Fostering orphan medicines development

IRDiRC conference, Dublin 2013

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Can regulators foster development?

Principal role is regulating medicines
- Can regulators be indifferent to failures or lack of development?

Need to stay away from being directly involved
- Data/results assessment, central to regulators, should be done independently
- Need to ensure there are no conflicts of interest

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Fostering orphan drug development

- Medicines development
- Economic incentives
- Support to research

Do we have a "regulatory" tool?

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Fostering orphan drug development

Medicines development

- Orphan designation and protocol assistance

Economic incentives

- Fee reductions and market exclusivity

Support to research

- COMP advisory role to EC on policy for orphan medicines

Regulation (EC) No 141/2000
Principles on orphan designation

Objective of Regulation (EC) No 141/2000

• provide incentives that stimulate research and development
• modify market conditions
• set up system of recognition for orphan medicines to be eligible for incentives:
  • Rarity (not more than 5 in 10,000)
  • Seriousness (life threatening / chronically debilitating)
  • Existence of alternative methods of treatment (significant benefit?)
Evolution orphan medicines designations
Protocol assistance

Provides Agency (EU Wide) advice on drug development

- **clinical** (90%; 51% exclusively) *
  *(most relevant key development step)*

- **preclinical** (44%)

- **quality** (27%)**
  **(most relevant development step for advanced therapies)**

Possibility of biomarker qualification

Following advice increases chances of marketing authorisation

(RR 1.48; failure rate non compliant 70%; compliant 2%)
Protocol assistance

![Bar chart showing scientific advice and protocol assistance from 2010 to 2012.]

-科学建议
-协议协助

2010: 332
2011: 347
2012: 332

2010: 68
2011: 79
2012: 81
Fee reductions

Annually EU allocated special fund to cover fee reductions (approx. 6 million Euro)

EMA has consistently kept maximum coverage for SMEs

Academia and SME responsible for 79% development of advanced therapies

Policy reviewed annually, needed revision in 2013 according to current budget
Allocation funds for fee reductions (2012)

Use EU fund

- Marketing authorisation: 60%
- Protocol assistance: 29.4%
- Inspections: 6.6%
- Post-authorisation activities: 3.9%
Status of Orphan Marketing Authorisation Applications: 78 granted to date

**Adopted positive opinion**

- 1 awaiting decision

**Ongoing applications in review process**

- 27 applications in review process

**Variations / Line Extensions in review process**

- 3 applications in review process

**Negative outcomes for orphan MAA**

- 56 applications withdrawn
- 10 negative decisions/refusals
COMP advisory role

Regular exchange of information with EC to identify high level research needs

Access to information on development

Regulators have direct contact experience with successes and failures

Direct access to a wealth of information

International collaboration between regulators (USA, Japan, Canada)
Of the 12 projects in the article nine for orphan designated products

Cordis website: three additional projects granted that involve development of orphan drugs:

- Drugsford (inherited photoreceptor degeneration)
- Eurofancolen (fanconi anaemia)
- Aipgene (intermittent acute porphiria)

<table>
<thead>
<tr>
<th>Rare disease project</th>
<th>Funding (million)</th>
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<tr>
<td>Neuromics: integrated European omics research project for diagnosis and therapy in</td>
<td>€12</td>
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<tr>
<td>rare neuromuscular and neurodegenerative diseases</td>
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<tr>
<td>RD-CONNECT: an integrated platform connecting registries, biobanks and clinical</td>
<td>€12</td>
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<tr>
<td>bioinformatics for rare disease research</td>
<td></td>
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<tr>
<td>EURenOmics: European Consortium for high-throughput research in rare kidney diseases</td>
<td>€12</td>
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<tr>
<td>BALANCE: development of a bioartificial liver therapy in acute liver failure</td>
<td>€6</td>
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<tr>
<td>DevelopAKUre: clinical development of nitisinone for alkaptonuria</td>
<td>€6</td>
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<tr>
<td>FIGHT-HLH: first targeted therapy to fight hemophagocytic lymphohistiocytosis</td>
<td>€6</td>
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<tr>
<td>GAPVAC: glioma actively personalized vaccine consortium</td>
<td>€6</td>
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<tr>
<td>MeuSIX: clinical trial of gene therapy for mucopolysaccharidosis type VI — a</td>
<td>€6</td>
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<tr>
<td>severe lysosomal storage disorder</td>
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<tr>
<td>Net4CGD: gene therapy for X-linked chronic granulomatous disease</td>
<td>€6</td>
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<tr>
<td>PREVENTROP: new approach to treatment of the blinding disease retinopathy of</td>
<td>€6</td>
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<tr>
<td>prematurity</td>
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<tr>
<td>PROFNAIT: development of a prophylactic treatment for the prevention of fetal/</td>
<td>€6</td>
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<tr>
<td>neonatal alloimmune thrombocytopenia</td>
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<tr>
<td>Traumakine: interferon-beta treatment of acute respiratory distress syndrome</td>
<td>€6</td>
</tr>
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Privileged access to knowledge

Suboptimal use:

• Lack of resources
• Confidentiality issues
Fostering orphan drug development

Medicines development
- Orphan designation and protocol assistance
- Scientific validation / guided development

Economic incentives
- Fee reductions and market exclusivity
- Economic viability

Support to research
- COMP advisory role to EC on policy for orphan medicines
- Knowledge “repository” and target identification – public regulatory intelligence