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Applied Translational Medicine

Early Patient Studies in Evolution

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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?

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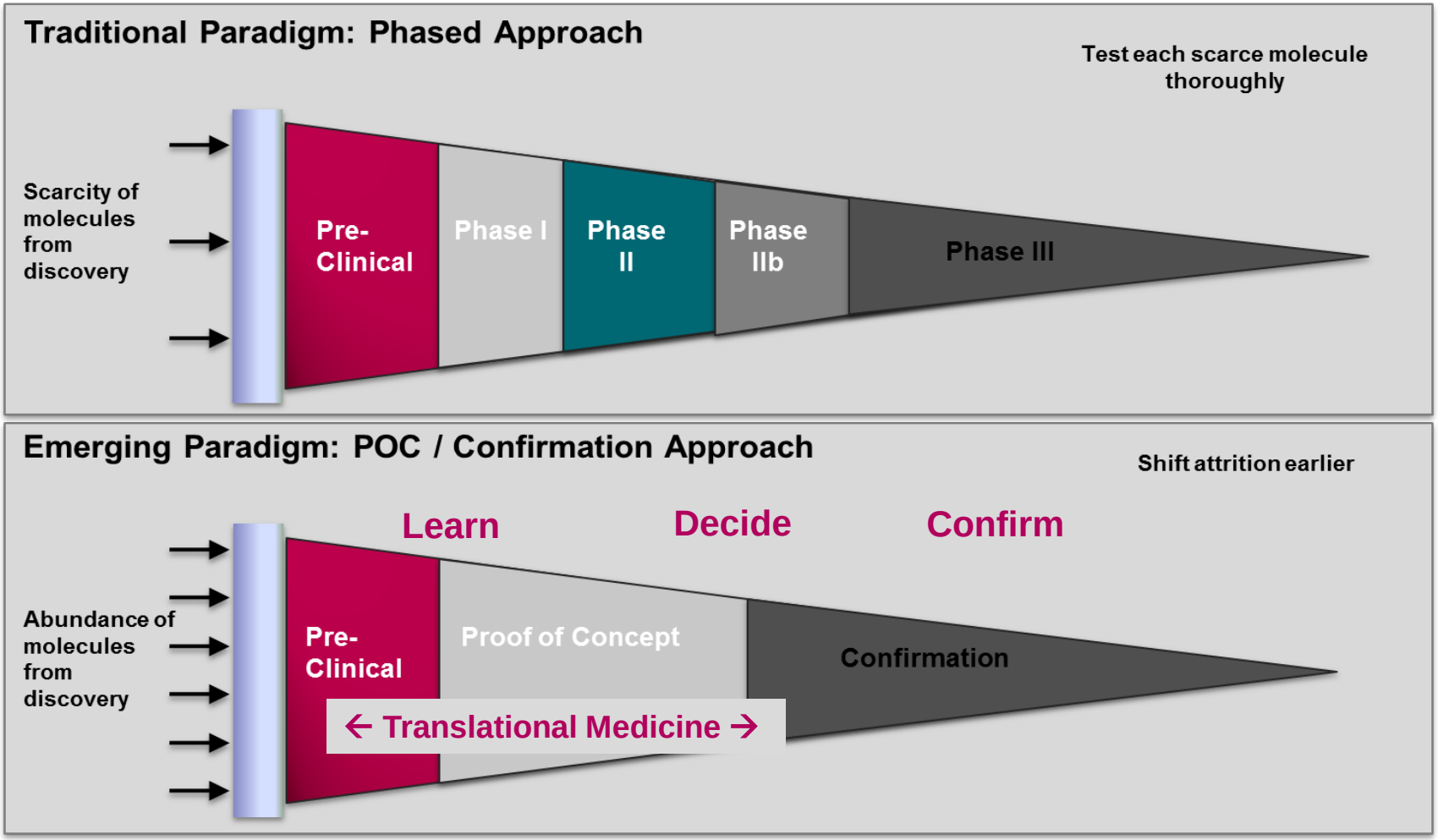
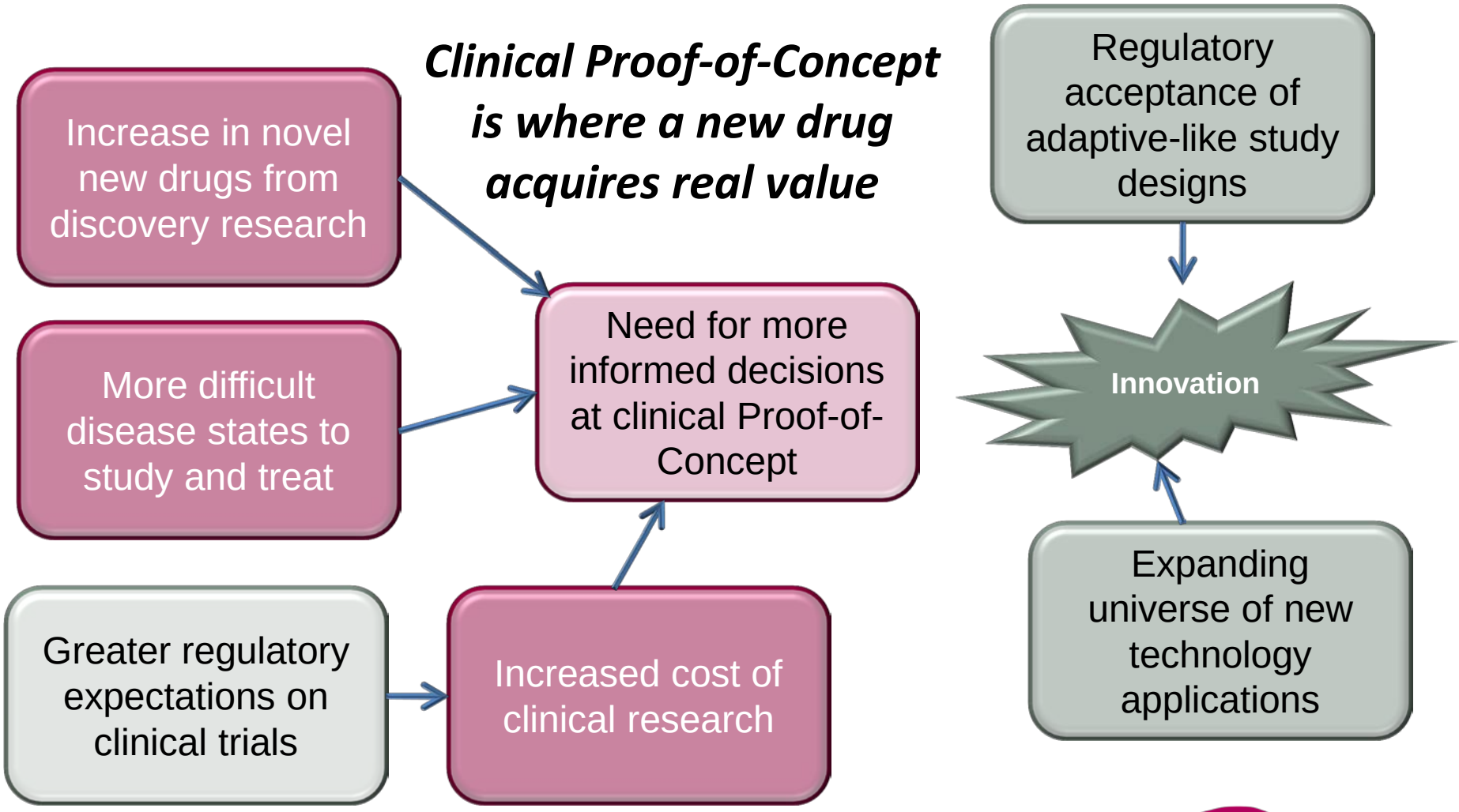
Emerging Paradigm



Source: William Blair & Company, (Bain and Company) Covance Investors Overview June 16, 2010

What's Driving Evolution of New Paradigm?



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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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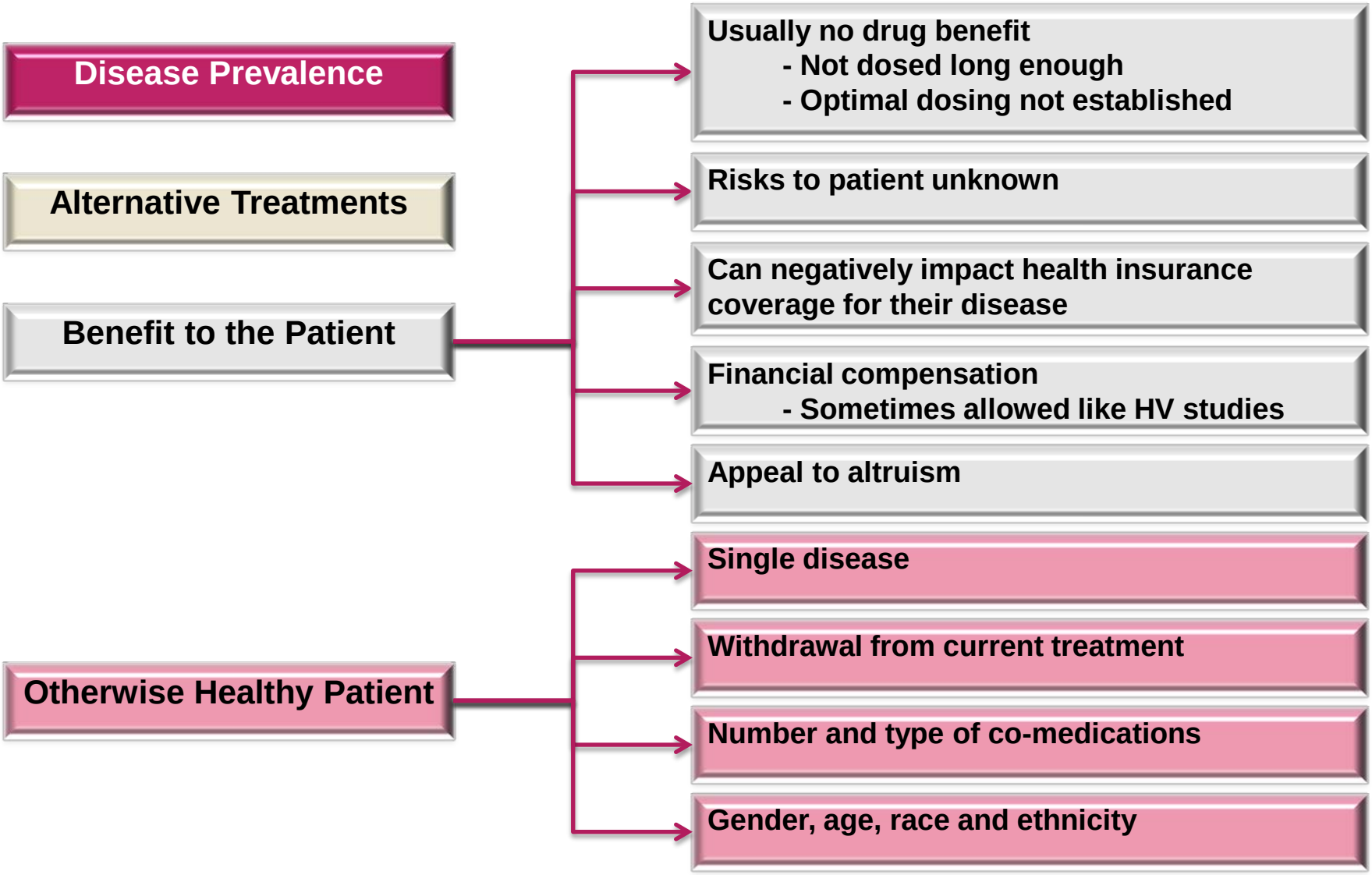
The Challenge of Recruiting Patients to Early Clinical Studies



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)

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Resources Dedicated to Research

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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

Patient Population	Internal	External Network
Respiratory and Inflammatory (asthma, COPD, cystic fibrosis)	Belfast	Strong network in UK and Germany (therapeutic cluster)
Ophthalmology	Belfast	Strong network in UK and Germany (therapeutic cluster)
Cardiovascular (hypertension, hypercholesterolemia, hyperlipidemia, thrombosis)	Belfast	Strong networks in Europe and Korea (therapeutic cluster)
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

Celerion Locations and Partner Sites

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