



**CBI**

# An overview with Hepatic Models

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**COMPARATIVE BIOSCIENCES, INC.**  
A TRANSLATIONAL APPROACH TO PRECLINICAL RESEARCH

# 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
- 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<sub>max</sub>, T<sub>max</sub>, 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
  - Renal and Hepatic Models
  - Anti-infective studies
  - Oncology and xenograft
  - Botulinum toxin
  - Central nervous system
  - Regenerative medicine
  - Surgical Models



# CCL4-INDUCED HEPATIC FIBROSIS

- CCL4 induces a robust and reproducible hepatic fibrosis in rats and mice
- CCL4 is administered twice weekly for 4,8 or 16 weeks resulting in hepatic bridging fibrosis, cirrhosis or micronodular hepatopathy respectively in rats
- Pirfenidone is a suitable positive control
- Hepatic enzymes including GGT, AST, ALT, AP are useful indices of hepatic injury
- Histopathology: HE, Trichrome
- IHC: Collagen, SMA, Stellate cell markers, vimentin

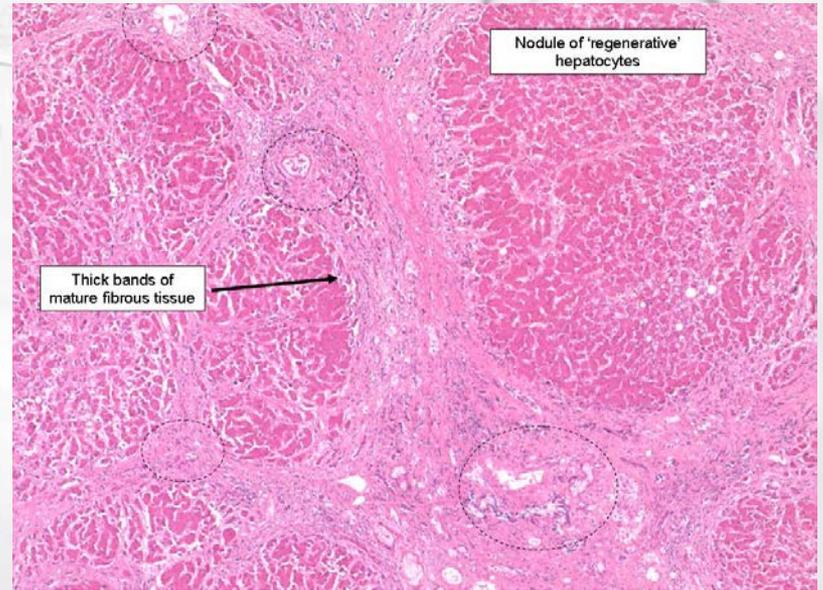
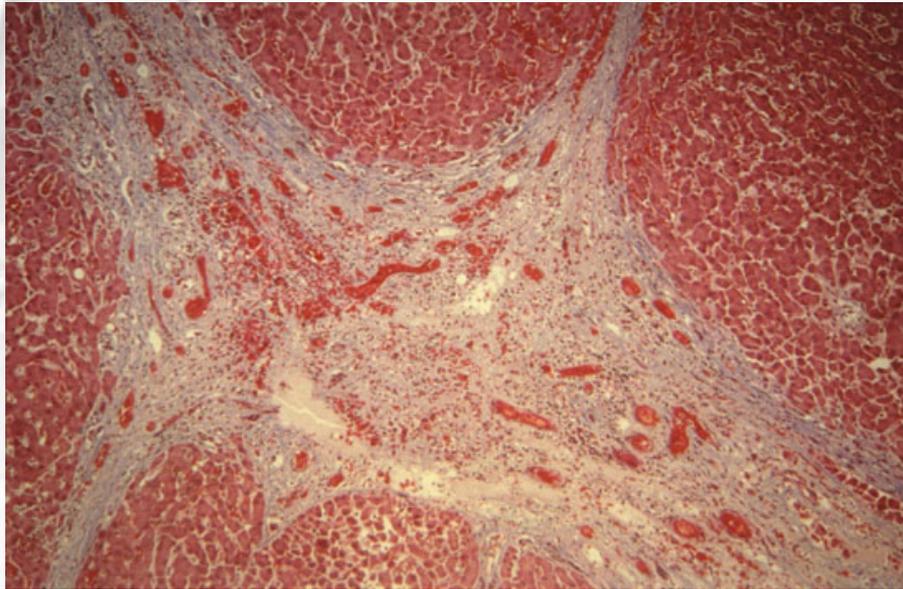
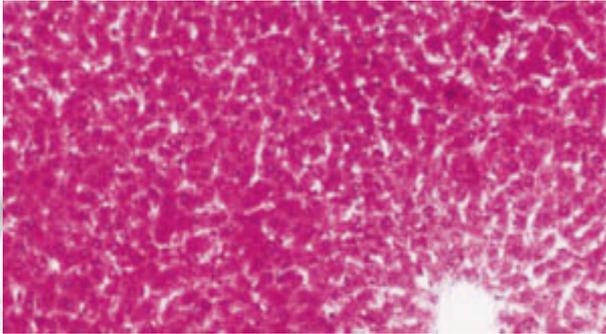


# CCL4-INDUCED HEPATIC FIBROSIS

- Typical Model Design
- Wistar or LE rats
- 10 males per group. Vehicle, test article at various dose levels, pirfenidone is a suitable positive control
- Twice weekly treatment with CCL4
- Daily clinical observations and weekly or twice weekly body weights
- Hepatic enzymes including GGT, AST, ALT, AP every other week (or more often) and necropsy
- Collect, weigh and fix liver at necropsy
- Histopathology: HE, Trichrome
- IHC: Collagen, SMA, Stellate cell markers, vimentin



# Histology: Normal liver, cirrhosis with bridging fibrosis, and micronodular fibrosis



## 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**

