Questions

- How are early phase studies evolving and 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 networks to enable more efficient and effective early clinical development programs?
Emerging Paradigm

Traditional Paradigm: Phased Approach

- Pre-Clinical
- Phase I
- Phase II
- Phase IIb
- Phase III

Test each scarce molecule thoroughly

Emerging Paradigm: POC / Confirmation Approach

- Learn
- Decide
- Confirm

Abundance of molecules from discovery

Pre-Clinical

Proof of Concept

Confirmation

↔ Translational Medicine ↔

What’s Driving Evolution of New Paradigm?

Clinical Proof-of-Concept is where a new drug acquires real value

- Increase in novel new drugs from discovery research
- More difficult disease states to study and treat
- Greater regulatory expectations on clinical trials
- Need for more informed decisions at clinical Proof-of-Concept
- Increased cost of clinical research
- Regulatory acceptance of adaptive-like study designs
- Expanding universe of new technology applications

Innovation
Key Aspect of Emerging Paradigm

For an early sense that a drug is working in humans as it was designed, you need access to:

**Patients**
- Relatively small number
- Stable disease
- Minimal confounding treatments
- Appropriately motivated

**Investigators / Clinical Trial Centers**
- Relatively small number of sites
- Scientifically / medically robust
- Controlled study setting
- Follow global GCP standards
- Ethical conduct
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The Challenge of Recruiting Patients to Early Clinical Studies

- **Disease Prevalence**
  - Usually no drug benefit
    - Not dosed long enough
    - Optimal dosing not established

- **Alternative Treatments**
  - Risks to patient unknown
  - Can negatively impact health insurance coverage for their disease
  - Financial compensation
    - Sometimes allowed like HV studies
  - Appeal to altruism

- **Benefit to the Patient**
  - Single disease
  - Withdrawal from current treatment
  - Number and type of co-medications
  - Gender, age, race and ethnicity

- **Otherwise Healthy Patient**
The Challenge of Recruiting Sites

- Resources
  - Dedicated for research
  - Performance standards for clinical studies
- Compounding Pharmacy
  - Sterile
  - Solid dosage forms
  - Suspensions
  - Solutions
- Complex sample processing/handling capabilities
- Deep operational expertise
  - Method development
  - Special capabilities (e.g. CSF sampling, glucose clamping, evoked potential testing)
Resources Dedicated to Research
Questions

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Global Clinical Pharmacology Unit Networks

- Most patient needs in early clinical research cannot be met by a single center
- Increasing the number of sites has its own challenges
- Need to evolve similar partnering and alliance models among groups of clinical pharmacology units
  - Work to same quality standards (undergo common systems QA audits)
  - Coordinated through a group which also brings in other study services as protocol preparation, bioanalysis, PK, DM and stats, CSR preparation
**Examples of networks and therapeutic clusters**

<table>
<thead>
<tr>
<th><strong>Patient Population</strong></th>
<th><strong>Internal</strong></th>
<th><strong>External Network</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory and Inflammatory (asthma, COPD, cystic fibrosis)</td>
<td>Belfast</td>
<td>Strong network in UK and Germany (therapeutic cluster)</td>
</tr>
<tr>
<td>Ophthalmology</td>
<td>Belfast</td>
<td>Strong network in UK and Germany (therapeutic cluster)</td>
</tr>
<tr>
<td>Cardiovascular (hypertension, hypercholesterolemia, hyperlipidemia, thrombosis)</td>
<td>Belfast</td>
<td>Strong networks in Europe and Korea (therapeutic cluster)</td>
</tr>
</tbody>
</table>
| Oncology (blood, breast, colon, prostate, lung, pancreatic, ovarian, skin) | Strong networks in Korea (therapeutic cluster)  
Good access in Europe  
Major academic cancer centers dominate NA |
| Renal or Hepatic Insufficiency | Strong network in US and Europe |
| Rheumatoid Diseases (RA, OA, SLE) | Belfast | Strong networks in Korea and in Europe (therapeutic cluster) |
| CNS /Neurology (Alzheimer’s, schizophrenia, anxiety, depression, pain, Parkinson’s, convulsion) | Collaborative neuroscience network in US  
Good access in Europe and Korea |
| Infectious Disease (HIV, HCV, HSV, influenza, bacterial) | HCV – Europe and Korean sites (Asian phenotypes), Influenza/bacterial: access in Europe and Korea |
Celerion Locations

- Lincoln, NE
- Montreal, QC
- Philadelphia, PA
- Belfast
- Zurich
- Seoul
- Singapore
Summary: Factors for Consideration

- Select right region(s)
  - Regulatory environment
  - Healthcare and socioeconomic status
  - Political stability

- Select right site
  - Experience and motivation of PI and study staff
  - Access to innovative technologies and biomarkers
  - Global acceptance of data

- Select right patient
  - Conmeds and concomitant diseases
  - Benefit to patient