

Achieving Successful Trial Outsourcing from the Perspective of Small Biotech Companies

Insights and Best Practices



Who am I

**Biomedical
Research**



Biochemistry & Molecular Biology
Toxicology

**Clinical
Study**



Project Manager
BD Director



Cancer Genomics



Director, Clinical Development

Connex Overview

- Connex is a clinical-stage biotech company developing recombinant therapeutics to improve the quality of life for patients.
- Connex pursues niche markets with high unmet needs and is developing high quality therapeutics based on platform bioprocessing technologies.



Company

Establishment: 25th of October 2017

Employees: 17

Location

HQ (R&D center): Daegu

Seoul office

Bundang office: Seoul National University Bundang Hospital Healthcare Innovation Park



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			Nonclinical	Phase 1	Phase 2	Phase 3
TLR5 AGONIST (Mitigating radiation toxicity)	CNT101	Acute GVHD	FIH study finished, IND approved by MFDS of Korea			
		Acute Radiation Syndrome	Phase 1 study finished			
	CNT102	Immuno-Oncology				
COLLAGENASE (Breakdown of abnormal collagen deposition)	CNT201	Dupuytren's Contracture	IND approved by the US FDA in June 2023 / Phase 1 underway			
		Peyronie's Disease				
		Cellulite				
	CNT202	Burn (Wound debridement)				

Agenda

1. Importance of Outsourcing in Small Biotech
2. Reason for Outsourcing Clinical Trials
3. Key areas of Outsourcing
4. Global vs. Local (small) CROs
5. Choosing the Right CRO
6. CRO Selection Process
7. Strategic Planning with Limited Resources
8. Case Study: CNT201 DC P1/2 study
9. Overcoming Outsourcing Hurdles: Challenges and solutions
10. Best Practices for Successful Outsourcing

Importance of Outsourcing in Small Biotech

- **Key Challenges:**

- ✓ Limited in-house expertise
- ✓ Budget and resource constraints
- ✓ Complex regulatory landscapes

- **Benefits of Outsourcing:**

- ✓ Access to expertise and infrastructure
- ✓ Faster project timelines
- ✓ Focus on core R&D

Reason for Outsourcing Clinical Trials

- **Cost Efficiency:**

- ✓ Outsourcing to a CRO can reduce infrastructure costs and operate on economies of scale, allowing them to perform tasks at a lower cost than in-house

- **Skilled Expertise:**

- ✓ CROs provide specialized knowledge in regulatory requirements, study design, and data management.
- ✓ Expertise in niche therapeutic areas or specific types of clinical trials (e.g., oncology, rare diseases).
- ✓ Experienced in navigating diverse regulatory landscapes, including FDA, EMA, and others

- **Geographic Reach:**

- ✓ CROs have local teams and infrastructure to conduct trials across countries, understanding regional regulations and cultural differences.

- **Scalability and Flexibility:**

- ✓ Outsourcing provides flexibility to scale up or down depending on project needs, which is especially beneficial for small biotech companies.
- ✓ Enables companies to focus on core activities, such as drug discovery or business development.

Reason for Outsourcing Clinical Trials (Cont..)

- **Data Quality and Compliance:**

- ✓ CROs use advanced tools and technologies (e.g., EDC systems, eTMF platforms) to ensure data quality, integrity, and compliance with global standards
- ✓ Familiarity with GCP guidelines ensures that trials meet regulatory expectations

- **Resource Constraints:**

- ✓ Small to mid-sized companies may lack the infrastructure or personnel to manage complex clinical trials internally
- ✓ Outsourcing allows them to leverage the CRO's resources without heavy upfront investment

- **Speed to Market:**

- ✓ Outsourcing enables faster development timelines, allowing companies to meet critical deadlines and bring products to market sooner
- ✓ Reduces the burden of managing trial logistics, enabling sponsors to focus on decision-making and strategy

Key areas of Outsourcing

- **Regulatory Services:**

- ✓ RA team: pre-IND, IND, NDA, CTA, HREC, IRB
- ✓ Clinical trial documents packaging (eCTD format)

- **Clinical Services**

- ✓ Study Management: CRO PM
- ✓ Site Management: feasibility, site contract, Committees (SRC, IDMC)
- ✓ Monitoring: CRA (SDV, communication with Sites)

- **Safety Services**

- ✓ Medical Monitor (Safety, SAE, SUSAR, protocol)
- ✓ Pharmacovigilance: PV team (DSUR)

- **Clinical Data Management & Statistics**

- ✓ DM (EDC (eCRFs), eTMF (regulatory and operational documents), CTMS, RTMS, ePRO (patient-reported outcomes), eCOA (Clinical Outcome Assessment), eConsent, DCT (decentralized clinical trial))
- ✓ Biostatistics: Statistician

Key areas of Outsourcing (Cont..)

- **Medical Writing:** Medical writer, protocol, IB, ICF, CSR
- **Labs/Imaging centers:** Central labs (PK, ADA, nAb, Image Reading (CT, MRI, endoscopy))
- **Material/IP Supply (Logistics):** Drug depot
- **Pre-clinical study (GLP):** Toxicology (CDISK SEND formatting), PK
- **Study IP Manufacturing (cGMP CMO):** DS, DP manufacturing, CMC documentation
- **Consultancy services**
 - ✓ SMEs: Regulatory consulting, CMC consulting, Clinical expertise, Medical expertise,
 - ✓ KOLs: SAB
 - ✓ Clinical Development Plan: Indication Prioritization, TPP, CDP
 - ✓ Legal & Accounting: Subsidiary incorporation, R&D incentive
 - ✓ Regulatory: Pre-IND meeting, IND submission, ODD application, DSUR, HREC
 - ✓ BD: Partnering meetings, NPV valuation, Market Access, Pricing & Reimbursement Strategy, Due diligence, Deal term sheet

Global vs Local (small) CRO

(The factors for Clinical CRO selection)

1. CRO Selection Factors

- ✓ Internal experts
- ✓ Consulting requirement
- ✓ Simple operation team
- ✓ Budget
- ✓ Alpha / beta team
- ✓ Agility
- ✓ Time difference
- ✓ Language barrier

2. Preparation for Clinical CRO selection

- ✓ Identify the needs and choose the best outsourcing model accordingly
- ✓ SWOT analysis
- ✓ Be clear on what you want done
- ✓ State expectations and explain your terms
- ✓ Prepare a detailed contract
- ✓ Request timely reports
- ✓ Utilize forums and conferences to meeting

Global vs Local (small) CRO

(SWOT analysis)

Global CRO

Strength	Weakness
<ul style="list-style-type: none"> ✓ Broad Expertise ✓ Global Infrastructure ✓ Regulatory Knowledge ✓ Standardized Processes ✓ Scalability 	<ul style="list-style-type: none"> ✓ Higher Costs ✓ Less Personalization ✓ Bureaucracy
Opportunities	Threats
<ul style="list-style-type: none"> ✓ End-to-End Solutions ✓ Established Reputation ✓ Access to Emerging Markets 	<ul style="list-style-type: none"> ✓ Priority Concerns ✓ Turnover ✓ Over standardization

Local (Small) CRO

Strength	Weakness
<ul style="list-style-type: none"> ✓ Cost-Effective ✓ Personalized Service ✓ Deep Local Knowledge ✓ Quick Decision-Making 	<ul style="list-style-type: none"> ✓ Limited Resources ✓ Geographic Restrictions ✓ Potential Gaps in Experience
Opportunities	Threats
<ul style="list-style-type: none"> ✓ Niche Expertise ✓ Local Relationships ✓ Collaboration Potential 	<ul style="list-style-type: none"> ✓ Capacity Issues ✓ Risk of Dependency ✓ Regulatory Challenges

Choosing the Right CRO

1. Define Your Project Needs and Goals

- ✓ **Therapeutic Expertise:** Look for CROs with experience in your specific therapeutic area. This ensures they understand the complexities and nuances of your trial
- ✓ **Trial Phase:** Select a CRO experienced in the phase of your trial (Phase I-IV)
- ✓ **Geographic Coverage:** If your trial spans multiple regions, choose a CRO with established local presence and regulatory knowledge

2. Assess Their Track Record

- ✓ Review their past performance in similar studies
- ✓ Ask for case studies, references, and metrics (e.g., on-time performance, patient recruitment success rates)
- ✓ Ensure they have expertise in handling trials for small biotech companies, which may require more personalized attention

Choosing the Right CRO (Cont..)

3. Evaluate Their Operational Capabilities

- ✓ **Project Management:** Assess their project management structure, including communication plans, escalation pathways, and resource allocation
- ✓ **Patient Recruitment:** Investigate their strategies and networks for patient recruitment
- ✓ **Technology and Systems:** Ensure they have advanced platforms for EDC (Electronic Data Capture), eTMF (electronic Trial Master File), and other essential trial systems

4. Regulatory and Quality Standards

- ✓ Verify their compliance with global regulatory requirements (e.g., FDA, EMA, ICH-GCP guidelines)
- ✓ Evaluate their internal quality assurance processes and audit readiness
- ✓ Confirm their track record with regulatory submissions and inspections

5. Flexibility and Scalability

- ✓ Determine if the CRO can adapt to changes in your trial design or timelines
- ✓ Ensure they can scale their resources to accommodate changes in trial size or complexity

Choosing the Right CRO (Cont..)

6. Financial Considerations

- ✓ Request detailed budgets and assess transparency in cost structures
- ✓ Balance cost with value—cheaper options may lack necessary expertise or infrastructure
- ✓ Confirm their ability to work within your budget without compromising quality

7. Communication and Collaboration

- ✓ Choose a CRO with a responsive, transparent communication style
- ✓ Meet their project team to ensure alignment in goals and expectations
- ✓ Ensure they are willing to act as a partner, offering strategic insights rather than simply executing tasks

8. Metrics and Reporting

- ✓ Confirm how they measure success and report progress
- ✓ Ensure you'll have regular updates and access to key performance indicators (KPIs)

Choosing the Right CRO (Cont..)

9. Cultural Fit

- ✓ Choose a CRO that aligns with your company's values and work culture
- ✓ Ensure they understand the unique needs and constraints of a small biotech firm

10. Conduct Due Diligence

- ✓ Visit their facilities, if possible, to evaluate their infrastructure and operations
- ✓ Speak with other sponsors who have worked with the CRO to gather firsthand feedback

11. Start Small if Necessary

- ✓ Begin with a pilot project or a smaller trial to assess the CRO's capabilities before committing to larger studies

Small biotech companies should prioritize flexibility, therapeutic expertise, and a partnership approach when selecting a CRO. A good fit will not only help execute the trial efficiently but also provide strategic insights to navigate challenges.

CRO Selection Process

1. Define Requirements

- ✓ Scope of Works (SOW): Trial management, Site selection & monitoring, DM, Regulatory
- ✓ Trial Specifications
- ✓ Budget Constraints

2. Identify Potential CROs

- ✓ Internal Database: Existing knowledge or recommendations from colleagues in the industry
- ✓ Market Research: Search for CROs specializing in the therapeutic area or trial type
- ✓ Industry Networks: Attend conferences or use platforms like ClinicalTrials.gov to identify experienced CROs

3. Request for Information (RFI)

- ✓ Expertise in therapeutic area
- ✓ Experience in similar studies
- ✓ Geographic Reach: Global and local presence
- ✓ Available resources and technologies (i.e. Vendors, EDC system, risk-based monitoring tools)

4. Request for Proposal (RFP)

- ✓ Scope of Works (SOW)
- ✓ Trial background and objectives
- ✓ Budget expectations
- ✓ Expected timelines and milestones
- ✓ Site feasibility: Questionary (interest, experience), Estimated recruitment rate

CRO Selection Process (Cont..)

5. Evaluate Proposals

- ✓ Scientific Expertise: Understanding of the therapeutic area and trial protocol
- ✓ Operational Capabilities: Site management, patient recruitment strategies, and quality control
- ✓ Experience: Track record in similar trials and regulatory environments
- ✓ Technology: Availability of tools for data management, analytics, and monitoring
- ✓ Cost and Flexibility: Alignment with the budget and adaptability to project changes

6. Bid Grid

- ✓ Line-item costs for services (i.e. PM, site monitoring, DM, MM, MW, Statistics)
- ✓ Pass-through costs: Site fees, Central labs, Drug depot, EDC system

7. (Bid Defense) Meetings

- ✓ Assess CRO's Understanding
- ✓ Evaluate Competence and Expertise
- ✓ Clarify and Discuss the Proposal
- ✓ Communication, Responsiveness, and Flexibility to project needs
- ✓ Problem-Solving Ability
- ✓ Team Chemistry
- ✓ Proposed timelines, budgets, and deliverables

CRO Selection Process (Cont..)

8. Study Team Interviews

- ✓ Interview Prioritization: PM >> MM > CRA
- ✓ Areas of Focus: Experience, Project Workload, Communication Skills, and Job Change History

9. Select and Negotiate

10. Master Service Agreement (MSA)

- ✓ Payment terms, Confidentiality clauses, IP rights, Dispute resolution

11. Work Order (WO)

- ✓ Service and Pass-Through Costs

12. Kick Off Meeting (KOM)

Strategic Decision-Making with Limited Resources

•Key Considerations:

- ✓ Prioritize critical trial components
 - Identify and focus resources on the most impactful aspects of the trial (e.g., efficient patient recruitment strategies, maintaining high data quality)
- ✓ Select a CRO that complements in-house strengths (e.g., regulatory compliance, data management, or global site coordination)
- ✓ Invest in strong vendor management processes
 - Clear communication channels, frequent updates, and defined deliverables
 - Assign dedicated in-house resources to monitor CRO performance and ensure alignment with project timelines and goals.

•Cost Optimization:

- ✓ Negotiate milestone-based payments:
 - Structure contracts to link payments to key deliverables (e.g., database lock, patient recruitment milestones, or site activation), Avoid large upfront payments
- ✓ Leverage combined or adaptive trial designs
- ✓ Optimize site selection to reduce costs
 - Choose trial sites with proven recruitment success, access to the target population, and cost-effective operations

Case Study: CNT201 DC Phase I/II trial

- **Objective:** Outsource and conduct a Phase I/II trial for CNT201 in Dupuytren's Contracture (DC) across Australian sites
- **Key Constraints:**
 - ✓ **Limited In-House Expertise:** The sponsor required external support for clinical trial execution
 - ✓ **Limited Clinical Sites:** Few sites were qualified and experienced in conducting DC trials
 - ✓ **Niche CRO Availability:** Scarcity of CROs with expertise in managing DC trials and navigating Australian regulatory requirements
- **Actions Taken:**
 - ✓ **Engaged SMEs and Consultants:** Utilized fee-based expertise to address gaps in internal capabilities
 - ✓ **Site Feasibility Assessment:** Identified experienced investigators and clinical sites with a strong track record in DC studies
 - ✓ **Strategic Site Partnerships:** Partnered with sites have track record in conducting DC studies
 - ✓ **Comprehensive CRO Selection:** Rigorously evaluated CRO candidates during the RFP process, emphasizing Phase I/II trial experience with small biotech / PM, MM, and CRA interview
 - ✓ **Site Engagement:** Strengthened relationships through site visits and PI meetings to ensure alignment and motivation
 - ✓ **Robust Communication Framework:** Implemented weekly progress reviews with the CRO to address challenges and monitor milestones
- **Outcome:** Accelerated trial progression, High-quality data, Enhanced Relationships

Outsourced Services

for CNT201 DC Phase I/II study

- **Pre-clinical Study:** Korea Institute of Toxicology (안전성평가연구소, KIT), Global GLP Organizations
 - ✓ Toxicology (Acute, SD, DRF, RD)
- **CMC:** Domestic & International cGMP Organizations
 - ✓ DS & DP manufacturing, CMC documentation
- **Study Development Plan:** Global Clinical Service CRO
 - ✓ Indication Prioritization, TPP, CDP
- **Regulatory Consulting (US):** Global Clinical Service CRO
 - ✓ Pre-IND meeting: IB, protocol synopsis, meeting request, Type-B MIP
 - ✓ IND prep & submission: Full study protocol, eCTD modules development, master ICF, Form 1572
 - ✓ IND maintenance: IND Amendments, safety reports, DSUR

Outsourced Services (Cont..)

for CNT201 DC Phase I/II study

- **Regulatory Consulting (Australia, EU):** Global Clinical Service CRO & RA Consultants
 - ✓ Australia: HREC, RGO / EU: Gap analysis, Clinical development strategy
- **Clinical Service (Australia):** Global Clinical Service CRO (ANZ)
 - ✓ Site feasibility, selection & contract
 - ✓ RA, PM, MM, DM, Site monitoring, Vendor management
 - ✓ Vendors: Central lab (PK, ADA), Drug depot, EDC, eTMF
- **Australia Subsidiary:** Corporate and advisory services (ANZ)
 - ✓ Company incorporation, Legal agreements, Accounting, Tax registration, R&D incentive
- **BD Consulting (US, EU and Japan):** Global & Local BD Consultants
 - ✓ Partnering meetings, NPV valuation, Market Access, Pricing & Reimbursement Strategy (Payer & Prescriber interviews)

Overcoming Common Hurdles

•Hurdle 1: Lack of internal experience

- ✓ **Challenge:** Small biotech companies often have limited in-house expertise in clinical trial management
- ✓ **Solution:**
 - Establish a small but experienced cross-functional team / Training and Upskilling
 - Leverage External Consultants
 - Define roles, responsibilities, and reporting structures

•Hurdle 2: Misaligned expectations with CROs

- ✓ **Challenge:** Miscommunication and unclear expectations can lead to delays and inefficiencies
- ✓ **Solution:**
 - Develop clear metrics and Key Performance Indicators (KPIs) in contracts
 - Schedule consistent meetings and progress reviews
 - Set Up Escalation Processes to create clear mechanisms for addressing and resolving issues quickly

Overcoming Common Hurdles (Cont..)

- **Hurdle 3:** Budget constraints

- ✓ **Challenge:** Limited financial resources make it difficult for small biotech companies to afford top-tier CROs or handle unexpected trial costs
- ✓ **Solution:**
 - **Explore Shared-Risk Models:** Partner with CROs offering shared-risk or milestone-based payment structures to distribute financial risk
 - **Negotiate Cost-Effective Packages:** Identify CROs that specialize in working with small biotech companies and offer tailored, budget-friendly service packages
 - **Optimize Site Selection:** Choose sites with high patient recruitment potential and cost efficiency to minimize travel and operational expenses
 - **Leverage Technology:** Use digital tools like eConsent, remote monitoring, and decentralized trial designs to reduce operational costs

Best Practices for Successful Outsourcing

1. **Define Clear Goals:** Ensure alignment on deliverables and timelines

- ✓ Clear outline of detail deliverables and set realistic timelines
- ✓ Hold a KOM with the CRO to discuss and finalize shared goals, ensuring both parties are aligned from the start

2. **Vendor Selection Process:**

- ✓ Use Request for Information (RFIs), Request for Proposals (RFPs), and reference checks effectively

3. **Robust Communication:**

- ✓ Establish Regular Meetings: Weekly or biweekly updates to monitor progress

4. **Performance Metrics:**

- ✓ Define success via measurable KPIs: e.g., recruitment rates, site activation timelines, data query resolution times, and protocol compliance
- ✓ Monitor regularly, and Address underperformance

5. **Continuous Monitoring:**

- ✓ Conduct site visits and PI meetings and Plan Audits
- ✓ Leverage Data Analytics

Closing

Key Takeaways

- ✓ Choose the CRO that aligns with your study's needs and resources
- ✓ Strategic planning is essential for small biotechs
- ✓ Effective communication and monitoring lead to success

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