Genomics-Enabled Drug Repurposing and Repositioning: A Workshop:

State of the Science: Industry

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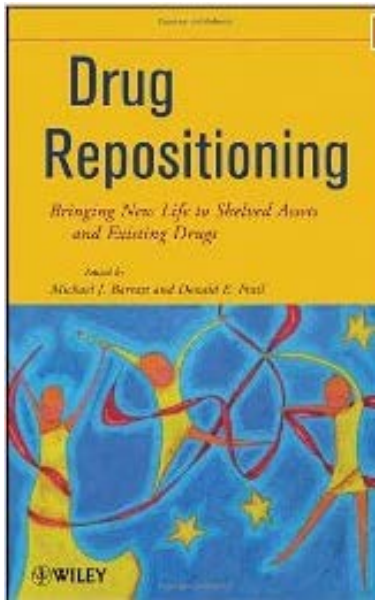
Institute of Medicine: June 2013



VIAGRA (sildenafil citrate) tablets
Angina to male sexual dysfunction...

Revatio sildenafil
...and on to PAH

Cymbalta duloxetine HCl
From depression to fibromyalgia

From hypertension to male pattern baldness

Rogaine

THALOMID (thalidomide) Capsules
From morning sickness to multiple myeloma

One View of Drug Repositioning

“Safe but discontinued compounds sitting on the shelf”

Another View of Drug Repositioning

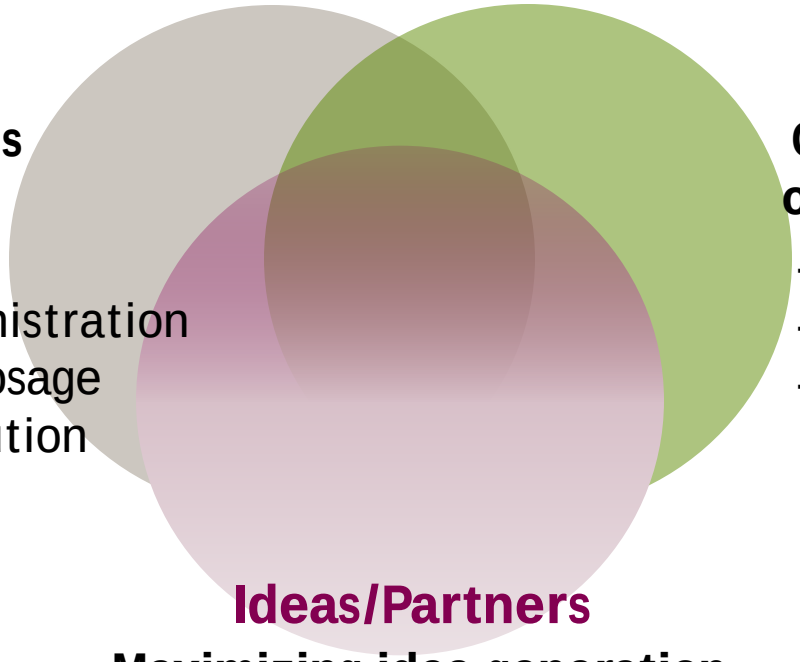
Three Key Strategic Elements

Compounds

Access to compounds

"Taking them off the shelf"

- Therapeutic index
- Length and route of administration
- Drug API, drug product, dosage
- Placebo, blinding, distribution
- Exclusivity: patent life, encumbrances



Indications

Core areas or opportunistic?

- True unmet need
- Standard of care
- Payer reimbursed

Ideas/Partners

Maximizing idea generation

- Knowledge mining
- Genetics/Transcriptional profiling
- Phenotypic screening
- in-silico
- **Open innovation/ Crowd sourcing**
- Many others…

Repositioning Efforts
Who's involved

Pharma
- "Business as usual"
- Dedicated group
  - Pfizer's Indications Discovery Group, AstraZeneca's "New Opportunities iMED; Takeda's efforts; GSK's "External Drug Discovery"

Biotechs
- e.g. Intellikine with PKD Foundation

Non-profits
- e.g. MJFF, LLS, PKD
- Cures Within Reach

Academia
- Funding bodies (e.g. MRC, NIH)
- A growing number of investigators

AZ-MRC Partnership For Translational Research

The power of open innovation

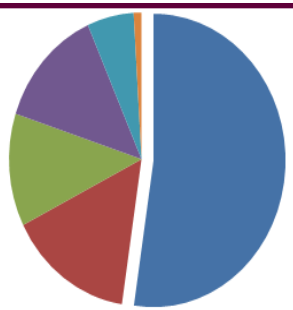
AstraZeneca

MRC Medical Research Council

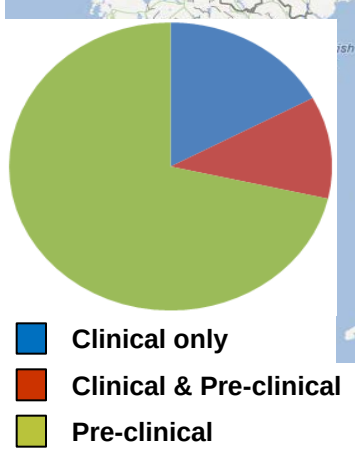
Investigators and academic institutions

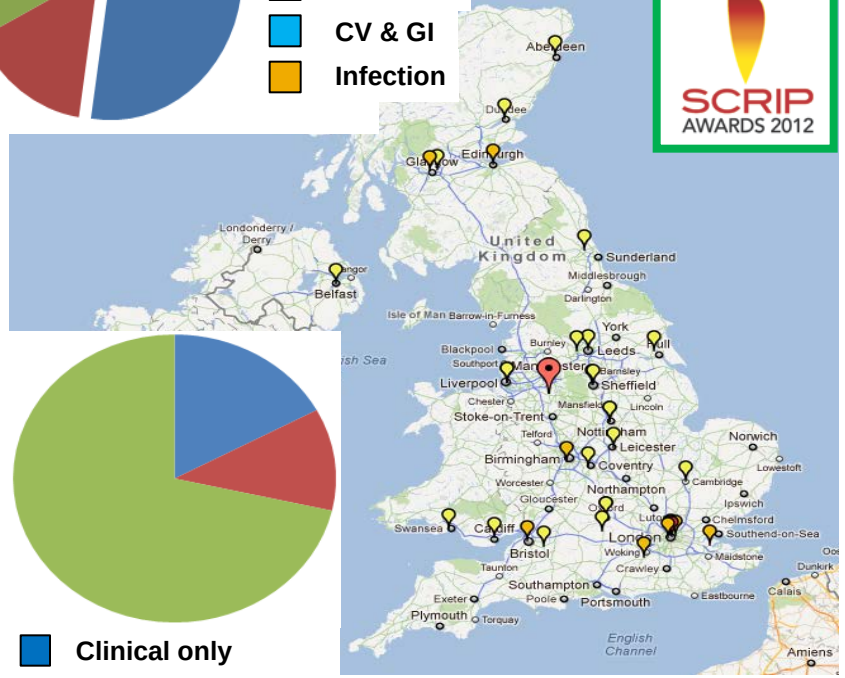
"...to provide funds for eligible academic researchers to access a collection of high-quality AstraZeneca compounds in order to support studies to investigate human mechanisms of disease and the development of potential therapeutic interventions".

- 22 compounds
- >100 clinical and pre-clinical proposals from 37 UK institutions
- Proposals submitted on all compounds & across a broad span of disease areas
- 8 preclinical and 7 clinical selected for funding by MRC (~$10M)



SCRIP AWARDS 2012





‘Open Innovation’ Alliance Models

Virtual iMED ’New Opportunities’ Forms Alliances to Explore Utility of Existing Drug Candidates in New Disease Areas

Academic partnerships

AstraZeneca
MedImmune
Development Compound Tool Box

- *AZ Development Compounds*
- *Information archive*
- *Know-how*

Dec, 2011

MRC Medical Research Council

- MRC committed up to £10M to fund studies on AZ compounds
- Proposals received in 8 week call period from 37 UK institutions
- Proposals span core and adjacent/white space indications
- Multiple preclinical and clinical collaborative projects being funded

May, 2012

National Institutes of Health

- **NIH “New Therapeutics for Existing Molecules” Initiative announced May 2012**
- **Up to $20M in 1st year; Eight partners**
- **Request for Proposals in June, 2012**
- **Clinical projects**

Next steps...

- **Evaluating models for broader open innovation**

Strategic partnerships with biotech and/or pharma e.g Alcon, Galderma

Repositioning In Industry

Potential barriers to committing to a dedicated strategy

- Companies typically declare areas of focus
  - Greater economies of scale
    - Leverages internal expertise, existing sales channels
- A distraction to the current project team and organization
- Considered part of the project team's responsibilities
  - Life cycle management
  - "What ifs?" – e.g. two indications with pricing differences
- Limited compounds
- Limited capital to invest
- Not considered innovative

Drug Repositioning With Discontinued Compounds

The challenges for industry…

- Updating the INDs, IBs
- All existing information – CMC, safety, clinical study reports
  - Program may have closed out before all data was in
  - Qualified drug product, clinical supply, package/labeling, placebo
- Analytical methods, PK of samples
- Safety review – human limits relevant to the proposed study
- Pharmacovigilence
- Infrastructure to support Investigator Initiated Studies or out-licensing
- Legal agreements – CDAs, Collaborative agreements, ISS agreements
- Patents, exclusivity – costs, remaining patent life, data exclusivity

Drug Repositioning With Live or Discontinued Compounds

Why some projects won't proceed…

- Company does not have an appropriate compound
- No patent or regulatory "exclusivity"
- Low probability of success
- Payer reimbursement challenges
- Market is too small (# patients or low price)
- No defined regulatory approval endpoints

Orphan Drug Space

The Opportunity

Highest priced orphan drugs

1. Solaris, nocturnal hemoglobinuria (Alexion) - $440,000/yr (~$1.1 B, 2012)
2. Elaprase, Hunter's Syndrome (Shire) - $375,000/yr ($590 M, 2012)
3. Naglazyme, Maroteaux-Lamy syndrome (Biomarin) - $365,000/yr ($257 M, 2012)
4. Cinryze, hereditary angioedema (ViroPharma) - $350,000/yr ($327 M, 2012)
5. Folotyn, peripheral T-cell lymphoma (Alios) - $320,000 ($53 M, 2012)

(source = Evaluate on-line)

Among the top Selling Orphan Drugs

- Rituxan – ~$7.0 B (2012)
- Revlimid - ~3.8 B (2012)
- Lucentis – ~$1.8 (2011)

(source = Evaluate on-line)

Orphan Drug Space

Participation by industry

Pharma:
- $28.8 B (11% of total revenue)
- e.g. GSK's Rare Diseases; Pfizer's Rare Disease Research Unit (RDRU); Sanofi's Rare Diseases

Specialty:
- $11.9 B (38% of total revenue)
- e.g. Shire, Celgene

"Pure Play":
-$3.7 B (81% of total revenue)
- e.g. Biomarin, Actelion, Cydan

Has the industry view of orphan diseases changed?
- A shift from primary care focus to specialty care focus
- A change in pharma blockbuster mentality???
- Is there a revenue "threshold" to pursue?

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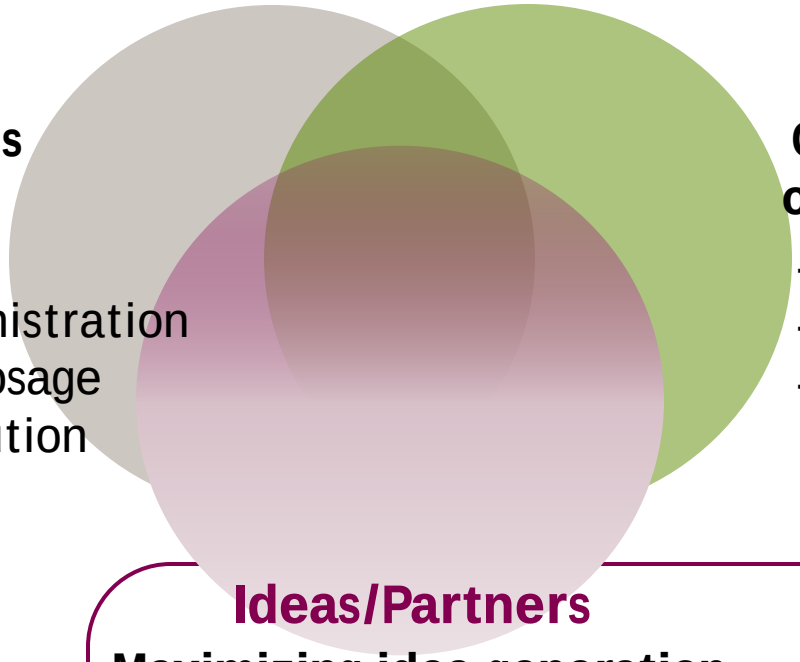

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Questions?