Testimonial from an industry partner

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AstraZeneca at a glance

• **Pure play pharmaceuticals business**
  – Cardiovascular/Metabolism & Gastrointestinal
  – Neuroscience
  – Respiratory and Inflammation
  – Oncology and Infection
  – Small Molecules and Biologicals

• Over 65,000 employees worldwide

• 12,000 people in R&D

• 26 manufacturing sites in 18 countries

• Extensive sales & marketing network dedicated to meeting our customers’ needs in over 100 countries.

• Sales 2008: 36.1 billion USD

• R&D spend 2008: over 5 billion USD
Why drugs fail in development and how these vary by phase?

Preclinical Phase I Phase II Phase III

Clinical Safety 26%

Efficacy
55%

Problem to be solved at EU level: Only 1 of 10 CDs may become a product
SAFE-T
(Safer and faster evidence-based translation)

- 3 target organs critical for drug-induced injury with non-appropriate clinical monitoring:
  - **Kidney**: Current standards (Serum Creatinine, BUN) are only increased when 50-60% of the kidney function is lost.
  - **Liver**: Current standards (AST, ALT, Bilirubin) are not specific and do not predict who will recover and who will develop fulminant liver disease.
  - **Vascular System**: There are currently no biomarkers to monitor drug-induced vascular injury in human.

- **Goal**:
  - To qualify translational safety biomarkers for monitoring DIKI, DILI and DIVI in humans.
SAFE-T: Partners

• EFPIA (11):
  – Novartis (Coordinator of the SAFE-T consortium)
  – Almirall
  – Amgen
  – Pfizer
  – Hoffmann La Roche
  – AstraZeneca
  – Bayer Schering Pharma AG
  – Boehringer Ingelheim
  – Eli Lilly
  – GlaxoSmithKline
  – Sanofi Aventis

• Academic (5):
  – Barcelona Cardiovascular Research Center
  – Charité Hospital
  – Groupe d’Etudes et de Recherches en Médecine Interne et Maladies Infectieuses - APHP
  – Groupe Hospitalier Pitié Salpêtrière - APHP
  – Natural and Medical Sciences Institute
  – Tel-Aviv (Souraski) Medical Center

• SMEs (4):
  – Firalis SAS (Coordinator of the Initial Applicant SAFE-T consortium)
  – Argutus Medical Limited
  – Experimental & Diagnostic Immunology GmbH
  – Interface Europe

• External Advisors:
  – European Medicines Agency
  – FDA (proposed)
SAFE-T: Project Overview

**WP1 - Development of generic scientific qualification strategy for translational safety biomarkers (BMs)**

**WP2 – DIKI BMs**
- Selection of candidate BMs and injuries/injury models to study
- **TWO STEP FORWARD BM QUALIFICATION APPROACH**
  - BM Proof of Translation (PoT) Studies
  - BM Proof of Performance (PoP) Studies
- Biologic/mechanistic studies to support BM qualification

**WP3 – DILI BMs**

**WP4 – DIVI BMs**

**WP6 - Integrative Data Analysis & Project Database**
- Project Database including human BM profiles
- Integrative data analysis of BM PoT, BM PoP and mechanistic studies Meta-analysis

**WP5 - BM Assay Development, Validation & Testing of Clinical Samples**
- Assay availability for selected candidate BMs
- BM assay development and validation
- Sample testing - BM PoT, PoP & mech. studies

**WP7 - Biobank for Qualification of Translational Biomarkers**
- Establishing guidelines and validation
- Sample management
- Maintenance
- Management
- BIOBANK
- COMMUNICATION, DISSEMINATION, TRAINING, EXPLOITATION

**WP8 - Dissemination / Communication / Training Plan**

**WP9 – SAFE-T Consortium Management**

**VALIDATED BM QUALIFICATION STRATEGY**

**DATABASE OF HUMAN BIOMARKER PROFILES**

**QUALIFIED BMS & VALIDATED ASSAYS for DILI, DIKI & DIVI**
SAFE-T: Facts and Status

• Duration: **5 years, 35.8 Mio €** research budget
• Kick off meeting June 15, 2009 – first IMI project that started
• Governance structure
  – Steering Committee (Project coordinator Frank Dieterle, Novartis)
  – Scientific Advisory Committee (Scientific coordinator Ina Schuppe Koistinen, AZ)
  – Work package leaders, task leaders
  – Ethical Committee, IP Committee
• Project work ongoing according to plan, first deliverables
  – Scientific biomarker qualification strategy
  – Prioritised list of DILI/DILI/DIVI biomarkers for qualification
  – Clinical study templates/plans
SAFE-T: Common Goal

EFPIA
- Is the compound safe in man?
- Can we select better follow up compounds?

Invests ~18 M€

EU
- How can we improve European drug R&D?
- How can we improve the diagnosis of drug-induced injury?
- How can we improve the monitoring of disease?

Invests ~14 M€

Academia
- How can we improve the monitoring of disease?
- Can we develop better tools?

Deliver new drugs to patients to improve the treatment of diseases

Open Information Day - 17 November - Brussels Expo
SAFE-T: management of IP

• A need for good communication between partners:
  – Identify the various interest
  – Define who brings what?

• SAFE-T: definition of a specific IP regime
  – Biomarker IP
  – Technology IP

• The preparation of the Project agreement need to be supported by a neutral body to ensure that all interests are met.
  – SAFE-T Project Agreement prepared and agreed in 4 months

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Some words of advise

- Study the Call text carefully
  - All components need to be addressed in the consortium
- Different from FP7:
  - Project coordination typically by EFPIA representative
  - Application + consortium formation process
  - The primary goal is not performing cutting edge research for the purpose of research but to achieve the stated objectives
- Include an appropriate number of partners
- Do not under-estimate the time required for preparation of the EOI
- Communication, communication, communication
Personal Reflections

• Focus on science
  – Interaction with Pharma as scientists sharing the same vision
  – Possible to reach broad scientific consensus on new safety biomarkers

• Focus on the common goal
  – New medicines for the treatment of diseases
  – Improved understanding of the molecular mechanisms of drug-induced injuries

• Recognise the power of the IMI-JU
  – Unique opportunity to work across disciplines
  – Large project budget
  – Cross-fertilisation EFPIA, Academia/SME and EMEA

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The Scientific Challenge is to qualify translational safety biomarkers and, ultimately, to understand the (patho)biology of the human organism!