Outsourcing in Early Development – Keys to a Successful Partnership

Clinical Trial Oversight Summit - Barnett

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celerion
Applied Translational Medicine

MERCK
Be well

Overview

	Introduction - Fully Outsourced Studies in Early Development
	Approach and Alignment Between Merck and Celerion
	Innovations in the Partnership
	Challenges
	Key Elements to a Successful Partnership
	Questions and Discussion

Introduction - Fully Outsourced Studies in Early Development

Why Outsource – what are Goals?

- Flexible resourcing with reduced fixed in house resources
- Leverage expertise of CRO/Celerion –use their processes, systems, resources
- Ensure compliance, subject safety, and study/data integrity

What is a Fully Outsourced Study?

- Protocol Concept Form (PCF) - Merck
- CRO - authors protocol, holds database, monitors and conducts study, authors CSR, provides agreed upon data deliverables (with various touch points)

What Studies are Outsourced?

- Drug-Drug Interactions
- ADME - Absorption, distribution, metabolism, and elimination
- Bioequivalence, Bio comparison, Bioavailability
- Special population - hepatic and renal insufficiency
- Thorough QT study

Approach and Alignment Between Merck and Celerion

Learning to Speak the Same Language

- Examples – need to define terms like SAS datasets, Functional Areas, Statistical and PK analysis, First Patient In, Risk Based Monitoring, Soft Lock, Database lock, Note to File, Amendment

Executive Sponsor and CRO Alignment - cascaded throughout each functional area in both organizations (SME to SME)

Approach

- What is being outsourced and what is being provided by Sponsor
- Process – who is doing what and when
- What are deliverables and timelines

Alignment and Agreement – with simplicity ("light touch") as a goal

- Study Designs – 34 design templates (dial up/down or "a la carte")
- Target Timelines – built for speed but adjusted based on experience
- Data Deliverables and Tracking

Innovations in the Partnership

- **Process**
  - Standard Study Designs – “Quality by Design”
  - Protocol Core and Process Definition
- **Business: “Flat Rate” Pricing**
  - Ease of Contracting
    - Decreases Overhead
    - Increases Speed
  - Predictability Enables Budgeting
  - Elimination of Change Orders

34 Standard Designs	
1 a-b	Bioequivalence, Bio Comparison
2 a-b	Food Effect
3 a-k	Drug-Drug Interaction
4 a-e	Thorough QT
5	ADME
6 a-b	Hepatic Impairment
7 a-b	Renal Impairment
8 a-d	Age/Gender/Ethnicity Safety&PK

Innovations - Novel Pricing Model

Select Study from Standard Design List

Drug (MK) Obj. of Study

34 Designs

#	Design
1a1	Bioequivalence/Relative Bioavailability Single-Dose, 2-way Crossover; Short half-life <24 hours; Early Development
1a2	Bioequivalence/Relative Bioavailability Single-Dose, 2-way Crossover; Short half-life <24 hours; Late Development
1b	Bioequivalence/Relative Bioavailability Single-Dose, 2-way Crossover; Long half-life >24 hours
2a1	Food Effect Single-Dose 2-way Crossover; Short half-life; Early Development
2a2	Food Effect Single-Dose 2-way Crossover; Short half-life; Late Development
2b	Food Effect Single-Dose 2-way Crossover; Long half-life
3a	Drug-Drug Interaction; Single Dose vs. Single Dose, Short half-life; Early Development
3b	Drug-Drug Interaction; Single Dose vs. Single Dose, Long half-life
3c	DDI: Inducer Single Dose vs. Multiple Dose; Short half-life; Early Development
3d	DDI: Inducer Single Dose vs. Multiple Dose; Long half-life

Identify study from list

Pricing by Standard Design

	Study Design
1a	Bioequivalence/Relative Bioavailability Single-Dose, 2-way Crossover; Short half-life <24 hours
1b	Bioequivalence/Relative Bioavailability Single-Dose, 2-way Crossover; Long half-life <24 hours
2a	Food Effect Single-Dose 2-way Crossover; Short half-life
2b	Food Effect Single-Dose 2-way Crossover; Long half-life
3a	Drug-Drug Interaction; Single Dose vs. Single Dose, Short half-life (2 way cross)
3a	Drug-Drug Interaction; Single Dose vs. Single Dose, Short half-life (3 way assay)
3b	Drug-Drug Interaction; Single Dose vs. Single Dose, Long half-life (2 way)
3b	Drug-Drug Interaction; Single Dose vs. Single Dose, Long half-life (3 way)
3c	DDI: Inducer Single Dose vs. Multiple Dose; Short half-life
3d	DDI: Inducer Single Dose vs. Multiple Dose; Long half-life
3e	DDI: Inducer Multiple Dose vs. Multiple Dose; Minimal Confinement, Mid-Long Range half-life
3f	DDI: Inhibitor Single Dose vs. Multiple Dose; Minimal Confinement, Short Half-life Substrate
3g	DDI: Inhibitor Single Dose vs. Multiple Dose; Minimal Confinement, Long Half-life Substrate
3h	DDI: Inhibitor Multiple Dose vs. Multiple Dose; Minimal Confinement, Mid-Range Half-life (fixed)
3h	DDI: Inhibitor Multiple Dose vs. Multiple Dose; Minimal Confinement, Mid-Range Half-life (crossover)

Pricing set for Standard Design or A la Carte

Best Pricing

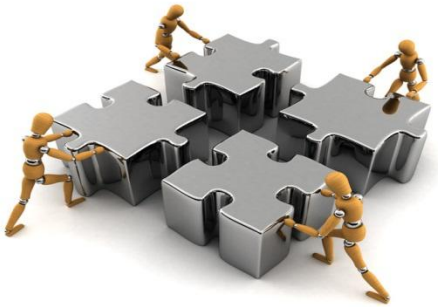
Continuing Innovations

- **CSR Process Improvements**
  - Timelines and Overall Metrics
  - Adjusted based on targets balanced with practicality
- **Risk Based Monitoring**
- **Growth of Relationship**
  - Early Development (SAD, MAD, POC)
  - Special Populations
- **Co-Developed Capabilities**
  - Merck Singapore Initiative
  - Celerion Korea

Merck and Celerion
Bio polis in Singapore

Challenges

- **Challenge: Balancing needs of all parties**
  - Management, Program team, Study team
  - Speed? Innovation? Simplicity? Consistency? Cost? Science?
- **Example: Management of Data**
  - Clinical Pharmacology team: Light touch, Style de-prioritized
  - Merck: Specific needs to allow inclusion into existing infrastructure
  - Data Management system
- **Resolution**
  - Identification of issues
  - Detailed discussions at every level
  - **Time consuming**



Compromise to minimize effort and defer costs, but allow study to proceed

Governance and Oversight

Governance and Escalation Path to Senior Management

- Operational Governance Team - members of both organizations meet quarterly
- Senior Team meetings – bi-weekly
- Executive Governance Meetings – quarterly

Practical Oversight and Quality Assurance (QA)

- Merck Vendor Management Oversight Plan – includes each functional area
- Feedback on audits/inspections - Celerion Internal and Merck-Initiated Audits

Ongoing Challenges

- **Many points of communication but need to move quickly**
- **Equal partnership requires pushing one another**

Example

- **Dosing procedure could have been more clear**
- **Celerion noted/queried but did not push hard enough**

Key Elements to a Successful Partnership

Key Elements

- Sponsor and CRO Alignment, Commitment, and plain ole “hard work”
- Communication– Routine, Planned, & Ad Hoc - as often as necessary
- Maturity of Partnership and Experience – “doesn’t happen overnight”
- Approach to Issue Resolution – challenges will arise, it’s how they are handled
- Mutual “skin in the game” – has to be mutually beneficial
- Partnership has to be flexible and evolve in order to meet changing business needs

Mutual Benefits of a Successful Partnership

Benefits to Merck

- Means to expand (and contract) with changing business demands
- Partnership willing to innovate (Singapore) and expand scope of work – FIH, POC (CSRs)
- Reliable, flexible, responsive partnership that can navigate & mitigate challenges

Benefits to Celerion

- Partnership willing to explore different business models and types of outsourcing
- Challenged to Innovate
- Rich scientific discussions and mutual learnings – scientific issues and drug development

Just that much closer to bringing new medicine to patients…

Questions and Discussion

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Thank you!

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