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Applied Translational Medicine

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

More than 750 beds globally

Phoenix, AZ
300 beds

Belfast, Northern Ireland
UK
78 beds

Bryan Health, Lincoln, NE
24 In-hospital beds

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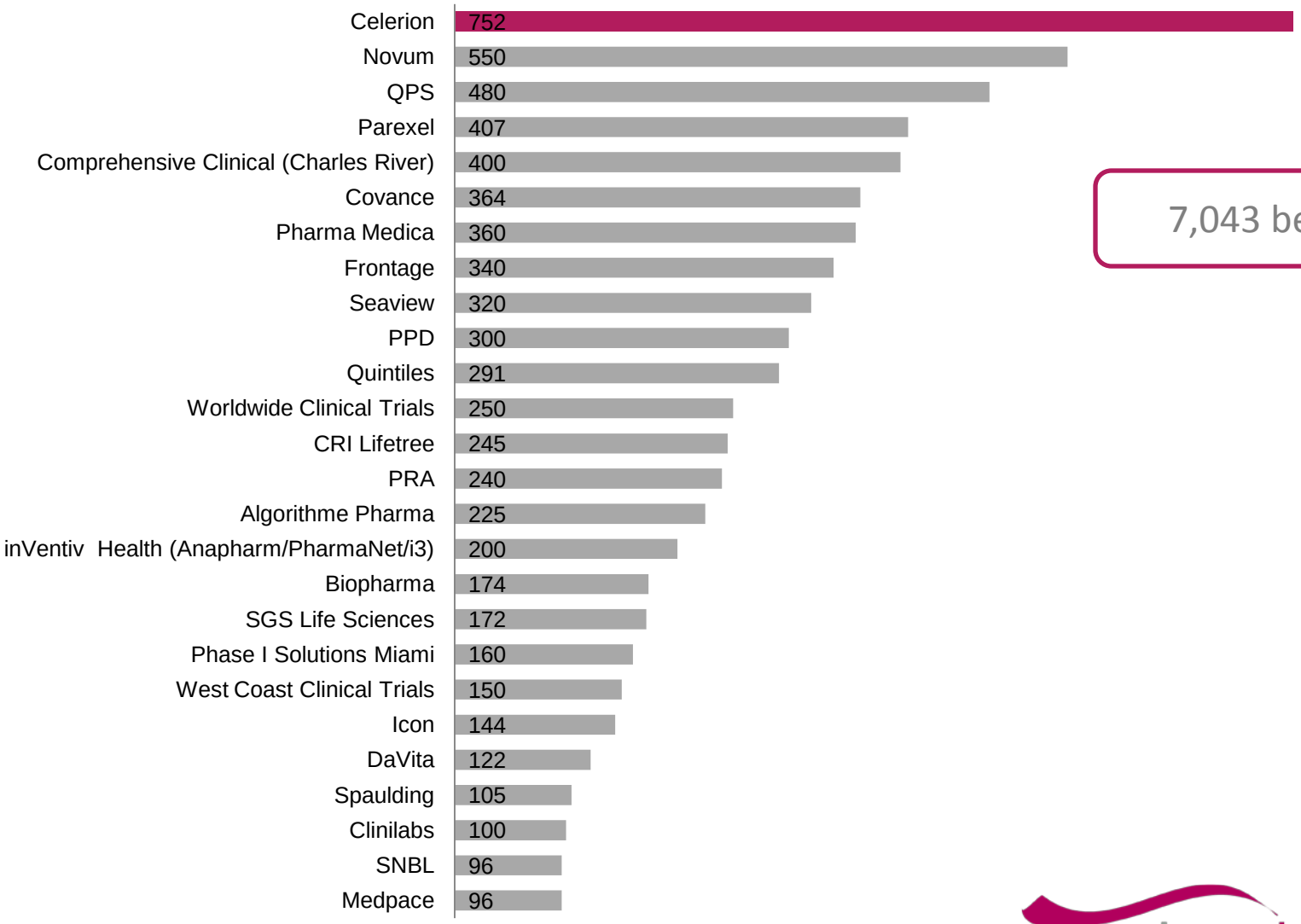
Top CROs (by Phase I Bed Capacity)



7,043 beds

Note: Data as of May 2013

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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

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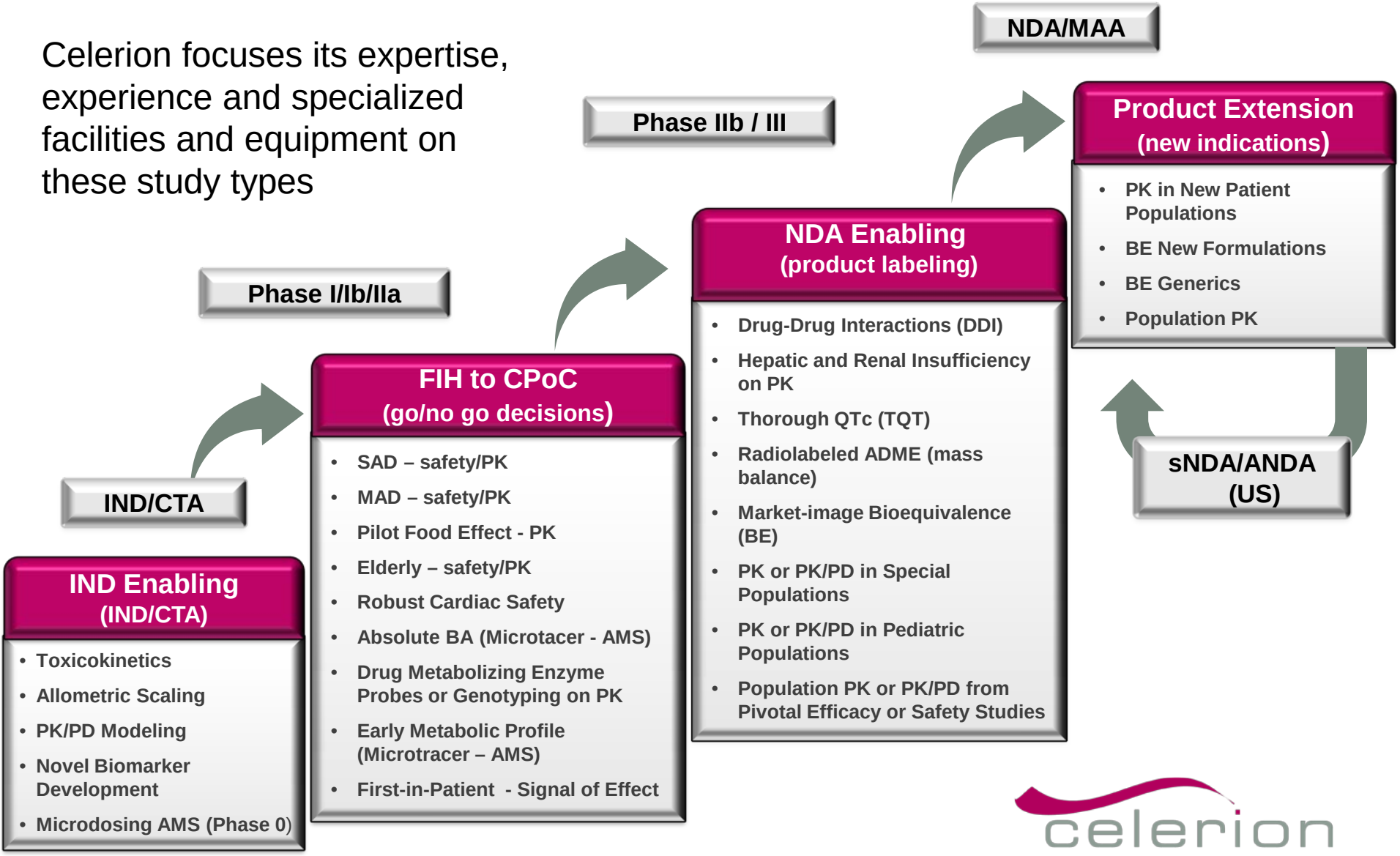
#1 Know Your Strengths

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



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

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#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

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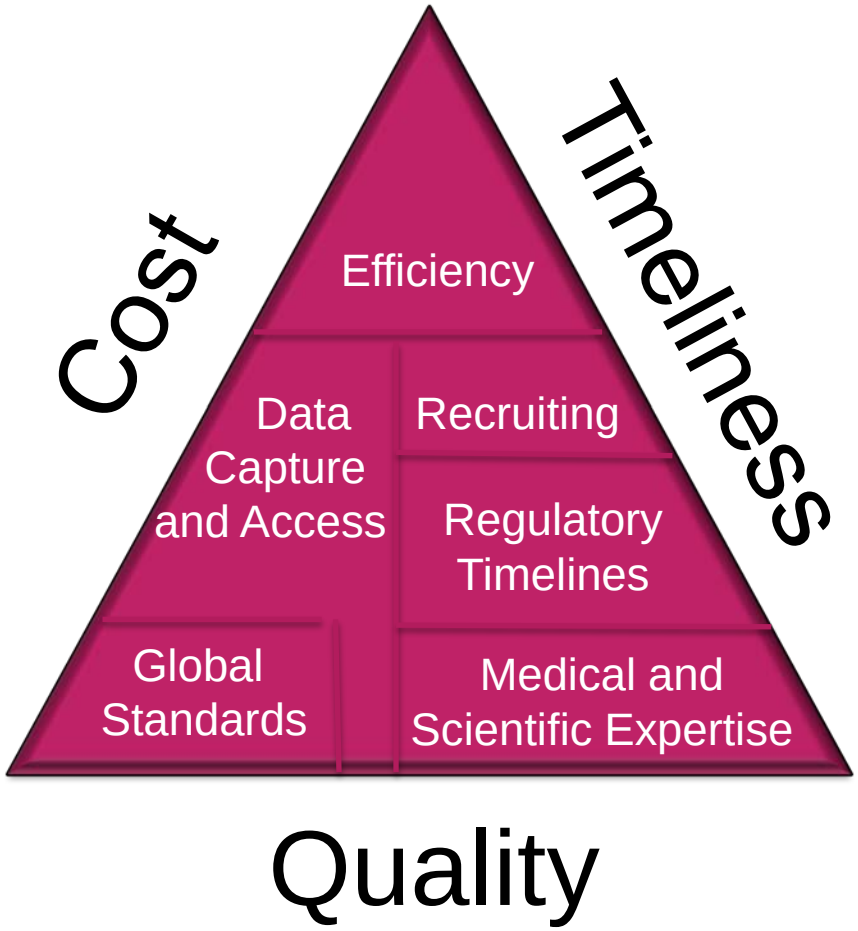
	Delivery & Preclinical	Phase I-IIa Early Clinical	Bio-analytical	Phase IIb-IV Global Clinical	Central Labs	Other	eClinical
	Early Stage testing: •Properties & effects (non-tox) •Harmful or fatal effects in animals (tox)	Determine impact of compound on human subjects (healthy or specific condition)	Analyzing 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 fro 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

#4 Build Efficiency into Clinical Operations to Control Cost and Improve Timeliness

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.
    - US – 21 CFR Part 11 compliance usually required.
  - 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.

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Example: Inflammatory Respiratory Diseases

Success Factor	Capabilities	
Expertise	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	✔
Experience	Celerion physicians and staff have several years experience with respiratory studies	✔
Facilities and Equipment	Confined clinic with specialized equipment (bronchoscopy, PFTs, body plethysmography)	✔
Access to Patients	Asthma, COPD, cystic fibrosis, pulmonary infections	✔
Access to Biomarkers	Assays for inflammatory markers in blood, sputum and broncheoalveolar lavage – GLP validated and qualified experimental	✔

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)

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

Scorecard provides a focus for investment to achieve success

Example: Oncology

Success Factor	Capabilities	
Expertise	PK/PD modeling experts. No oncologist on staff. Oncology many diseases requiring different experts. Work with academic sites and oncology focused CROs	
Experience	Performed two multi-site studies in blood cancers. Not a focus for Celerion in past or present	✔
Facilities and Equipment	Celerion's hospital unit could accommodate. Celerion provide study ops support to academic units	
Access to Patients	No access through Celerion recruitment Must work with oncology focused AROs and CROs	
Access to Biomarkers	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.	✔

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.
   - *Cost. Timeliness. Quality.*
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.*

Perspectives on Clinical Pharmacology in Asia

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