Partnerships in Early-phase Biopharmaceutical Development:

Views from a specialist early phase clinical trial service provider

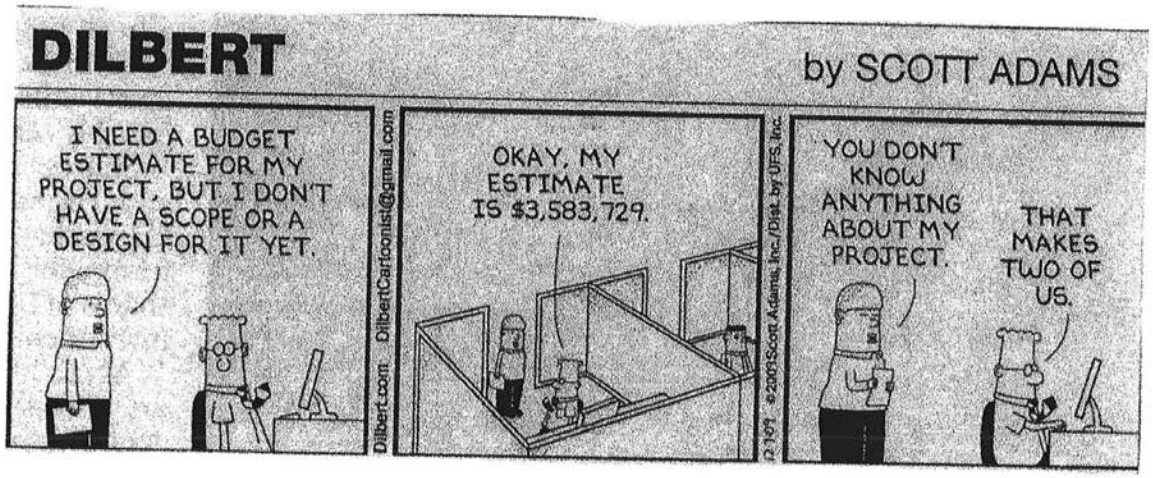
AusBiotech 2011 National Conference

Q-Pharm Pty Limited

What are the considerations for clinical research?

- Costs and timelines
- Regulatory requirements
- Outsourcing to the ‘experts’
- Nature of the product
- Participants
- Trial Design

Clinical trials: Costs and timelines



Regulatory considerations for clinical research

- Regulatory pressures are at an all time high
- Premium placed on effectiveness
  - Driven by Govt. needs to control health costs
- Trials are more stringent and need more data
- Demonstrate true improvement over existing treatments (both efficacy and cost)
- Increasing attention on safety concerns

To which Regulator will the data be submitted?

How to overcome economic and regulatory challenges in clinical research?

- Increasing economic and regulatory pressures

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- Increasing duration, size, complexity & cost of trials

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- Decreasing success of later stage clinical trials

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- Biotech needs to be smarter about early phase clinical development in order to succeed

OUTSOURCING is crucial to success

INNOVATION is critical to success

Clinical Trials: Outsourcing is the model

- Companies acutely aware that R&D beyond the proficiencies of any single company
  - Many Biotech's are 'virtual' entities
- Need for externalisation stronger than ever
  - opportunities to access new technologies and novel therapies
  - Big Pharma: 1/3 of compounds originate outside of the company – within years expected to reach 70% (past = 0) = Opportunity!
- However: sourcing funding is extremely difficult
  - Want R&D costs to be predictable – Impossible!?!?
  - Outsourcing at fixed cost: Australia for early phase clinical studies (experts), + Other countries for later phase (patient pool)

Clinical Trials: Outsourcing is the model

- Specialist Phase 1 units in Australia: Controlled conditions
- Location and Facilities
  - Access to emergency equipment and emergency services
  - Quality system (ICH-GCP compliance)
- Staffing
  - Expertise with early phase product development
  - Basic and Advanced Life Support
  - Training (Emergency, Product specific AE and treatment)
  - Level of staff – workflow and procedures
- Input into Clinical Trial Design
  - Protocol and ICF development
  - Risk assessment (staffing, product type, visit schedule etc.)
  - Dose escalation

Nature of the investigational product

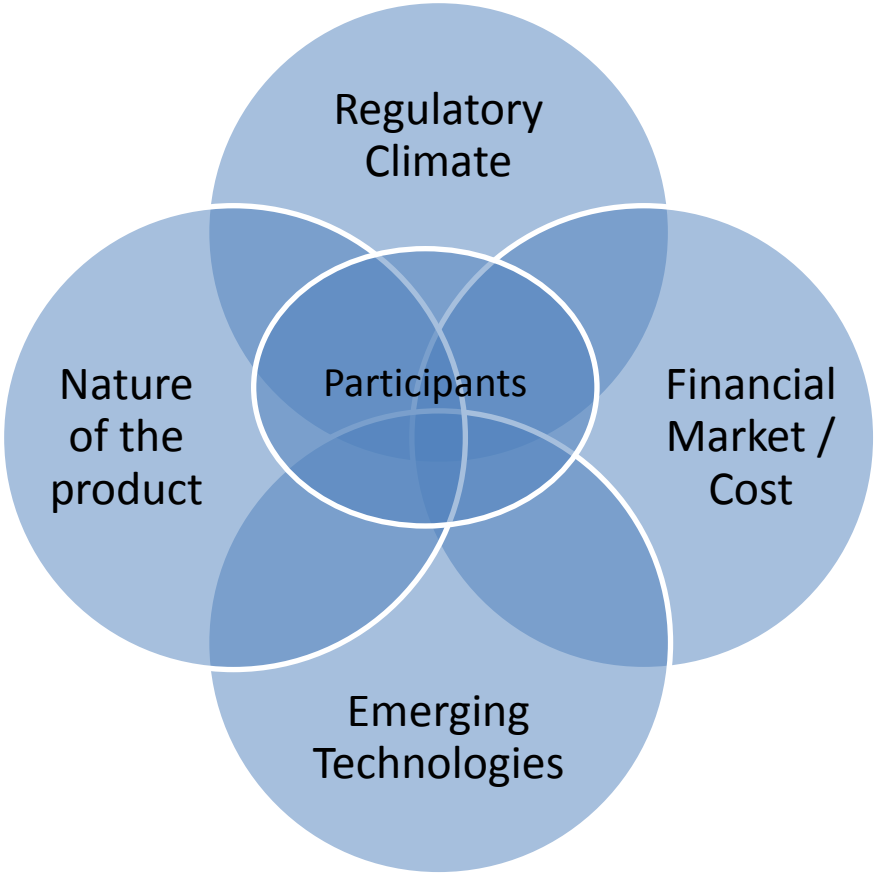
- Small molecule or Biological
- Manufacturing
- Choice of pre-clinical studies
- Dose Selection
- Assessment of Risk
  - Ethics
  - Trial design - sentinels
  - Dose escalation process

CONSULT THE APPROPRIATE EXPERTS

Study Participants: Healthy or Patient?

- What is the objective of the study?
- **IS THE CLINICAL TRIAL RECRUITABLE?**
- Most Phase 1 studies (safety) = healthy participants
- Phase 2 and beyond = patients
- Number of patients available and ability to 'cohort' – stage of disease = time and cost implications
- Females v Males
  - Toxicology, risk
  - Females: Post-menopausal (tested) or On two forms of contraception (documented)
  - Males: partner risk and requirements
- Eligibility – Strict criteria (waivers)? Restrictions (Diet, Meds, exercise)?

What does this all mean for Clinical Trial Design?



How to overcome these Challenges?

- Clinical Trial designs to **"Fail Early and Fail Cheap"**
- **Innovation** - New clinical trial designs
  - Adaptive design
    - SAD/MAD + Food Effect arms; Dose reformulations
    - Phase 1 in Healthy Volunteers and Patients (same protocol)
    - Provision for variation in dosing regimen
  - Microdosing (Phase 0)
    - Sub-therapeutic dosing (~ 100 times lower)
      - exploratory IND for subtherapeutic dosing with minimal animal safety testing OR
      - in Phase 1 using 14C exposures that are truly as low as reasonably achievable
      - Requires specialised equipment and extreme sensitivity
  - Targeted therapies
    - Biomarkers/molecular diagnostics to identify what treatment & who
- **Outsourcing** - Embracing Technological and Scientific Innovation