Hypertrophic scar formation in rabbits
Premier Preclinical Contract Research Organization

- **18 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
Hypertrophic scar formation in Rabbits

• Creation of a circular lesion with removal of the perichondrium elicits a proliferative fibrosis resulting in scar formation on the rabbit ear

• This lesion can be measured and effects of test article determined

• Typical study setup:
  – 6 weeks with dosing at day of wound formation
  – After formation of scar (~3 weeks) with 3-4 weeks treatment
    • With 2-3x weekly assessments and followed by histopathology for each

• Test article may be applied topically or intralesion injection

• Recommended group size is 5-6 animals per group with 4 lesions per ear

• Vehicle and test article applied to lesions
Hypertrophic scar formation in Rabbits

Top: Appearance immediately post surgically

Middle: Untreated lesions—there is clear scar formation present

Bottom: Triamcinolone treated: There is more healing and less scar formation
Hypertrophic scar formation in Rabbits

• Screening study-proposed design

<table>
<thead>
<tr>
<th>Group</th>
<th>No Rabbits</th>
<th>In life observations</th>
<th>Necropsy</th>
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<tr>
<td>Vehicle and sham</td>
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<td>Photos of lesions 1x week for 6 weeks</td>
<td>• Histopathology (including IHC) and quantitative assessment of scar formation</td>
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<td>TA low dose</td>
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<td>• qPCR of Scar Samples</td>
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<td>TA mid dose</td>
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<td>TA high dose</td>
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• Quantitative Histology Assessment
  – Scar Elevation Index (SEI)
    • Morris et al. (1997)
Hypertrophic scar formation in Rabbits

- Normal Rabbit
- Scar at 3 weeks
Hypertrophic scar formation in Rabbits

- Three weeks, scar induction, no treatment
- Three weeks, scar induction, no treatment, demonstrating area measured for histomorphometry
Hypertrophic scar formation in Rabbits

• Three weeks, scar induction, no treatment

• Three weeks, scar induction, treatment with Test Article
Hypertrophic scar formation in Rabbits

• Study Summary, SEI of Wounds Treated

Please note
- Decreased SEI compared to vehicle shows efficacy
- TA 1 shows no efficacy at both doses
- TA 2 shows efficacy only in high dose
- TA 3 shows efficacy in both doses
Hypertrophic scar formation in Rabbits

• Histopathology Scores

Inflammation

Collagen Formation
Hypertrophic scar formation in Rabbits

- qPCR – gene of interest expression

Please note:
- High gene expression in vehicle & TA 1 correlates with lack of efficacy.
- Low gene expression in TA 3 correlates with efficacy seen.
Hypertrophic scar formation in Rabbits

- IHC

Immunohistochemical detection of Periostin in Hypertrophic Scar. The test article was applied intralesional (A) or topical (B). Periostin leads to altered regeneration through TGF-Beta Signaling.
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.