Operating an Efficient and Profitable Clinical Trial Center in the US and Europe: Are US and European Experiences Relevant in Asia?

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Celerion Operates Five Commercial Clinical Trial Centers in US and UK

Lincoln, NE
200 beds

Neptune, NJ
150 beds

Phoenix, AZ
300 beds

Belfast, Northern Ireland
UK
78 beds

Bryan Health, Lincoln, NE
24 In-hospital beds

More than 750 beds globally
Top CROs (by Phase I Bed Capacity)

<table>
<thead>
<tr>
<th>CRO</th>
<th>Beds</th>
</tr>
</thead>
<tbody>
<tr>
<td>Celerion</td>
<td>752</td>
</tr>
<tr>
<td>Novum</td>
<td>550</td>
</tr>
<tr>
<td>QPS</td>
<td>480</td>
</tr>
<tr>
<td>Parexel</td>
<td>407</td>
</tr>
<tr>
<td>Comprehensive Clinical (Charles River)</td>
<td>400</td>
</tr>
<tr>
<td>Covance</td>
<td>364</td>
</tr>
<tr>
<td>Pharma Medica</td>
<td>360</td>
</tr>
<tr>
<td>Frontage</td>
<td>340</td>
</tr>
<tr>
<td>Seaview</td>
<td>320</td>
</tr>
<tr>
<td>PPD</td>
<td>300</td>
</tr>
<tr>
<td>Quintiles</td>
<td>291</td>
</tr>
<tr>
<td>Worldwide Clinical Trials</td>
<td>250</td>
</tr>
<tr>
<td>CRI Lifetree</td>
<td>245</td>
</tr>
<tr>
<td>PRA</td>
<td>240</td>
</tr>
<tr>
<td>Algorithme Pharma</td>
<td>225</td>
</tr>
<tr>
<td>inVentiv Health (Anapharm/PharmaNet/i3)</td>
<td>200</td>
</tr>
<tr>
<td>Biopharma</td>
<td>174</td>
</tr>
<tr>
<td>SGS Life Sciences</td>
<td>172</td>
</tr>
<tr>
<td>Phase I Solutions Miami</td>
<td>160</td>
</tr>
<tr>
<td>West Coast Clinical Trials</td>
<td>150</td>
</tr>
<tr>
<td>Icon</td>
<td>144</td>
</tr>
<tr>
<td>DaVita</td>
<td>122</td>
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<tr>
<td>Spaulding</td>
<td>105</td>
</tr>
<tr>
<td>Clinilabs</td>
<td>100</td>
</tr>
<tr>
<td>SNBL</td>
<td>96</td>
</tr>
<tr>
<td>Medpace</td>
<td>96</td>
</tr>
</tbody>
</table>

Note: Data as of May 2013

7,043 beds
What Defines an Enduring Business

- Consistently provides a valuable service to customers
- Provides satisfying work for employees
- Contributes to global and/or local communities
  - Geographical, societal and professional
- Makes money for owners/investors

Keeping Business Balance

More revenue
Add new services
Better data for better decisions

Lower operating costs
Focus on core competencies
Faster results for faster decisions

Invest in potential “game-changing” technologies
Five Learnings From a US and Europe Focused Early Clinical Phase CRO

1. Know your strengths
2. Know the marketplace and how it is changing
3. Know what the customer cares about most
4. Constantly be building efficiencies that reduce cost and shorten timelines
5. Create a strategic approach to growth
#1 Know Your Strengths

Celerion focuses its expertise, experience and specialized facilities and equipment on these study types:

**IND/CTA (Phase I/Ib/Ila)**
- Toxicokinetics
- Allometric Scaling
- PK/PD Modeling
- Novel Biomarker Development
- Microdosing AMS (Phase 0)

**FIH to CPoC (go/no go decisions)**
- SAD – safety/PK
- MAD – safety/PK
- Pilot Food Effect - PK
- Elderly – safety/PK
- Robust Cardiac Safety
- Absolute BA (Microtracer - AMS)
- Drug Metabolizing Enzyme Probes or Genotyping on PK
- Early Metabolic Profile (Microtracer – AMS)
- First-in-Patient - Signal of Effect

**NDA Enabling (product labeling)**
- Drug-Drug Interactions (DDI)
- Hepatic and Renal Insufficiency on PK
- Thorough QTc (TQT)
- Radiolabeled ADME (mass balance)
- Market-image Bioequivalence (BE)
- PK or PK/PD in Special Populations
- PK or PK/PD in Pediatric Populations
- Population PK or PK/PD from Pivotal Efficacy or Safety Studies

**Product Extension (new indications)**
- PK in New Patient Populations
- BE New Formulations
- BE Generics
- Population PK

**NDA/MAA**

**Phase IIb / III**

**sNDA/ANDA (US)**
Celerion Differentiators

- **Focus** – only early clinical research, NDA-enabling studies and bioanalysis
- **Size** – capacity and capability coupled with flexibility and responsiveness
- **Industry knowledge** – “hands-on” drug development experience throughout the company
- **History** – first free standing contract research organization
- **Innovative** service offerings - better data, faster and lower cost
#2 Know the Marketplace and How it is Changing

Confined Clinical Pharmacology Studies

- Number of studies done in US and Europe per year grew steadily until peaking in 2005-2006 then leveled off with some recent decline.
- Cutbacks in large pharmaceutical companies mean fewer new drug candidates entering early clinical research but more outsourcing.
- Global growth projected to come from Asia-Pacific as more drug candidates discovered in these regions enter the global drug development pipeline.
- There is an increasing number of adaptive and fusion protocols in early clinical research.
- There are more first-in-human (SAD/MAD) protocols that have patient arms so that early signals of drug effect can be seen.
- There are more experimental medicine studies that evaluate the utility of certain new biomarkers as tools to help understand drug effects on disease.

Access to patients is emerging as a critical business driver
The Outsourced Drug-Development Market

Celerion

Delivery & Preclinical | Phase I-IIa Early Clinical | Bio-analytical | Phase IIb-IV Global Clinical | Central Labs | Other | eClinical
---|---|---|---|---|---|---
Early Stage testing: • Properties & effects (non-tox) • Harmful or fatal effects in animals (tox) | Determine impact of compound on human subjects (healthy or specific condition) | Analyzing samples from preclinical or early clinical to test for specific physiological impacts | Managing patient recruitment and administration of clinical trials for new compounds | Analyzing human samples from clinical trials to test for specific physiological impacts | Includes preclinical supplies, research models, formulation, and manufacturing | Includes electronic data capture, IVRS, RTSM, medical imaging

| Addressable Market | $9.2bn | $9.4bn | $1.0bn | $30.5bn | $1.4bn | $10bn | $1bn |
| Outsourcing Penetration | 33% | 45% | 40% | 35% | 100% | 50% | 50% |
| CRO Market | $3.0bn | $4.2bn | $0.4bn | $10.7bn | $1.4bn | $5bn | $0.5bn |

About $5 billion annually for clinical pharmacology studies and PK assay support

Source: Madison Williams and Company; Equity Research; Pharmaceutical Services (August 17, 2011)
#3 Know What Customers Care About Most

## Challenges for Asian CTCs
- Distance from global pharma R&D headquarters
- Ethnic differences in drug metabolism or drug response
- Overcoming quality perceptions
- Regulatory timelines in some countries

## Opportunities for Asian CTCs
- Access to patients
- Strong medical and scientific expertise
- Electronic data systems
- Large future markets for new drugs
- Growing domestic drug discovery industry
Managing a clinic and laboratory is a high fixed cost business. *What can we control?*

- **Size of Clinic**
  - US: large clinics (100-300 beds) are most efficient
  - Europe: smaller clinics (70-120 beds) are effective
  - Asia: ?

- **Staffing Flexibility**
  - US: can use variable-hour employment contracts
  - Europe: employment laws more restrictive
  - Asia: ?

- **Computerized Recruiting Tools**
  - Computerized participant/patient databases essential today for assessing feasibility and quickly reaching potential participants using social media, email, call centers
  - Patients? Privacy issues in some countries
  - Asia: most hospitals have fully computerized and searchable patient records
Build Efficiency into Clinical Operations to Control Cost and Improve Timeliness

What can we control (continued)?

- **Automated Data Capture**
  - Electronic capture of routine clinic data (sample collection times, vital signs, results from clinical safety labs) speeds process and reduces human errors compared to paper systems.
  - Integrating study management characteristics into system also effective
    - e.g. system that relates conduct of activities to training records
  - Use of electronic laboratory notebooks improves productivity in the GLP-regulated bioanalytical laboratory.
    - e.g. Celerion’s use of eLab Notebook increased bench time for chemists from 55% to 85% because of reduced time to maintain GLP compliance with records

- **Deployment of Innovative Equipment and Systems**
  - Costly new equipment or systems need to have at least a 5-10 years lifespan of full utility – also need trained staff to operate and maintain
  - Huge potential if properly thought through and deployed
    - e.g. Celerion’s highly automated high definition Holter ECG analysis system took 2 years to develop but can cut cost of TQT studies in half.
#5 Create a Strategic Approach to Growth

- Celerion’s business is “applied translational medicine” – demonstrating whether or not nonclinical evidence of drug effect actually translates to human participants and patients.

- Identify key factors for being successful in applying translational medicine to various areas of medical research.

- Create a scorecard to determine where there are strengths and where further investment is needed.
### Example: Inflammatory Respiratory Diseases

<table>
<thead>
<tr>
<th>Success Factor</th>
<th>Capabilities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Expertise</td>
<td>Collaboration between Celerion Belfast Clinic and Professor Stuart Elborn, Queen’s University – a global expert in inflammatory respiratory disease – UK Center of Excellence for Respiratory Research</td>
</tr>
<tr>
<td>Experience</td>
<td>Celerion physicians and staff have several years experience with respiratory studies</td>
</tr>
<tr>
<td>Facilities and Equipment</td>
<td>Confined clinic with specialized equipment (bronchoscopy, PFTs, body plethysmography)</td>
</tr>
<tr>
<td>Access to Patients</td>
<td>Asthma, COPD, cystic fibrosis, pulmonary infections</td>
</tr>
<tr>
<td>Access to Biomarkers</td>
<td>Assays for inflammatory markers in blood, sputum and bronchoalveolar lavage – GLP validated and qualified experimental</td>
</tr>
</tbody>
</table>

Celerion is well positioned to support early clinical research and translational medicine studies for products treating inflammatory respiratory diseases
# Example: Metabolic Syndrome (Diabetes and Obesity)

<table>
<thead>
<tr>
<th>Success Factor</th>
<th>Capabilities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Expertise</td>
<td>No diabetic expert on staff. Celerion recruited a leading researcher to head up Translational Medicine in Metabolic Disease</td>
</tr>
<tr>
<td>Experience</td>
<td>Celerion has successfully performed studies at Celerion clinics in diabetic and obese participants</td>
</tr>
<tr>
<td>Facilities and Equipment</td>
<td>Confined clinic. No glucose or insulin clamping capabilities. Celerion adding clamping capabilities in 2014</td>
</tr>
<tr>
<td>Access to Patients</td>
<td>Celerion has successfully recruited mild type 2 diabetics and obese patients to studies in the last 3 years. Larger database needed to support demand.</td>
</tr>
<tr>
<td>Access to Biomarkers</td>
<td>Celerion has a validated (GLP, CLIA) collection of diabetes biomarker assays</td>
</tr>
</tbody>
</table>

Scorecard provides a focus for investment to achieve success
### Example: Oncology

<table>
<thead>
<tr>
<th>Success Factor</th>
<th>Capabilities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Expertise</td>
<td>PK/PD modeling experts. No oncologist on staff. Oncology many diseases requiring different experts. Work with academic sites and oncology focused CROs</td>
</tr>
<tr>
<td>Experience</td>
<td>Performed two multi-site studies in blood cancers. Not a focus for Celerion in past or present</td>
</tr>
<tr>
<td>Facilities and Equipment</td>
<td>Celerion’s hospital unit could accommodate. Celerion provide study ops support to academic units</td>
</tr>
<tr>
<td>Access to Patients</td>
<td>No access through Celerion recruitment. Must work with oncology focused AROs and CROs</td>
</tr>
<tr>
<td>Access to Biomarkers</td>
<td>Can support PK, clinical markers of safety and Immunogenicity assays. No genomics or flow cytometry capabilities in Celerion laboratories. Would require close collaboration with genomic AROs.</td>
</tr>
</tbody>
</table>

Scorecard indicates that considerable investment would be needed – possible solutions in Asia and Central/Eastern Europe.
Applying These Learnings to an Asian ARO/CTC

1. Know your strengths
   - *Expertise? Technology? Study types?*

2. Know the marketplace and how it is changing.
   - *Access to patients.*

3. Know what the customer cares about most.

4. Constantly be building efficiencies that reduce cost and shorten timelines.
   - *Right size. Leverage efficiencies (e.g. electronic). Partner with other sites?*

5. Create a strategic approach to growth.
   - *Vision. Tools (scorecards) that direct future investment.*
Rapid growth in number of Phase II/III clinical studies

More future involvement in early clinical pharmacology research

Many governments want better access to new medicines

Government support for developing clinical study centers

High percentage of patients get care at large medical centers

Good access to patients for clinical studies

Well trained medical staff

Strong interest in medical research

Emerging domestic drug development industry

Growing demand for early clinical research in originating country

Strength in electronic tools industry

Future global leaders in electronic data capture and management
Daedanhi Kamsahamnida