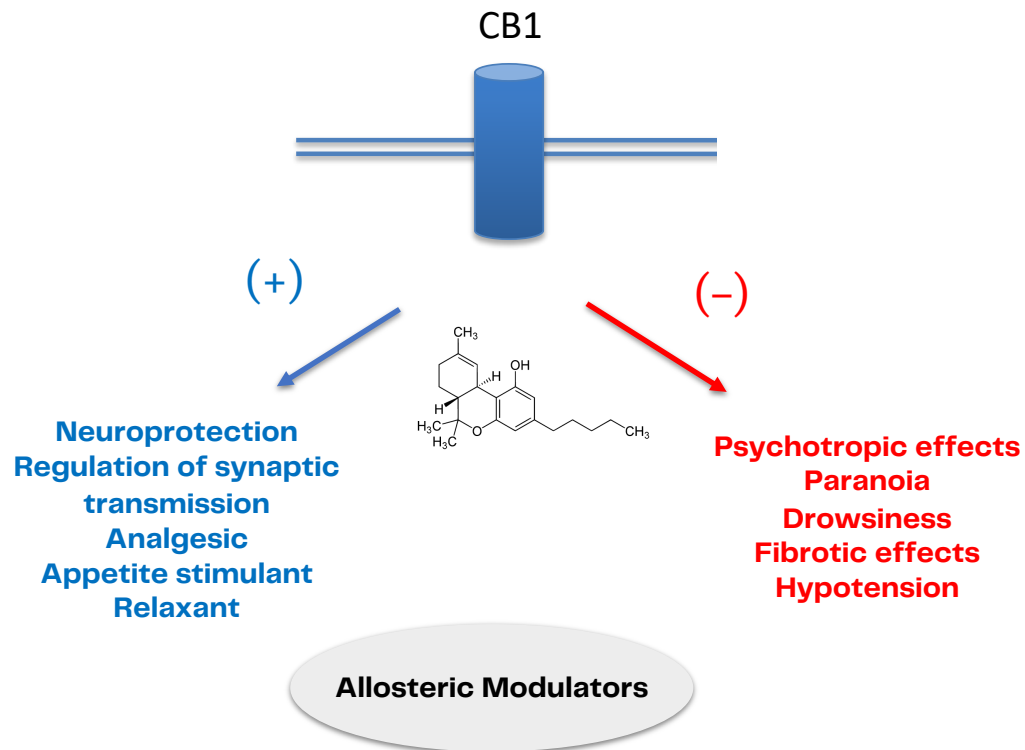


CB₁R activation with THC, one of the major cannabinoids in the plant, has been associated with important therapeutic benefits in different preclinical models.

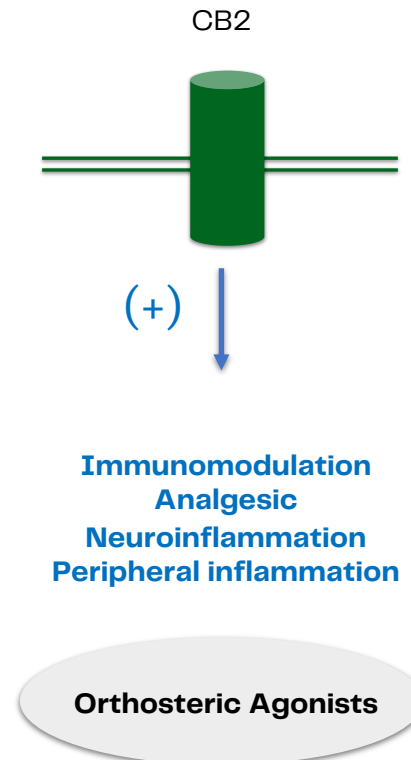


CANNABINOID RESEARCH

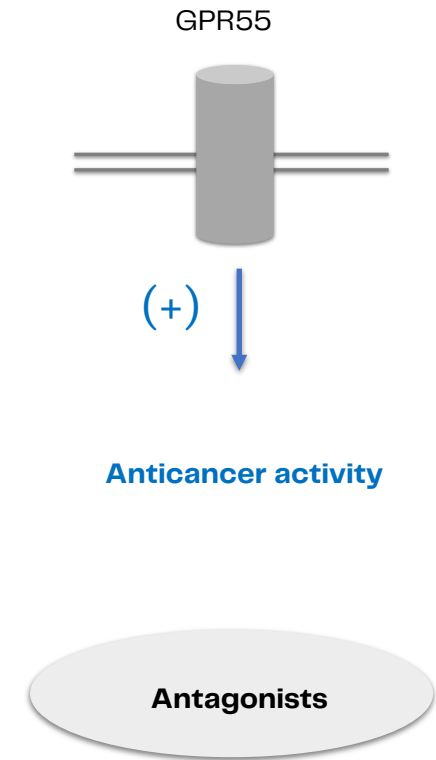
Systemic activation of CB₁R with cannabinoids (THC) may lead to positive and negative effects



No side effects described for CB₂R agonists

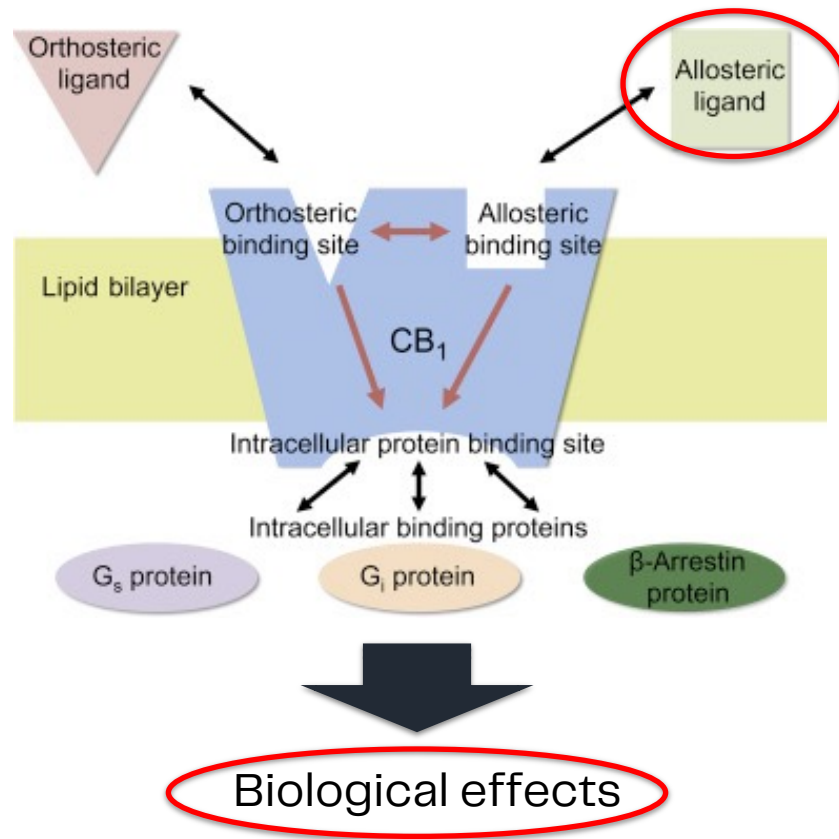


GPR55 activation is associated with cancer



AREAS OF RESEARCH IN THE CANNABINOID FIELD (CB₁R)

“Next generation” of CB₁R modulators inspired in natural cannabinoids



Positive Allosteric Modulators (PAMs)

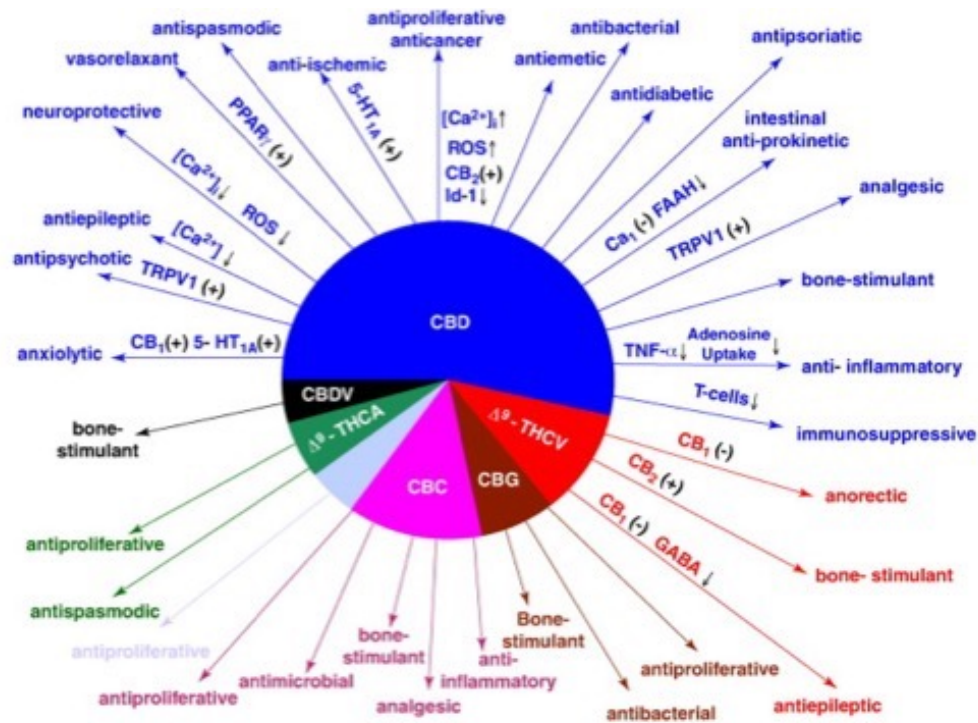
“Benefit of CB₁R activation without side effects”

Negative Allosteric Modulators (NAMs)

“Benefit of CB₁R inhibition without side effects”

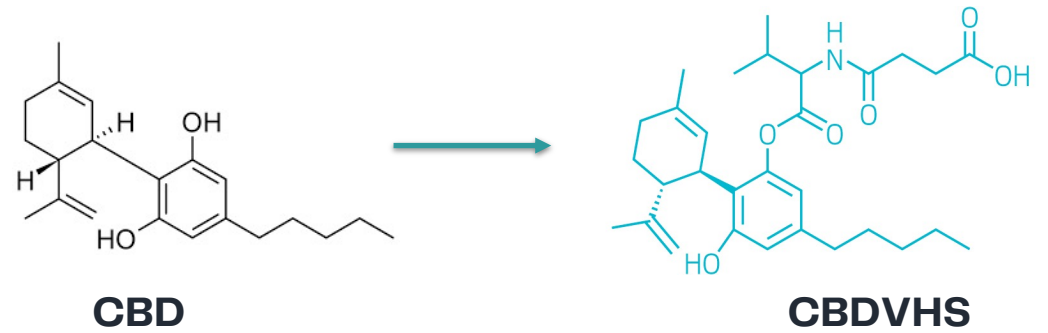
CBDVHS

CBD is a pleiotropic cannabinoid widely used for different indications



TRENDS in Pharmacological Sciences

However, its oral absorption is very low and limits its biomedical application in most diseases



CBD

CBDVHS

CBDVHS IS LIKE CBD, BUT BETTER...

CANNABINOID PHARMACEUTICAL INNOVATION PROGRAM

- ❖ Preclinical development of CBDVHS for unmet medical needs
- ❖ Identification of novel allosteric modulators of CB₁R:
 - Positive allosteric modulators: pain, inflammatory diseases, neurological diseases...
 - Negative allosteric modulators: fibrotic diseases, metabolic diseases...
- ❖ Generate a wide portfolio of patents and IP
- ❖ Preclinical development of novel PAMs and NAMs for CB₁R
- ❖ Drug discovery on CB₂R agonists and GPR55 antagonists



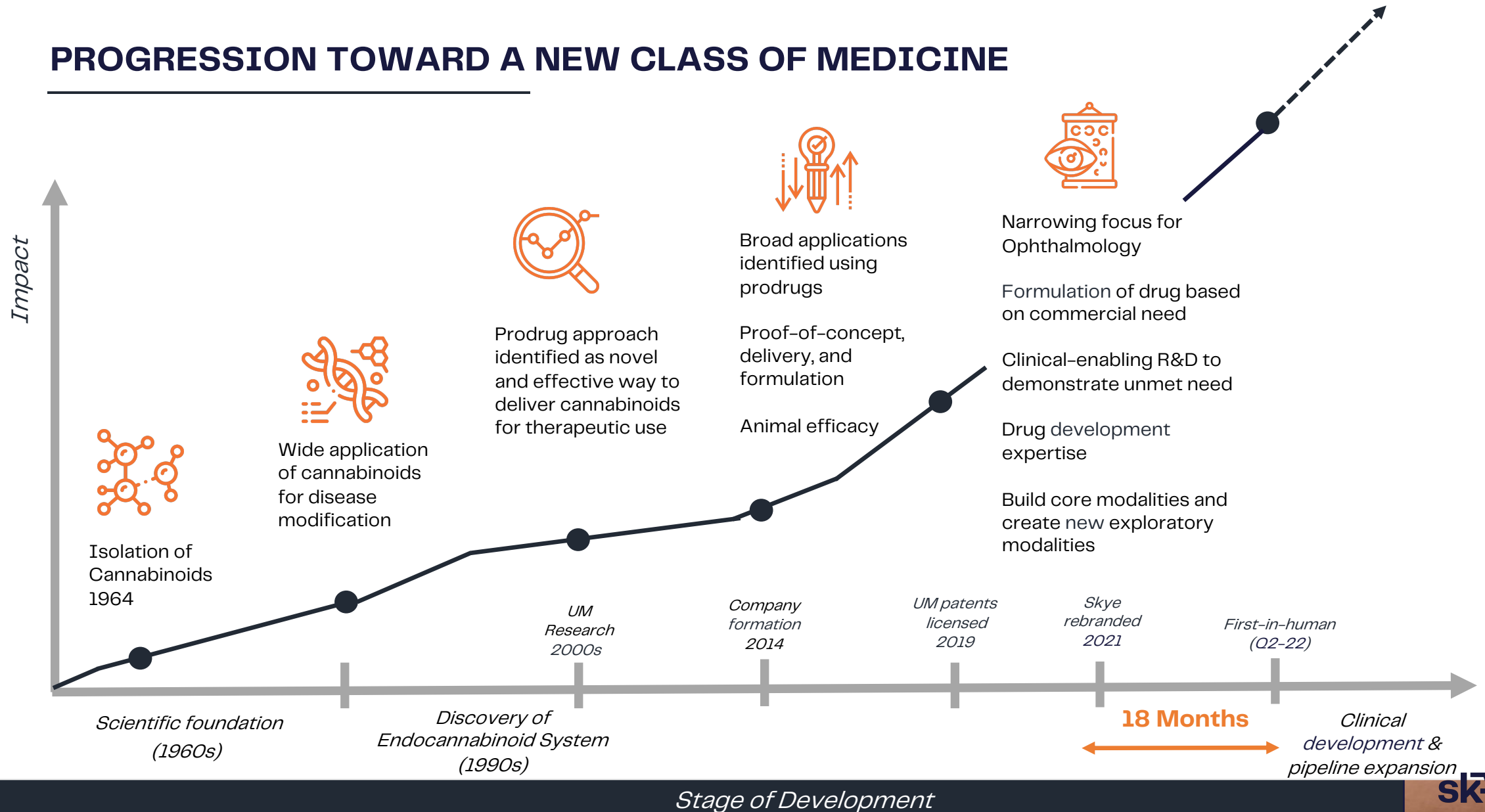
CLOSING REMARKS

PUNIT DHILLON

CEO & CHAIR

SAN DIEGO, CA

PROGRESSION TOWARD A NEW CLASS OF MEDICINE



A LOT HAS CHANGED IN 12 MONTHS

Objective	Achievements
Strengthen new product development capability	<ul style="list-style-type: none"> - Cannabinoid pharmaceutical innovation program; expanded team and budget - Pipeline expansion focused on novel cannabinoid pharmaceuticals addressing unmet needs beyond ophthalmology
Enhance organization structure & process	<ul style="list-style-type: none"> - Expanded BOD, CAB, SAB - Key hires to support organizational focus - Instill financial and operational discipline
Develop Clear Strategic Plan	<ul style="list-style-type: none"> - Focused clinical development plan for SBI-100 - Expanding ophthalmology pipeline - Rebranded company to align with renewed focus
Implementation of capital-efficient plan	<ul style="list-style-type: none"> - Tighter financial controls; improved balance sheet & cash flow - Elimination of costly consulting/third-party professional arrangements (i.e. accounting) - Focused spending on key studies to support first-in-human studies
Extend Cash Runway	<ul style="list-style-type: none"> - \$21M raised since August 2020; path to long-term sustainability - 15+ months cash runway

SKYE ACADEMIC COLLABORATIONS



THE UNIVERSITY OF
MISSISSIPPI



UNIVERSIDAD DE CÓRDOBA



IMIBIC

MAIMONIDES BIOMEDICAL
RESEARCH INSTITUTE OF
CORDOBA

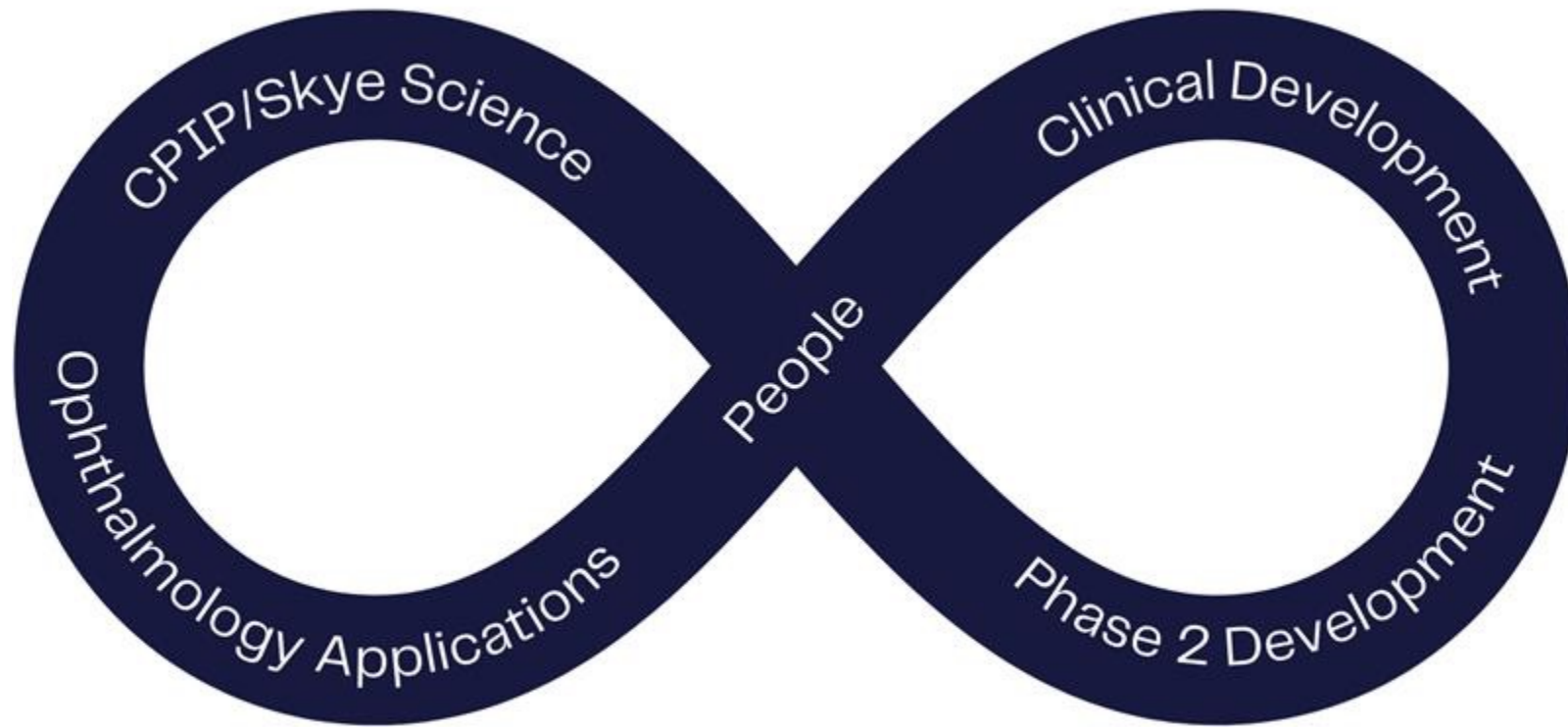


Stanford
University



UNIVERSITÀ DEL PIEMONTE ORIENTALE

LONG-TERM VISION: CANNABINOID PHARMACEUTICAL INNOVATION PROGRAM



UPCOMING CATALYSTS TO ADVANCE OUR GROWTH

SBI-100

- Neuroprotection study results from assessment of SBI-100 potential to spare vision loss
- Results of GLP toxicology studies assessing safety of topical delivery of SBI-100 and systemic exposure to THC
- Pre-IND meeting with the FDA to discuss Phase 2 study in the US and beyond
- Phase 1 safety interim data
- Phase 2 efficacy study initiation

ADDITIONAL MILESTONES

- CPIP/early-stage research & pipeline expansion
- Expand ophthalmology pipeline
- Product-driven intellectual property
- Efficient corporate growth to support objectives

INVESTMENT HIGHLIGHTS



Transformative new class of ocular therapeutics

Cannabinoid receptors discovered in the eye demonstrated to impact multiple ocular disease indications.

Lead glaucoma program SBI-100 demonstrated proof-of-concept that CB1 receptors can be targeted with synthetic cannabinoids

Animal models consistently indicate that SBI-100 performs better than Latanoprost and Timolol at reducing IOP.

Patent protection: SBI-100 through 2027, SBI-200 through 2034

Pipeline expansion focused on novel cannabinoid pharmaceuticals addressing unmet needs beyond ophthalmology

Capital-efficient plan to get to a meaningful clinical inflection point

THANK YOU



Have questions?
Email us at ir@skyebioscience.com