TripleHelix Science

CELL AND GENE THERAPIES

Olivers Mouse Study

ROI Analysis Cradle to Grave

NOTE: There are many ways to calculate the ROI depending on ones perspective. In this analysis, I'm assuming one wants to do the study and take the output to market.

Competitive Landscape Adjusted

Executive Summary

This analysis evaluates ROI for a 10-gene longevity study with a streamlined $12M preclinical budget, incorporating full development costs and realistic competitive pressures.

Cost Structure

Phase 1: Preclinical Study ($12M)

As per original budget:

- Animal housing: $3.12M
- Vectors: $2.48M
- Assays: $3.3M
- Personnel/Equipment: $2.48M
- Contingency: $1.12M
- **Total Preclinical: $12.5M** (rounded to $12M)

Phase 2: Clinical Development Costs

Based on competitive landscape and 10-gene portfolio:

IND-Enabling Studies (Years 4-5)

- GLP toxicology (3 lead genes): $15M

- GMP manufacturing scale-up: $25M
- Regulatory filings: $5M
- **Subtotal: $45M**

Clinical Trials - Lead Genes (Years 5-15)

Tier 1 Genes (hTERT, Follistatin, Klotho)

- Phase I (each): $15M × 3 = $45M
- Phase II (each): $40M × 3 = $120M
- Phase III (each): $150M × 3 = $450M
- **Subtotal Tier 1: $615M**

Tier 2-3 Genes (2 additional advanced)

- Phase I/II combined: $30M × 2 = $60M
- Phase III: $120M × 2 = $240M
- **Subtotal Tier 2-3: $300M**

Commercialization (Years 12-15)

- Manufacturing facility: $100M
- Launch and marketing: $150M
- Post-market studies: $50M
- **Subtotal: $300M**

Total Investment: $1,272M

- Preclinical: $12M
- Clinical development: $960M
- Commercialization: $300M

Revenue Projections with Competition

Short-Term Revenue (Years 1-10)

Early Licensing (Before Clinical Data)

- **Years 2-4**:
  - 4 non-lead genes licensed: $3M upfront each = $12M
  - Milestones: $8M
  - Research tool licensing: $5M

Clinical-Stage Licensing

- **Years 5-10**:
  - 2 genes partnered after Phase I: $20M each = $40M
  - Clinical milestones: $60M
  - Co-development deals: $35M

Ancillary Revenue

- Biomarker licensing: $15M
- Research model licensing: $10M
- Veterinary applications: $25M

Total Short-Term: $220M

Long-Term Revenue (Years 11-25)

Market Analysis by Gene (Competition-Adjusted)

Tier 1: High-Value Markets (Lower Share Due to Competition)

- **hTERT**: Sarcopenia/muscle wasting
  - Market size: $8B by 2035
  - Achievable share with competition: 10%
  - Annual peak sales: $800M
- **Follistatin**: Muscle/metabolic disorders
  - Market size: $6B
  - Achievable share: 12%
  - Annual peak sales: $720M
- **Klotho**: Cognitive decline/aging kidneys
  - Market size: $10B
  - Achievable share: 8%
  - Annual peak sales: $800M

Tier 2: Moderate Value (Less Competition)

- **FGF21**: Metabolic syndrome
  - Market size: $5B
  - Achievable share: 15%
  - Annual peak sales: $750M
- **SIRT6**: Broad anti-aging
  - Market size: $4B

    - Achievable share: 10%
    - Annual peak sales: $400M

Revenue Scenarios (Risk-Adjusted)

Conservative Scenario (40% probability)

- 3 genes reach market (hTERT, Follistatin, Klotho)
- Combined peak sales: $2.32B/year
- 10-year market revenue: $15B
- Probability-adjusted: $6B

Base Scenario (40% probability)

- 5 genes reach market
- Combined peak sales: $3.47B/year
- 10-year market revenue: $22B
- Probability-adjusted: $8.8B

Optimistic Scenario (20% probability)

- 7 genes reach market + combinations
- Combined peak sales: $5B/year
- 10-year market revenue: $32B
- Probability-adjusted: $6.4B

Total Risk-Adjusted Long-Term Revenue: $21.2B

Additional Revenue Streams

- Diagnostic tests: $300M
- Combination therapies: $800M
- International expansion: $1.5B
- Next-gen formulations: $600M
- **Additional Revenue: $3.2B**

ROI Calculations

Cumulative Cash Flow Analysis

Years 1-5 (Preclinical + Early Development)

- Investment: -$57M ($12M + $45M)
- Revenue: $25M
- Net: -$32M

Years 6-10 (Clinical Development)

- Investment: -$400M
- Revenue: $195M
- Net: -$205M

Years 11-15 (Late Clinical + Launch)

- Investment: -$815M
- Revenue: $3.2B
- Net: $2.38B

Years 16-25 (Market Phase)

- Investment: -$0
- Revenue: $21.4B
- Net: $21.4B

ROI Metrics

Overall Program ROI

- Total Investment: $1,272M
- Total Revenue: $24.62B ($220M + $21.2B + $3.2B)
- **Gross ROI: 1,836%**
- **NPV @ 10% discount rate: $5.8B**
- **IRR: 24.5%**
- **Payback Period: 13 years**

Preclinical Investment ROI

- Preclinical cost: $12M
- Attributable to preclinical success:
  - Early licensing: $220M
  - Value creation for clinical: ~$2B (estimated)
- **Preclinical-specific ROI: 17,500%**

Risk-Adjusted Returns by Investment Stage

1. **After Preclinical ($12M invested)**

    - Expected value created: $220M
    - ROI: 1,733%
2. **After Phase I ($102M invested)**
    - Expected value created: $1.2B
    - ROI: 1,076%
3. **After Phase II ($342M invested)**
    - Expected value created: $3.5B
    - ROI: 923%
4. **Full Investment ($1,272M)**
    - Expected value: $24.62B
    - ROI: 1,836%

Competitive Impact Analysis

Market Share Erosion Factors

- **Year 1-5**: First-mover advantage, 20-25% share possible
- **Year 6-10**: Competition enters, share drops to 10-15%
- **Year 11-15**: Biosimilars emerge, share stabilizes at 8-12%
- **Year 16-25**: Next-gen therapies compete, maintain 5-10%

Competitive Advantages from 10-Gene Approach

1. **Portfolio diversification**: Not dependent on single mechanism
2. **Combination data**: Unique IP position
3. **Biomarker suite**: Patient selection advantage
4. **Multiple indications**: Broader market access

Sensitivity Analysis

Critical Success Factors

1. **Number of genes reaching market**: Each additional gene adds $3-4B value
2. **Market share**: Each 1% share = $200-300M annual revenue
3. **Time to market**: Each year delay = $500M lost revenue
4. **Partnership terms**: 10% better terms = $2B additional value

Downside Protection

Even if only 2 genes succeed:

- Revenue: $8-10B
- ROI: 600-700%
- Still exceeds industry benchmarks

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Conclusion

With a streamlined $12M preclinical investment:

1. **Overall program ROI of 1,836%** despite $1.27B total investment
2. **Preclinical phase generates exceptional 17,500% return** through early value creation
3. **Risk mitigation through 10-gene portfolio** reduces binary failure risk
4. **Competitive positioning** via combination data and biomarkers

Key Advantages of $12M Budget Approach:

- Lower initial capital risk
- Faster decision-making on lead candidates
- More attractive to early investors
- Flexibility to expand based on results

Recommendation:

The $12M preclinical investment offers outstanding risk-adjusted returns. The 10-gene portfolio approach provides multiple paths to success even in a competitive landscape, with break-even achievable through licensing alone if only 2-3 genes advance successfully.

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Specialities:

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