



CBI

Capabilities Overview

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COMPARATIVE BIOSCIENCES, INC.

Premier Preclinical Contract Research Organization

- **20 years** of experience
- Conveniently **located in the heart of Silicon Valley**, amidst many biotech companies
- **State of the art, purpose-built facility**
- Approximately **30 employees**
- **Highly experienced staff**
- **GLP, OECD, FDA, USDA, OLAW**
- **AAALAC Accreditation**



Scientific Overview

We specialize in developing a custom study plan in order to best meet your pre-clinical research needs and prepare for regulatory submission.

- GLP and Non-GLP
- Toxicology
- Efficacy
- Pharmacokinetics
- Pharmacology
- Ocular studies
- In-house histopathology, immunohistochemistry & TCR



CBI Animal Facility

- **Dedicated Rooms:**
 - Six small animal and four large animal rooms
 - Two procedure rooms, two surgery rooms
 - Two rooms with ventilation for immuno-compromised animals
- **Air Quality Systems:**
 - HVAC, light control in each room
 - 10-15 air changes per hour with positive air flow and filtered air
- **Cleanliness:**
 - Dual corridor system with pass-thru Basil cage washer
 - Daily environmental monitoring
 - Regular disease, bacterial and water surveillance
- **24/7 Staff**



Species

- **Mice and Rats:** transgenic, knockout, immunocompromised, and wild-type strains
- **Guinea Pigs, Hamsters, Gerbils**
- **Rabbits:** New Zealand White, Dutch Belted
- **Ferrets**
- **Chinchillas**
- **Dogs:** Lab Beagles
- **Mini-Pigs:** Gottingen, Yucatan



Test Articles

- **Small molecules**
- **Biologics**
 - Peptides
 - Antibodies
 - Vaccines
 - siRNA & Nucleic Acids
- **Stem cells & cell therapies**
- **Devices**
- **Device and drug combinations**
- **Regenerative Medicine**



Toxicology Studies

- **GLP and Non-GLP studies**
- **Single-dose and multiple-dose studies**
- **All routes of administration**
- **Acute & chronic studies**
- **Discovery and Investigative toxicology**
- **Non-standard routes of administration**
- **Complete, prompt reports**



Pharmacokinetic Studies

- **GLP and Non-GLP studies**
- **Single-dose or multiple-dose studies**
- **Sample analysis from blood, urine, CSF, feces**
- **Measure C_{max}, T_{max}, AUC**
- **Metabolic and pharmacodynamics studies**
- **Non-standard routes of administration**



Pharmacology and Efficacy Studies

- **Pharmacology and efficacy modeling in multiple areas**
- **Custom model development**
- **Surgical modeling**
- **Investigative studies**
- **Combination GLP efficacy and toxicology**



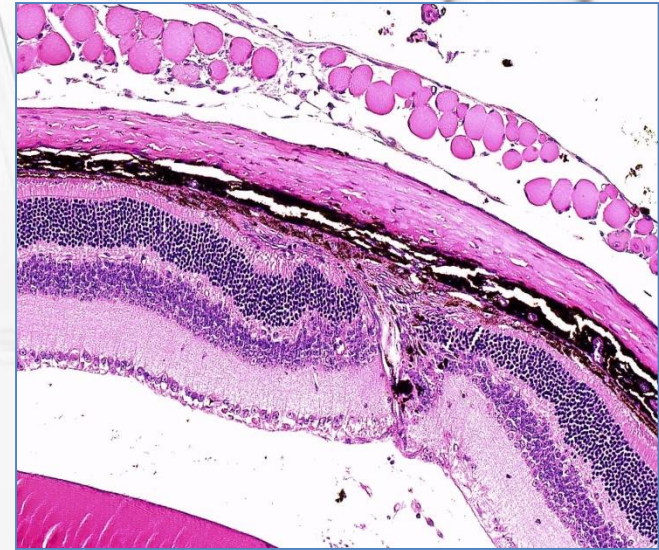
Pharmacology and Efficacy Studies

- **Animal Disease Models for Multiple Indications**
 - Ocular
 - Otic
 - Cardiovascular
 - Inflammation
 - Dermatology
 - Arthritis
 - Allergic and Immune Mediated studies
 - Wound healing and scarring
 - Fibrotic: skin and lung
 - Anti-infective studies
 - Oncology and xenograft
 - Botulinum toxin
 - Central nervous system
 - Regenerative medicine



Histopathology Services

- **Complete In House Laboratories**
 - Paraffin, cryotomy, plastic
 - Immunohistochemistry
 - Special Stains
- **Digital Image Analysis
and Histomorphometry**
- **Highly skilled staff**
 - Trained technicians
- **Validated pathology data acquisition system**
- **Evaluation and report by Board Certified Pathologist**



Ocular Capabilities

- **Ocular toxicology**
- **Ocular pharmacokinetics**
- **Ocular efficacy testing in animal models**
- **Unusual routes of ocular administration**



Ocular Capabilities

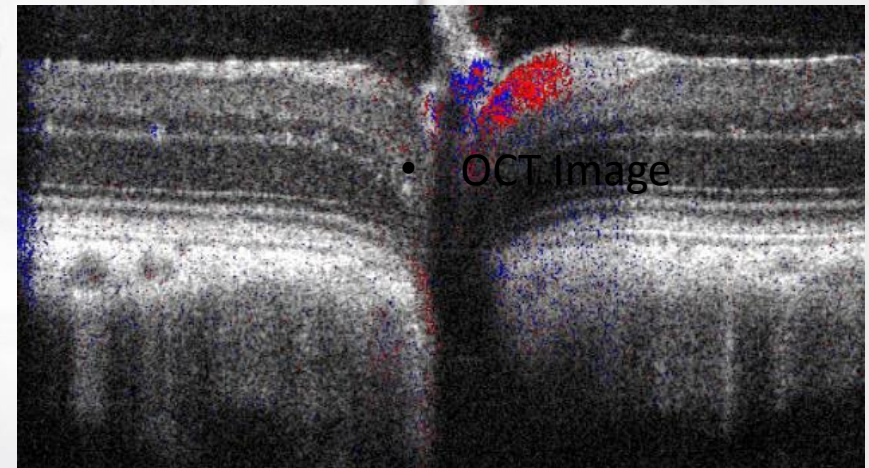
- Ocular Test Articles:
 - Small molecule
 - Large molecule
 - Stem Cells
 - Contact Lens
 - Medicated contact lens
 - Ocular implants
 - Antibodies
 - Proteins
 - Gene therapy/AAV
 - Punctal plugs
 - Ocular devices



Ocular Capabilities

– Equipment and procedure capabilities

- Optical Coherence Tomography
- Retinal scanner
- ERG
- Schirmer test
- Aqueous or vitreal protein
- Fundus examination
- Fundus photography
- Corneal fluorescein staining
- Fluorescein angiography
- Oxygen chamber for OIR
- Optic nerve staining
- Surgical microscope
- Tonometry (IOP)
- Retinal lasering
- Slit lamp examination
- Pachymetry (corneal thickness)



*OCT image

Ocular Capabilities

- Ocular routes of administration
 - Topical
 - Anterior and posterior chamber
 - Conjunctival or subconjunctival
 - Subtenon
 - Intra or transclera
 - Periocular
 - Lacrimal glands
 - Intravitreal
 - Subretinal
 - Intrastromal
 - Retrobulbar
 - Ocular Implants



Ocular Capabilities

Ocular tissue sampling

| | |
|---------------|---|
| Aqueous humor | Vitreous humor |
| Ciliary body | Retina |
| Conjunctiva | Choroid |
| Cornea | Ocular muscles- adenexa – lacrimal glands |
| Iris | Optic nerve |
| Lens | Sclera |
| Tear fluid | Retinal pigmented membrane |



Toxicology Studies

Ocular focus

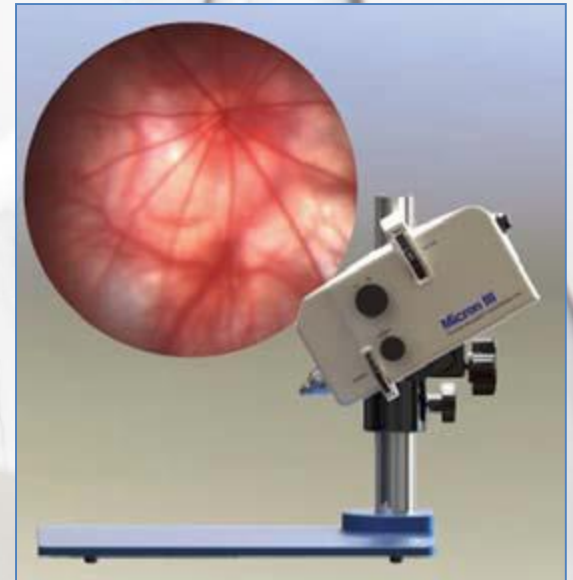
- Topical, adenexal, anterior chamber, intravitreal, implantation, subconjunctival
- Ocular assessment by boarded Ophthalmologist (DACVO)
 - Slit lamp, tonometry, pachymetry, fundus photography, funduscopy assessments
 - Specialized ocular histopathology
 - *in vivo* ERG assessments in all species



Ocular Pharmacology and Efficacy Capabilities

CBI offers a robust variety of validated ocular models for assessment of test article activity

- Retinopathy models
- Dry eye models
- Inflammation models
- Immune-mediated inflammation models
- Glaucoma and ocular hypertension
- Ocular pain models



Ocular Pharmacology and Efficacy Capabilities

- Models of angiogenesis and retinopathy
 - Laser induced choroidal neovascularization (CNV) model in mice, rats, minipigs
 - Oxygen-induced retinopathy (OIR) in neonatal mice and rats
 - PVR (Proliferative vitreoretinopathy)
 - Streptozotocin-induced diabetic retinopathy in rats.
 - VEGF-induced retinal vascular leakage
 - Corneal pocket or suture model
 - Angiotensin II induced retinal vascular leakage



Ocular Pharmacology and Efficacy Capabilities

- Models of Ocular Inflammation
 - LPS-induced acute uveitis in rodents and rabbits
 - F40 80-induced acute uveitis in rabbits
 - Albumin-induced conjunctivitis in rabbits
 - Bacterial and viral induced keratitis model



Ocular Pharmacology and Efficacy Capabilities

- Dry eye models
 - Scopolamine-induced dry eye in mice
 - Botulinum-induced dry eye in mice
 - ConA-induced model in rabbits
 - Glycopyrrolate-induced model in rabbits.
 - Benzalkonium chloride-induced model in rabbits



Ocular Pharmacology and Efficacy Capabilities

- Glaucoma and ocular hypertension
 - Laser induced glaucoma in rodents
 - Corticosteroid-induced
 - Water loading
 - Chymotrypsin



Ocular Pharmacology and Efficacy Capabilities

- Ocular Pain
 - Capsaicin-induced
 - Formalin-induced
- Immune-mediated inflammation
 - Melanin associated antigen induced anterior uveitis in rats
 - IRBP or S-antigen induced posterior uveitis in mice and rats



Ocular Pharmacology and Efficacy Capabilities

- Surgical ocular models
 - Ocular device-drug combinations
 - Artificial/replacement lens
 - Corneal abrasion/laceration
 - Vitreous replacement studies
 - Ocular hypertension/Glaucoma



Service and Quality

- ***Thoroughness in planning and execution is key to a successful study.*** All protocols are vetted and approved by multiple personnel. Our QAU has a rigorous training program. All non-GLP studies are conducted in the spirit of GLP.
- ***We believe in sound science.*** Our ratio of scientists to non-scientists is one of the highest in the industry. Every study director is a PhD-level scientist.
- ***We believe in communication.*** Timely responses to your inquiries and frequent updates on your study are mandatory.
- ***We welcome visitors.*** You are always welcome at CBI to meet the staff, tour the laboratory and discuss the progress and results of your study.



Our Staff

- **Study Directors**

- PhD level scientists
- Appointed by management for each job
- Serves as single point of control and is responsible and accountable for study conduct and scientific interpretation
- Experienced attentive and communicative
- Rapid study initiation and report preparation

- **Research Associates**

- Bachelor Level Scientists
- Extensive technical training

- **Quality Assurance**

- Rigorous Training Program



Summary

- **CBI provides state of the art:**
 - Toxicology
 - Pharmacokinetics
 - Efficacy
 - Pharmacology
 - In house histopathology
- **Experienced attentive and communicative study directors**
- **Rapid study initiation and report preparation**
- **Established, stable business**
- **Regulatory compliance**
- **Favorable pricing structure**

