celerion

Applied Translational Medicine

Industry Academic Collaboration: A Key to Successful Involvement of Patients Early in Clinical Development

Aernout van Haarst PhD

Director, European Corporate Development

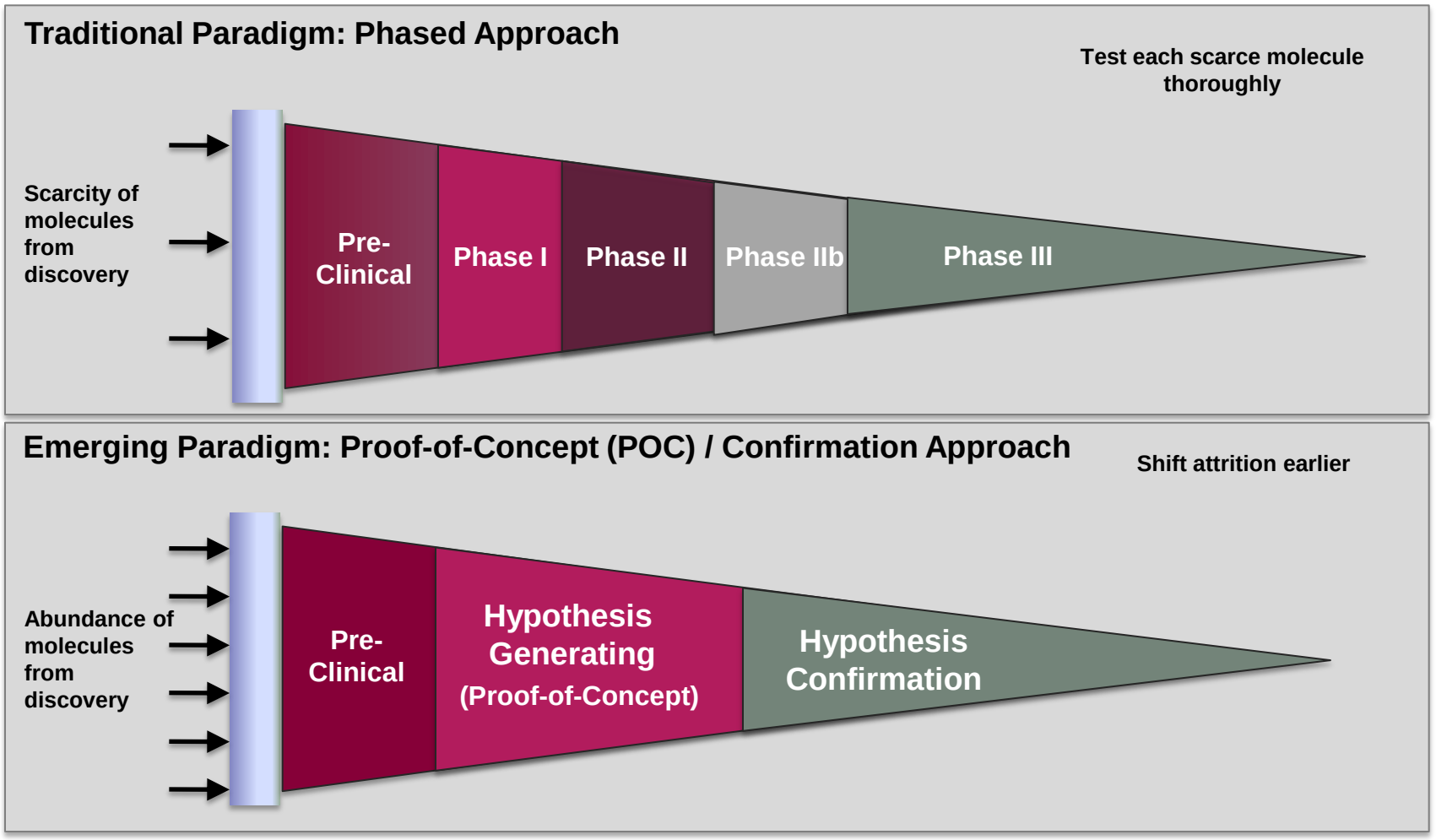
Feb 2016

Industry Academic Collaboration - Trends

- Pharma and academia: from separate worlds to team approach
  - Academia leveraging IP (“valorization”)
  - Knowledge exchange
  - Combined resources
- Expanding role for CROs in setup and conduct of studies
- Increased patient involvement in early stage

celerion

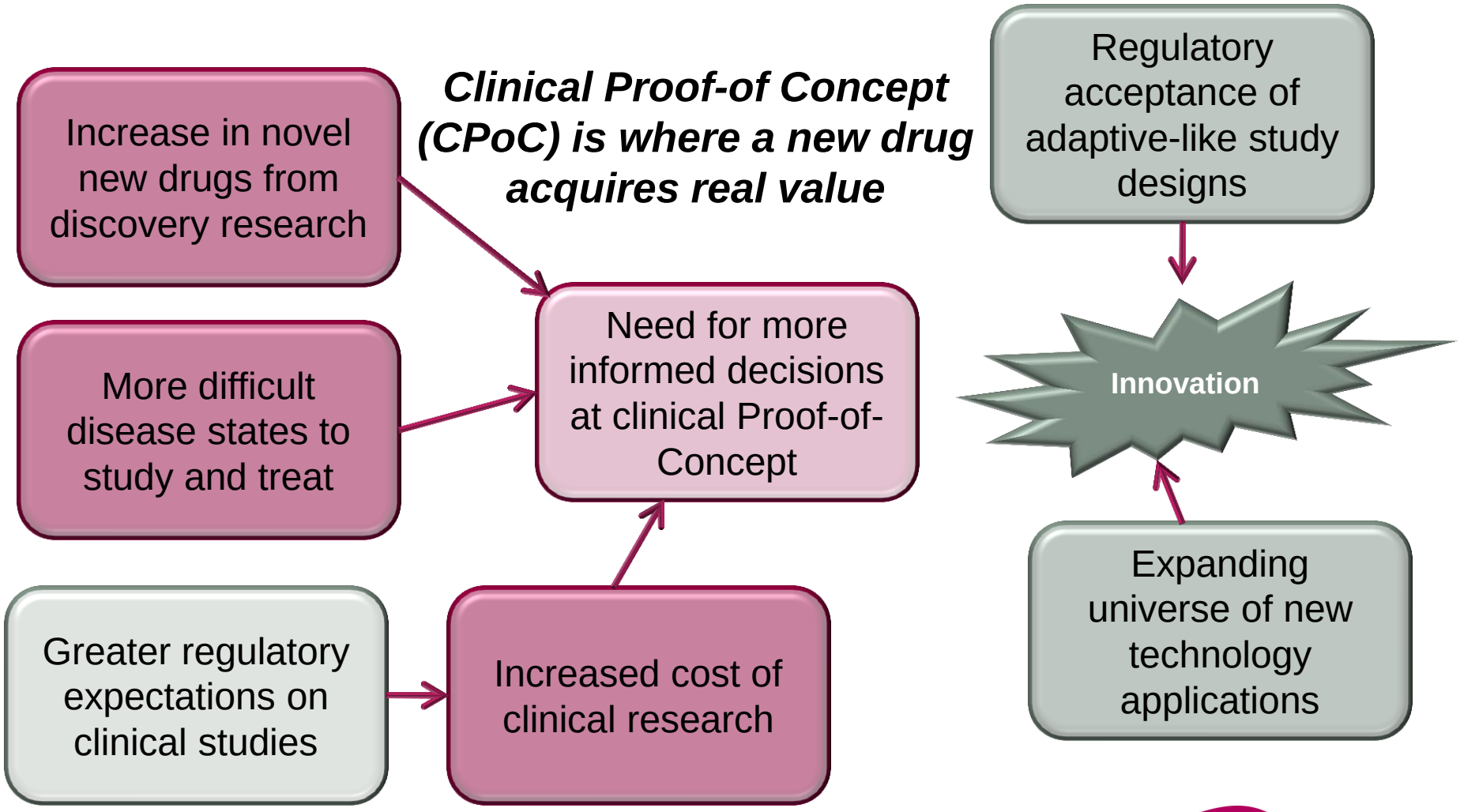
Clinical Development is Evolving



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

celerion

What's Driving Evolution of New Paradigm?



celerion

Does the Drug Work in Humans?

- **Proof-of-Presence**
  - Does the drug get to its site of action?
  - Value Add: $

- Pharmacokinetics
- Tissue concentrations
- Healthy subjects (HS) or patients

- **Proof-of-Mechanism**
  - Does the drug affect the biological target as it was designed?
  - Value Add: $$$

- Biomarkers reflecting target engagement
- Biomarkers of toxicity (liver, kidney effects)
- Healthy subjects or patients

- **Proof-of-Concept**
  - Is there a sufficient signal that the drug favorably impacts the disease with an acceptable risk of toxicity that would stimulate further investment in the drug?
  - Value Add: $$$$$

- Biomarkers reflecting impact on disease
- Biomarkers of toxicity (liver, kidney effects)
- Patients

celerion

Bridging Strategy to CPoC

- **Start design of CPoC study first**
  - What is “Proof”? Endpoints?
  - What patients? How many?
- **How to get to CPoC?**
  - What can I do in healthy subjects?
  - Are biomarkers available?
  - Develop novel biomarkers?
    - Biochemical assays
    - Imaging and imaging agents
    - MicroRNA panels
  - Can PK/PD modeling be applied?
- **What preclinical work is needed to support the early clinical program?**

The Three Constraints

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

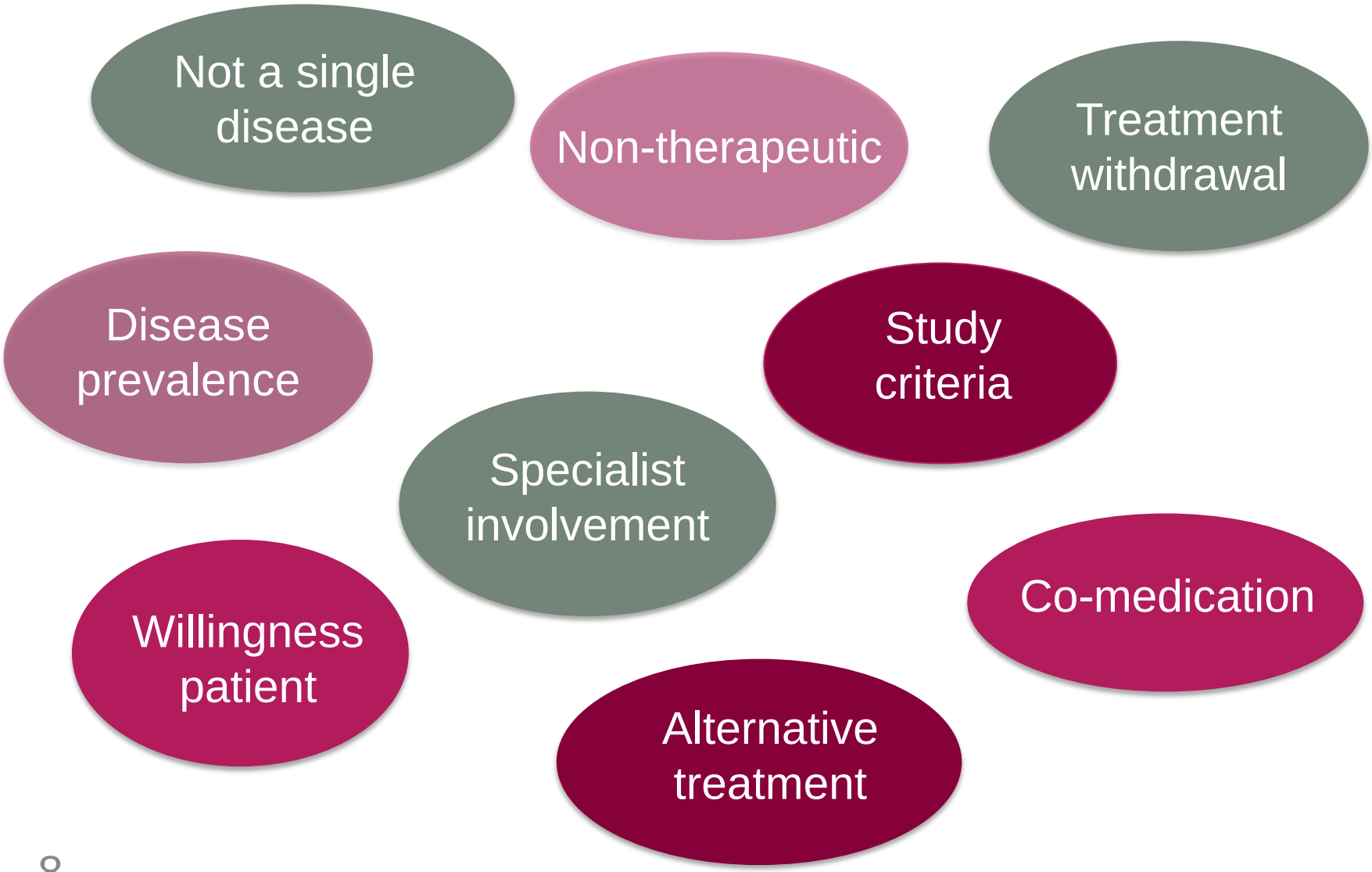
- Small number
- Stable disease
- Minimal confounding treatments
- Appropriately motivated

Investigators / Clinical Trial Units

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

celerion

The Challenge of Involving Patients in Early Clinical Studies



Collaboration with Queen's University, Belfast

- Partnership with Prof. Elborn at Queen's University Belfast (QUB)
  - Focused on Respiratory – asthmatics, COPD and Cystic Fibrosis
- Collaboration
  - Queens University provides scientific expertise, specialized procedures and access to patient populations
  - Celerion provides access to a high level of clinical recruitment, conduct and ability to analyze large amounts of data to high standards
- Expansion
  - Based on the success of respiratory, expanded to other areas, most recently Ophthalmology

celerion

Expertise and Skills In-house

Lung Clearance Index

Bronchoalveolar Lavage

Challenge Models

Fractional Exhaled Nitric Oxide Testing

Body Plethysmography

Spirometry

Partnering with Queen's University: A Case Study

- Background
  - Biotech company
  - First-in-Patient study in **cystic fibrosis** patients
  - Aim to assess safety and tolerability
  - Explore pharmacodynamics
- Study design
  - Multiple ascending dose
  - 15 day treatment
  - Parallel RCT (double-blind & placebo)

celerion

Case Study: Challenges

- Cystic Fibrosis (CF) patients are very difficult to recruit
  - Rare disease
  - Willingness
  - Eligibility criteria?
- End point selection may be cumbersome
  - Reliable outcomes?
  - Feasibility in CF patients?
- Complex methodologies
- Patient management
  - Infection risk
  - Variable health status

celerion

Case Study: Approach

- Leveraged Queen's University expertise throughout study design, recruitment, conduct and reporting
- Specialized methodologies transferred to Phase I setting
  - Lung function tests, LCI
  - Sputum collection
- Patients in a controlled research environment
  - Minimize risk of cross-infection
- Flexible schedule to accommodate variable health status

celerion

Case Study: Outcomes

- Inclusion of 17 Cystic Fibrosis patients
- Fast turn-around of results allowing rapid dose-escalation
- First Patient In – Last Patient Out: 14 months
- Drug in general well tolerated (adverse events mostly mild)
- Changes in biomarkers reflected drug's Mechanism-of-Action

celerion

Five Key Elements in Translational Medicine

- **Expertise:** Scientific and medical staff with study skills
- **Experience:** Operational know-how (e.g. high density sampling)
- **Facilities and Equipment:** Modern confinement clinics and labs equipped with innovative technologies
- **Access to Patients:** Effective subject recruitment
- **Access to Biomarkers:** Capabilities to ascertain drug effect in humans

1 + 1 = 3

celerion

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 Quality Assurance audits)
  - Coordinate through a group which also brings in other study services such as protocol preparation, bioanalysis, pharmacokinetics, data management and statistics, and clinical study report preparation

celerion

Celerion Locations and Partner Sites

A Global Network of Specialty Clinics and Labs

celerion

Celerion's Strategic Expansion of Patient Access by Leveraging Qualified Sites

- **Offices in South Korea and Singapore**
  - Modern clinical trial centers at major academic medical centers
    - Patient access in controlled clinical research settings
    - Supporting biomarker assays and imaging capabilities
  - Highly qualified investigators and well-trained, motivated staff
  - Superb access to patients
    - Various cancers, RA, infectious diseases, liver and brain disorders.
- **Acquisition of Assign Clinical Research, Vienna Austria**
  - Based throughout Europe (strong academic-CRO collaborations)
  - European and global Phase I-III studies
  - Strong expertise in multi-site patient studies
  - Key: new oncology treatments, immunology drugs and vaccines
  - Complements Celerion's early clinical research expertise in respiratory and metabolic diseases.

celerion

Conclusion

- Earlier engagement of patients in studies (PoC)
- Need to implement operational setting near clinician
- Multiple centers may be required in early clinical research
- Replication of “Belfast model” and alliance model of clinical pharmacology units preferred approach

celerion

Thank You!