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Applied Translational Medicine

Celerion's Symposia Series: Bridging the Gap from Phase I to Proof-of-Concept

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Applied Translational Medicine

Access to Patients Earlier in Clinical Development: Think Global

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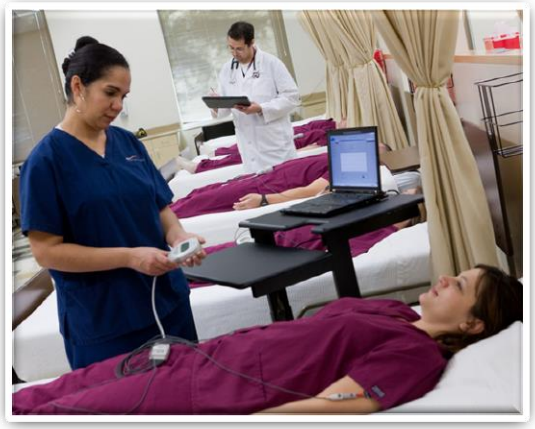
Questions

- Why the push for studying patients earlier in clinical development?
- What are some challenges and strategies for engaging patients in early studies?
- How can we leverage global differences in healthcare practices to enable more efficient and effective early clinical development programs?
- How does Celerion manage early patient studies differently than conventional approaches that don't meet the time and cost demands of today for early clinical research?

Health Participants: Is Their Role Changing?

- HPs still provide the most resilient human population if adverse events occur
  - TeGenero (2006). Starting dose: 1/500 NOAEL, 4/6 multi-organ failure in healthy male participants. What if they were patients?
- HPs allow us to proceed with clinical development with incremental increases in clinical risk
- HPs may be more ethical FIH approach than patients for drug development that traditionally has gone straight to patients (e.g. oncology)
- HPs are only way to isolate drug effects on each other from disease complications (e.g. Drug-Drug Interaction studies)



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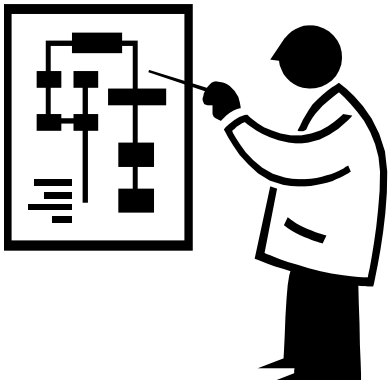
What Can we Learn from Patients?

- Is the safety profile different in patients?
  - Consider the indication
  - Comorbidities?
  - Preclinical signals for concern?
- Is drug distribution or exposure potentially different in patients?
  - Drug metabolized or excreted by liver?
  - Drug eliminated by kidney?
- Can we get a signal (hint) of efficacy?

What is a Signal or Hint of Efficacy?



- Will knowing this impact a go-no go decision?
  - Almost always tied to further funding
- What endpoints will be used?
  - Sensitivity and variability of assessment
- Will the early clinical research study be powered statistically to see a difference or will data trends be sufficient to support the go-no go decision?
- Are biomarkers available?
  - Signal of target engagement
  - Signal to verify mechanism
  - Signal of drug effect

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Applied Translational Medicine

- **Applied Translational Medicine** is the science of confirming whether the properties of new drugs suggested by non-clinical testing are important when the drug is given to humans.
- By “applying” such “translation” of non-clinical tests to carefully designed and conducted clinical studies, Celerion helps drug developers answer key questions related to efficacy, patient safety and drug-drug interactions.
- These studies are particularly important in managing investment risk early in clinical drug development.

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Early Signals of Clinical Safety and Efficacy are the Key to Applied Translational Medicine

To get an early sense that a drug is working in humans as it was designed, you need:

Patients

- Small number
- Stable disease
- Minimal confounding treatments
- Appropriately motivated

Investigators / Clinical Trial Units

- Small number of sites
- Scientifically / medically robust
- Controlled study setting
- Follow global GCP standards
- Ethical

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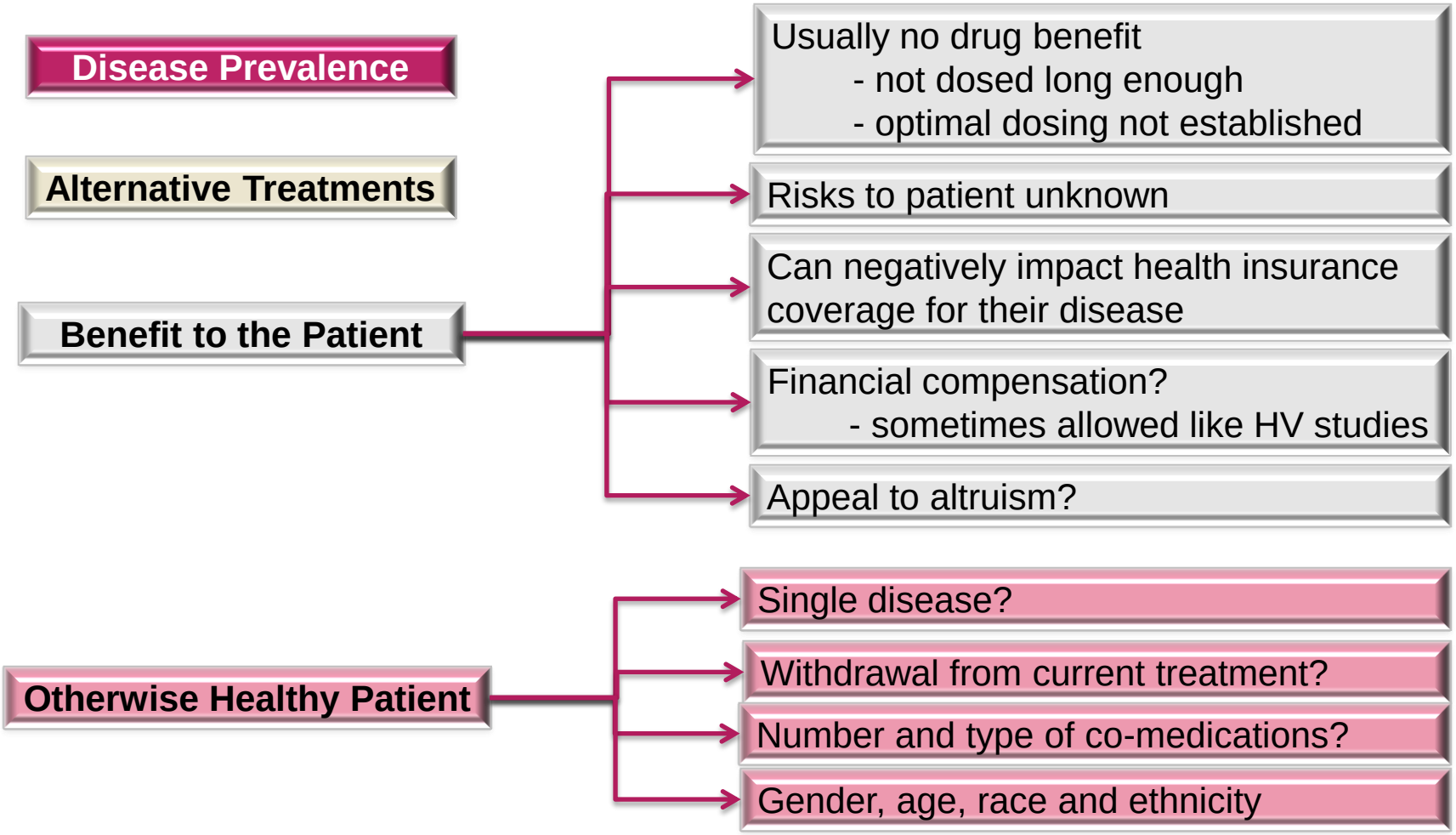
The Challenge of Recruiting Patients to Early Clinical Studies



What's Changing at Clinical Pharmacology Units?

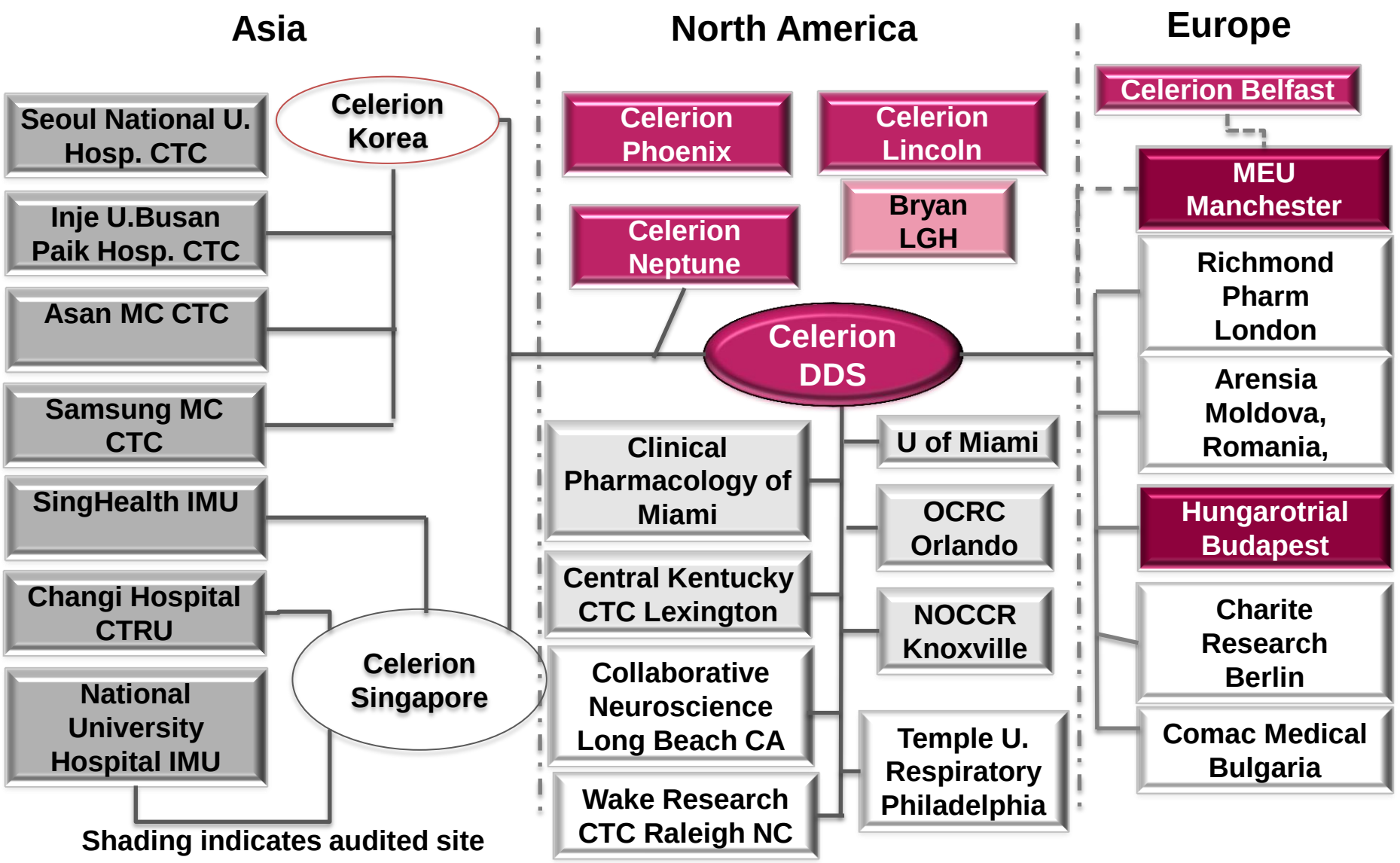
- R&D cost cutting forcing closure of in-house clinical pharmacology units at major pharma companies
- Private clinical pharmacology clinics or hybrid academic-CRO clinical pharmacology units becoming experts in innovation around robust execution
  - Hiring ex-pharma expertise
  - Building platforms for innovative technologies that provide better data, faster
  - Expertise evolves from broad experience to many situations (pay for "minds" as well as "hands")
- Global digital communications
  - Expectation of real time data sharing and rapid digital analysis
  - Deploying smart devices in study recruiting, data capture and oversight

The Need for Global Clinical Pharmacology Unit Networks

- Most patient needs in early clinical research cannot be met by a single center
- Need to evolve similar partnering and alliance models among groups of clinical pharmacology units
  - Share patient recruiting, costs and revenues
  - Work to same quality standards (undergo common systems QA audits)
  - Valued professional relationship among PIs and/or centers
  - Coordinated through a group (CRO) which can also bring in other study services that the sponsor would need (protocol preparation, bioanalysis, PK, DM and stats, CSR preparation)

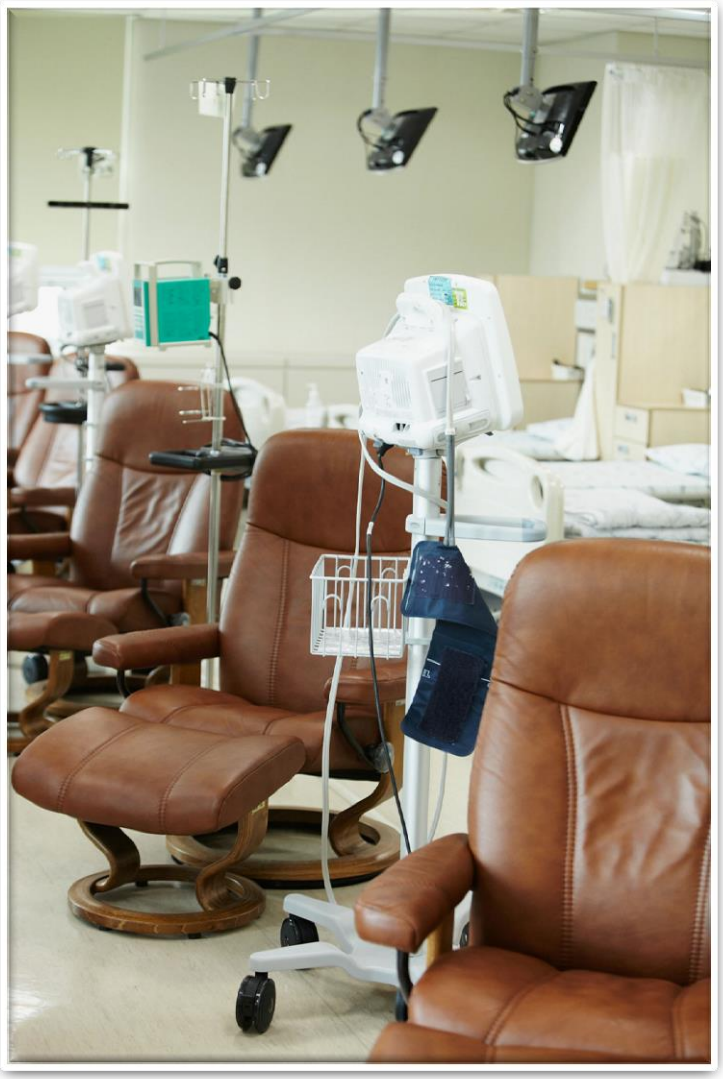
In Feb 2014 Celerion Established Official Presence in Asia

Celerion's global clinical site network Feb 2014



Celerion's Global Network

SNUH Clinical Trial Center



What patient populations can Celerion access today in US, Europe and Asia?

Patient Population	Internal	External Collaborations
Diabetes and Obesity	Celerion Phoenix	Augment expertise in glucose clamping and other techniques available at Celerion
Cardiovascular (hypertension, hypercholesterolemia, hyperlipdemia, thrombosis)		Taking patients off existing medications can limit recruitment Good access in CEE and Korea
Respiratory and Inflammatory (asthma, COPD, cystic fibrosis, RA, OA)	Celerion Belfast, Neptune	C-TRIC (N. Ireland) – patients for Belfast MEU – Manchester Temple U – Philadelphia JSMC – Rutgers – patients for Neptune
Renal Insufficiency	Celerion Neptune	Strong network in US plus Neptune Expert sites in CEE and experience in Korea
Hepatic Insufficiency		Strong network in US Expert sites in CEE and access to HBV/HCV patients in Korea
Rheumatoid Diseases (RA, SLE)	Celerion Belfast	Strong networks in Korea and in Europe
CNS /Neurology (Alzheimer's, schizophrenia, anxiety, depression, pain, Parkinson's, convulsion)		Collaborative Neuroscience Network, CRI Lifetree in US Good access in CEE and Korea
Oncology (blood, breast, colon, prostate, lung, pancreatic, ovarian, skin)		Good access to patients in CEE Excellent research clinics with large patient access in Korea Major academic cancer centers dominate NA - pricey
Infectious Disease (HIV, HCV, HSV, influenza, bacterial)		HCV – OCRC, EE, Korean sites (Asian phenotypes), HIV EE Influenza/bacterial: access in CEE and Korea

Five Key Elements of Clinical Success in Applying Translational Medicine

- **Expertise:** Scientific and medical staff with the portfolio of skills to design, conduct and interpret complex clinical studies
- **Experience:** Leveraging knowledge gained from conducting early clinical pharmacology studies with high density sampling
- **Facilities and Equipment:** Modern confinement clinics and laboratories equipped with innovative technologies to meet the varying and evolving demands of early clinical research
- **Access to Patients:** Recruiting the right participant or patient to meet the needs of specific study designs in a timely and ethical way.
- **Access to Biomarkers:** Leveraging capabilities resident within the participating clinics or laboratories or with qualified vendor labs to create the appropriate palate of tests to ascertain the drug's effect in humans

Questions?