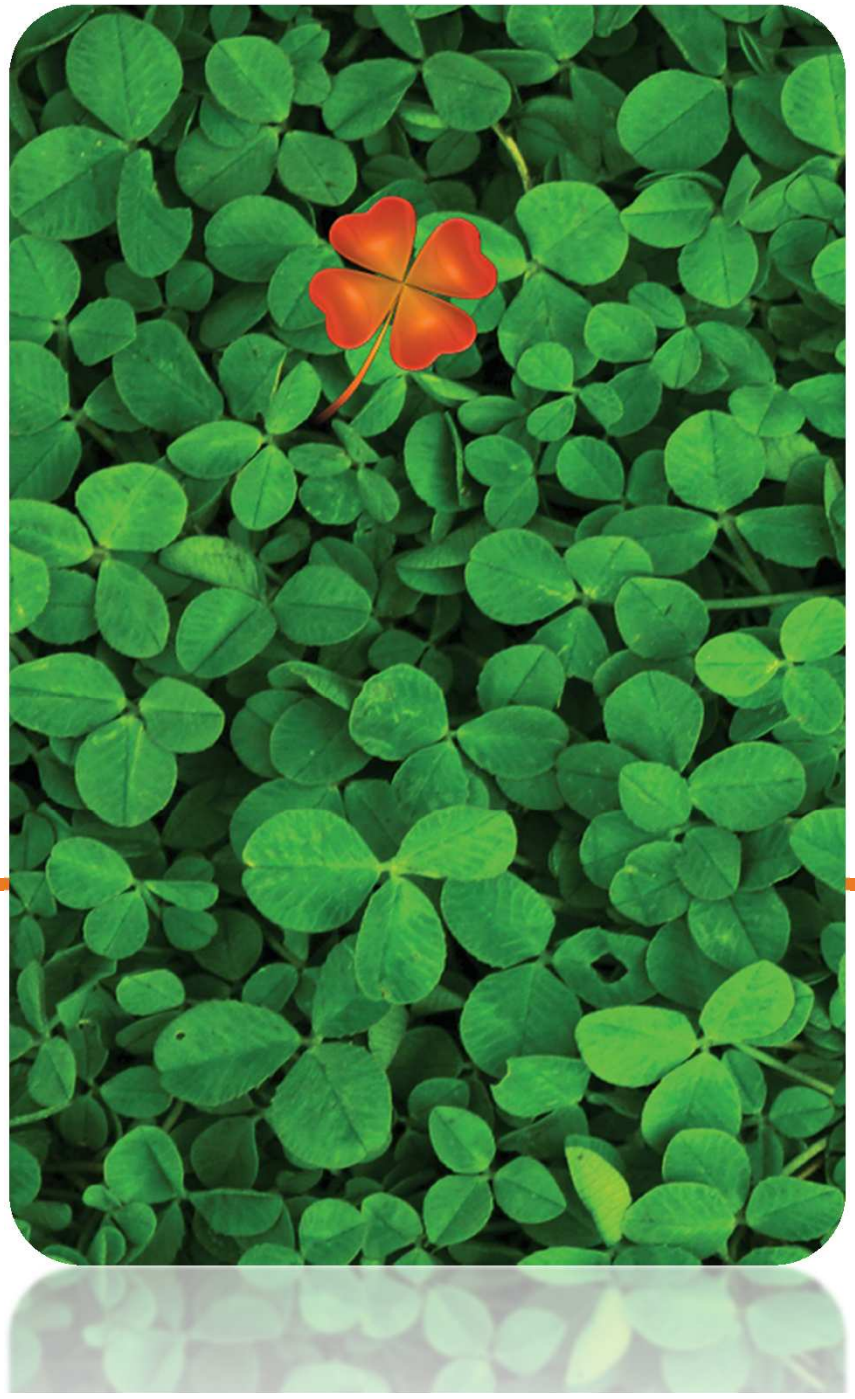
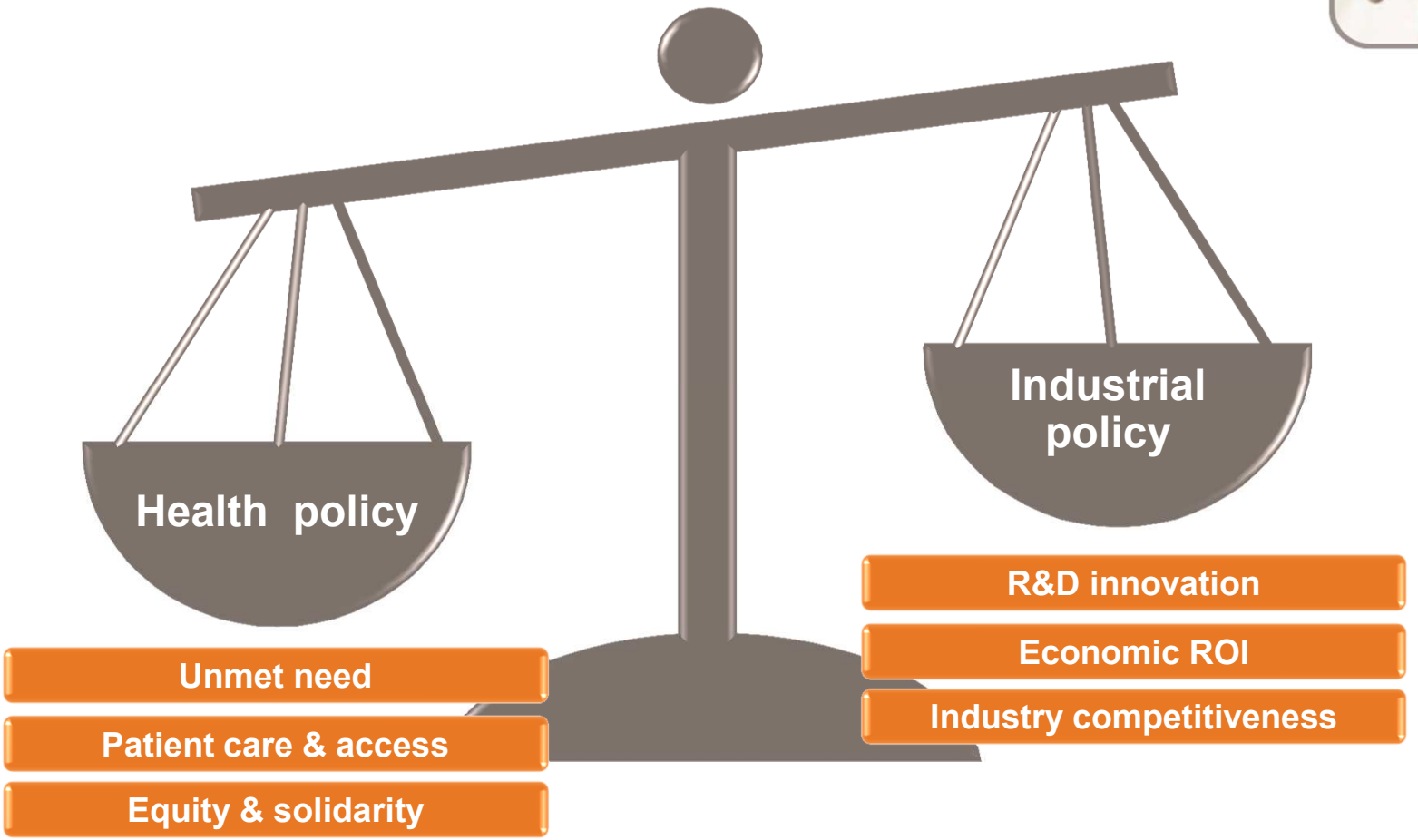


Value & Specificity of Rare Diseases Business Model

Is the pursuit of this societal priority sustainable?

Marc Dunoyer
ECRD- Brussels
24th May 2012

Value & Specificity of the Rare Diseases Model the Policy Equation



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Outline

- Rare Diseases is one of the healthcare challenges
- “Learn from the rare!” - a major source of R&D innovation
- Reward of innovation based upon unmet need & patient outcome
- Importance of orphan policy incentives
- Sustainable Rare Diseases access model
- Early dialogue between sponsor-regulator-payer-patient groups

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Rare Diseases Unmet Need
A Societal Priority

Severity

Life threatening,
devastating diseases

Lack of treatments

7.000 rare diseases
1% covered by approved treatments in EU**

Social impact

Families' daily life suffering
&
psychological despair

60% of families affected have a lower income***

EQUITY & SOLIDARITY

« Patients suffering from rare conditions should be entitled to the same quality of treatment as other patients with more frequently occurring disorders »

OD in Legislation: EC 141/2000 Preamble 7, Article 3.1.b

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*Nature July 2010
**Source: 68 Orphan drugs approved in EU by 2010
*** Eurordis council May 2011

Rare Diseases – Treatments

Scientific Advances Lead to New Breakthrough Therapies for Patients

Technology platforms

- Cell therapy
- Gene therapy
- Small molecules
- RNA interference
- Monoclonal antibodies
- Pharmacological chaperones

Patient outcome

- Curative
- Disease modification
- Disease symptoms control

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Rare Diseases a Dynamic Source of R&D Innovation

- Significant R&D investments inflow*
  - OD R&D expenditures in the EU have increased 2X faster than overall Pharma (year 2000 to 2008).
  - R&D in ODs represent an increasing proportion of total R&D in the general biopharmaceutical industry.
- R&D innovation impact – France case study**

	All drugs	Orphan drugs
• ASMR I & II	32%	52%

(share in total drugs reimbursed) 2001 to 2009

- A major contributor to the economy*
  - Employment in companies working on orphan drugs in EU has more than doubled between 2000 and 2008

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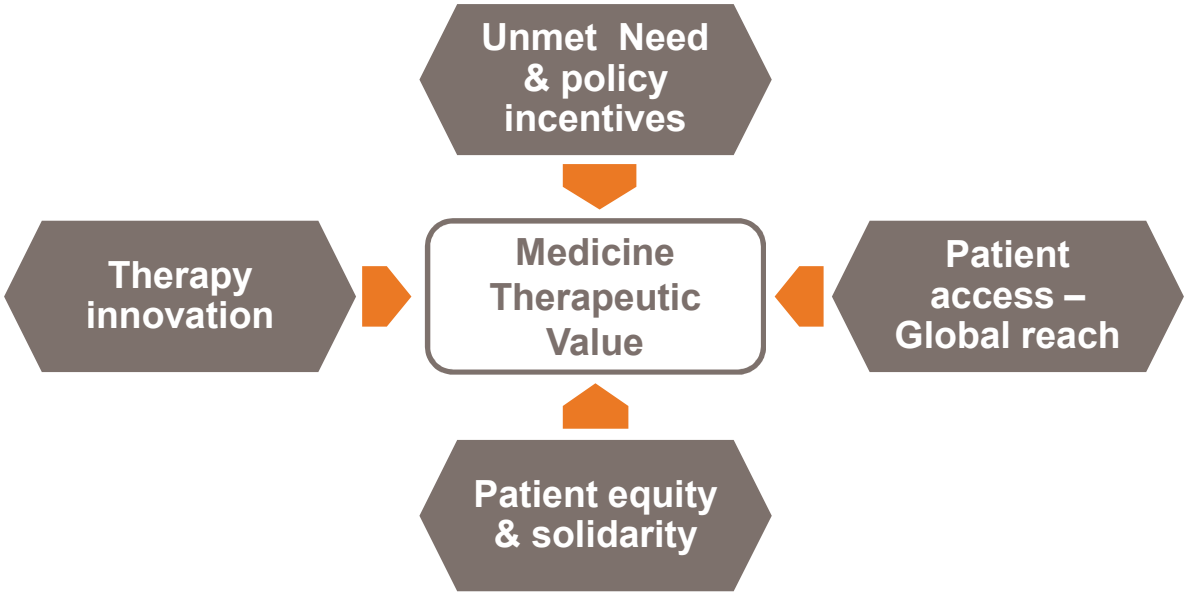
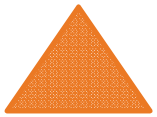
* OHE Consulting report Nov 2010 /
** AFM report Feb 2011

Rare Diseases Sustainability for Health Care Systems? Key Factors of Change

Affordability





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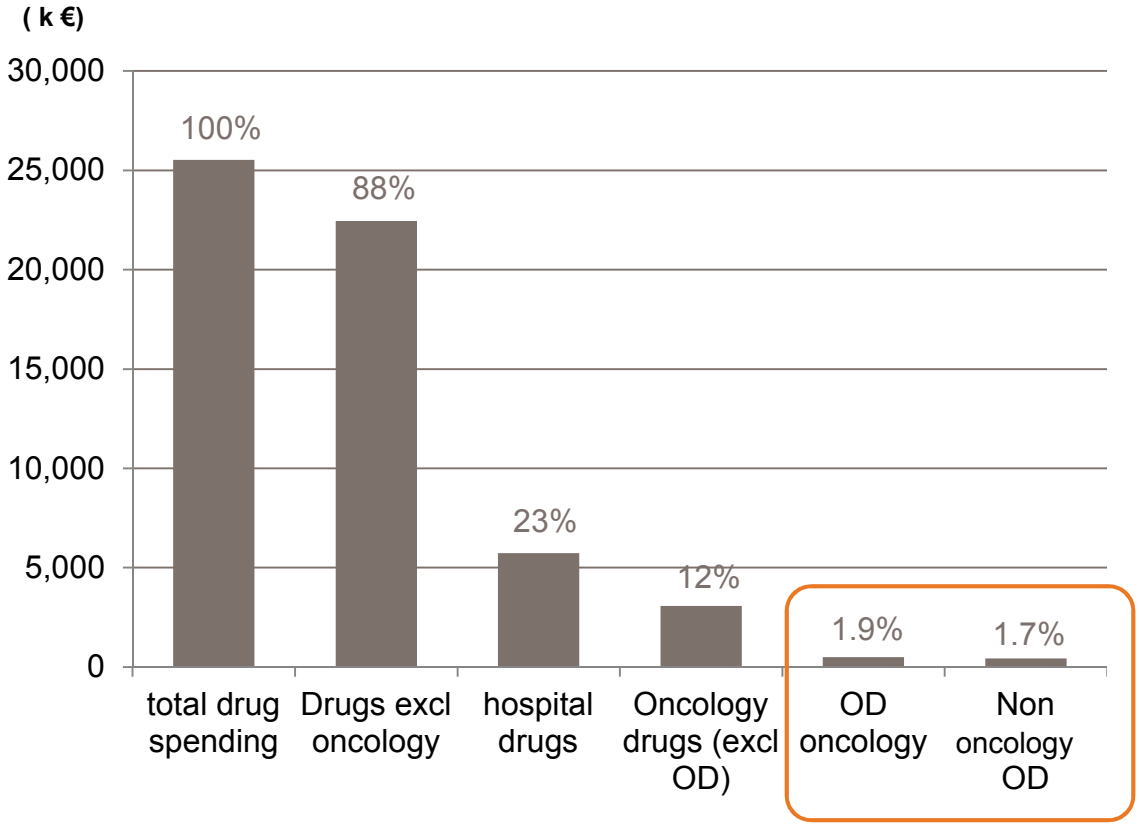
Orphan Drugs – Low Budget Impact

France case study – Drug spending (2009***)



EU overview 2009
ODs in total drug spending (%)
Germany 2.5%*
Italy 2.1%**
Spain 2.5%*
France 2.4 %*
UK 1.8%*

6%-8%
of population

* 2009 OD sales compared to total pharmaceutical sales; IMS data
** Rapporto OSMED 2010
*** CEPS report 2009

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Orphan Drugs Budget Impact Dynamics Concentrated & Likely to Plateau

Class	N drugs	- % OD spending	(YTC range k €)
Oncology OD	5 drugs 49%	62%	(20-50 k €)
	15 drugs 13%		(4 - 180k €)
Non Oncology OD	LSD 14%	38%	(100-700 K €)
	CVS 14%		(15-60 K €)
	Other ODs 10%		(10 – 400 K €)
2010 estimated budget impact*		100%	

Estimated 2016 budget impact

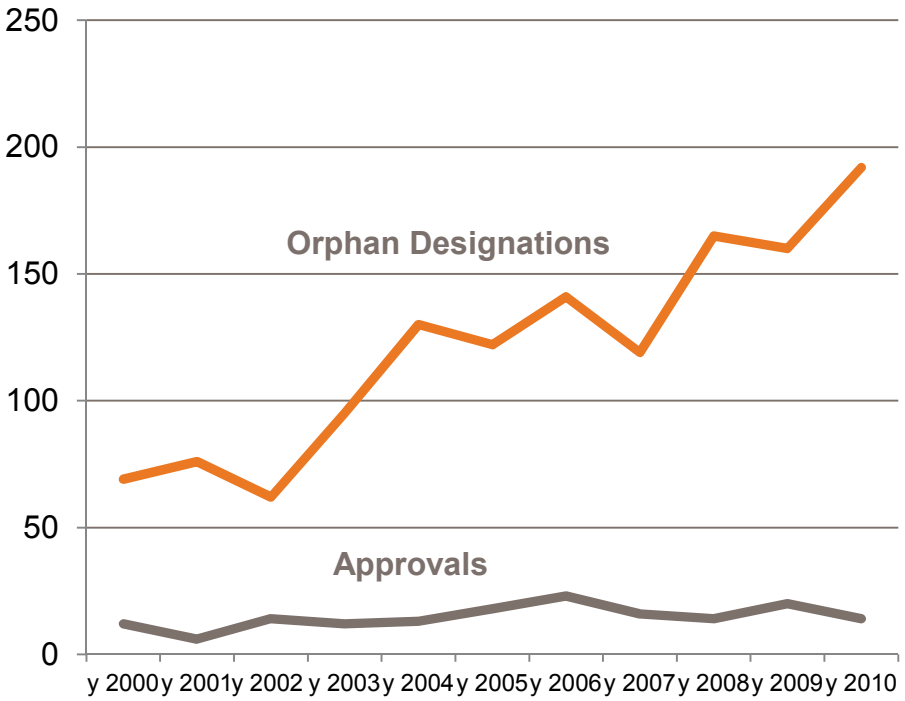
Orphan drug spending in EU likely to plateau at 4% - 5% of total drug spending**

*AFM report Feb 2011 /
**C Schey 2011

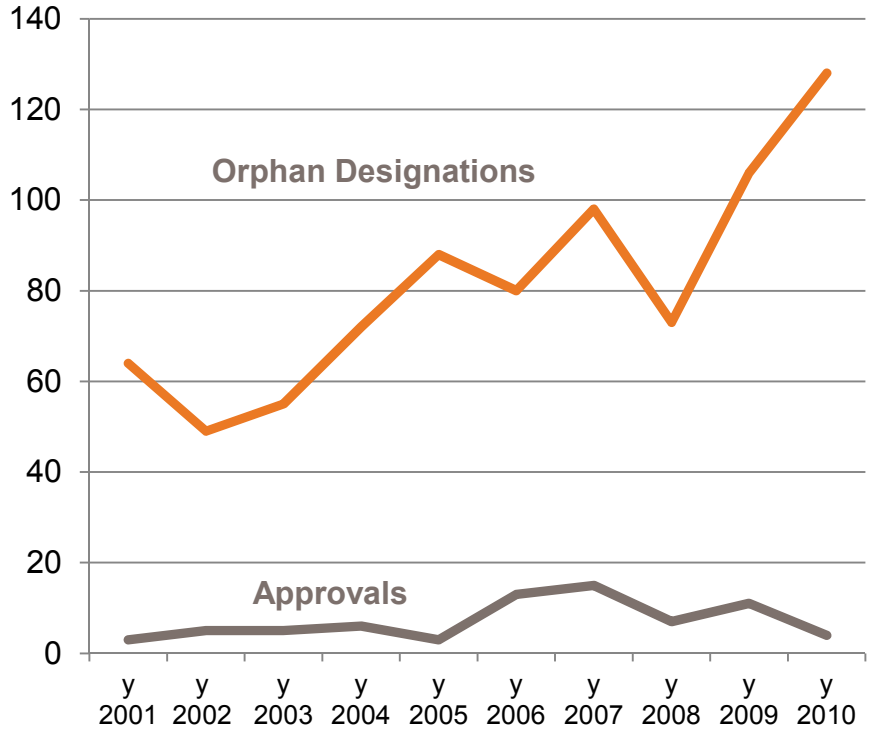
Rare Diseases Business Model

Rate of Orphan Product Approvals Remain Flat

All Orphan Designations and Approvals (USA)



All Orphan Designations and Approvals (EU)



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Rare Diseases Drug Development a Challenging Reality

- **Substantial heterogeneity of patient population**
  - Difficulty in clearly defining the patient population – clinical presentation, disease subtype
- **Small patient populations**
  - Difficulty in demonstrating statistical significance
  - Geographically dispersed patients – recruitment
- **Limited clinical experiences**
  - Common problems for medical sites, industry and agency
  - Challenge of defining practical clinical endpoints
- **Traditional study designs often not feasible**
  - Randomization of trials and inclusion of control arms can be untenable
  - Double-blind design with placebo or standard of care is often difficult to apply

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High Risk Pharma R&D Innovation Model

Discovery Pre clinical → **Phase I** → **Phase II** → **Phase III** → **Marketing Authorization (EMA)** → **Reimbursement (National)**

	Common diseases	*Rare diseases*	*drivers*
1. Time R&D financing cost Cost of capital	10 y to 14 y* (from pre clinical to launch)	**< =**	• therapeutic area • Disease rarity (ultra orphan)
2. Risk (attrition)	P-O-S = 8%* (from pre clinical to launch)	**< =**	• Diseases pathways • repurposed vs « pure » OD
3. Costs	1.8 -2.2 Bio $* (capitalized at 11%)	0.5 – 1.5 Bio $ (capitalized at 11%) **> cost per patient**	• > N countries (rarity) • complexity recruitment • > relative n patients in trials (up to 15% of prevalent population)

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* Source: “how to improve R&D productivity”, S Paul, Nature(2010).

Investment Dynamics & Returns Depend on the Sources of Innovation

Sole designations

80%

Re-purposed

15%

Expansion strategy

5%

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Access to Rare Diseases Treatments Opportunities for Policy Optimisation

iscovery | AOP, published online 24 June 2011; doi:10.1038/nrd3493

Nature Reviews Drug Discovery

COMMENT

Accelerating access to treatments for rare diseases

Marc Dunoyer

Changes in regulatory policy and legislative incentives to promote the development of drugs for rare diseases — orphan drugs — have led to increases in the number of orphan drug designations, but the rate of such products reaching the market remains frustratingly flat. This article highlights areas in which novel approaches could facilitate regulatory approval and access to treatments for rare diseases.

10 solutions to accelerate access to treatments in rare diseases

1. Importance of continued flexible orphan incentives
2. Role of Patients' disease registries & post-approval studies
3. Global Simplification-Harmonization of regulatory requirements

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Patient Timely Access to Rare Diseases Treatments Development Process as a Continuum

REGULATORY FOCUS

April 2012

Perspective: A Modern Progressive Approval System for Rare Diseases

By Marc Dunoyer

The recent dramatic increase in the number of orphan drug designations has prompted patient groups, pharmaceutical companies, legislators and many other stakeholders to look for ways to accelerate the delivery of innovative new medicines to people with rare diseases. In particular, patients suffering from illnesses for which there are no adequate licensed therapies want access to promising new products earlier in the drug development cycle.

Against this backdrop, there is a growing urgency to rethink the regulatory review process itself. One option certainly worth exploring is a more progressive assessment and approval mechanism under which potential therapies for rare diseases are reviewed.

Certain dynamics make rare diseases ideal subjects for such regulatory innovation. These include the relatively small patient populations, the concentration of clinical research activities at medical centers of excellence and the high level of specialization of the treating physicians. Another unique feature of rare diseases is the wealth of scientific knowledge among patients and their families and, as a result, the extent to which they can interact with specialist doctors about diseases and their evolution.

Taken together, these factors make the rationale for 'experimenting' with less conservative regulatory mechanisms very compelling.

1. Accelerated and Conditional approval should become the default pathway in this priority population provided sufficient dialogue has taken place between patients, physicians, drug developers and HTA.

2. Progressive assessment and approval mechanism as a standard practice

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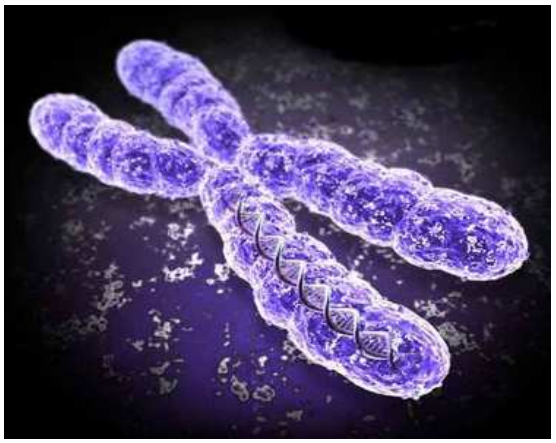
Reward of Innovation Based Upon Unmet Need & Patient Outcome



GSK Rare Diseases Portfolio

75% of targeted diseases
have no approved treatments

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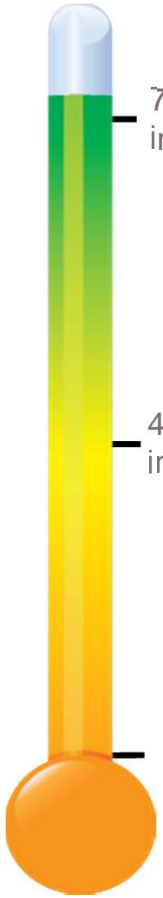
Define Medicine Therapeutic Value



Medicine Therapeutic Value

Rare Disease Unmet Need

- Treatment available
- Disease Clinical severity
- Disease Social Impact

Medicine Therapeutic Benefit

- Treatment innovation
- Treatment Clinical Benefit and outcome
- Treatment Social outcome

Value attributes
Value criteria definition

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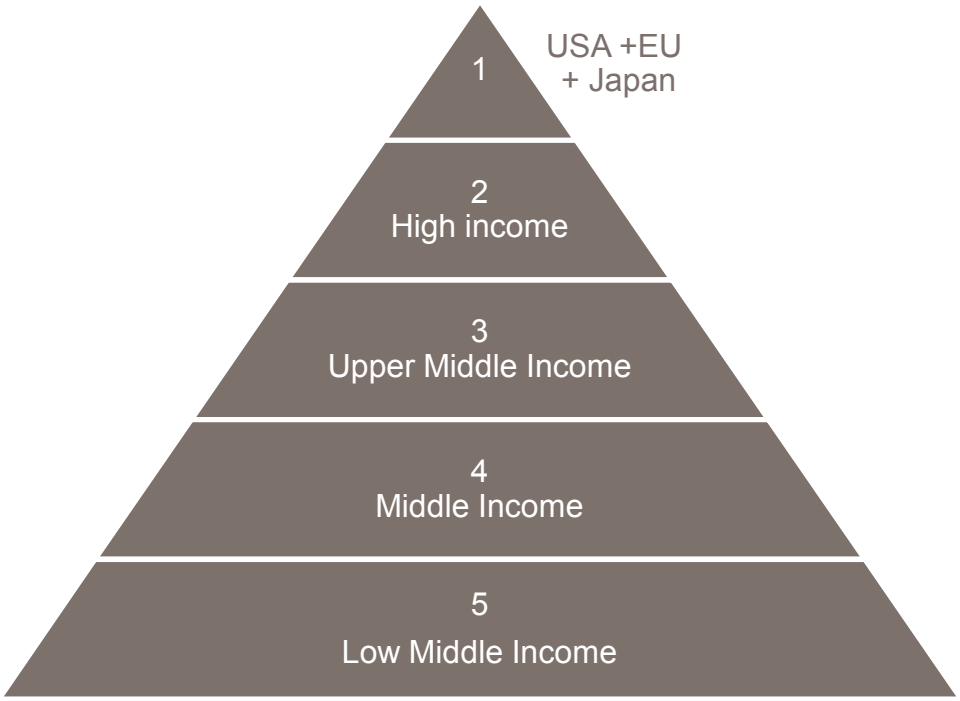
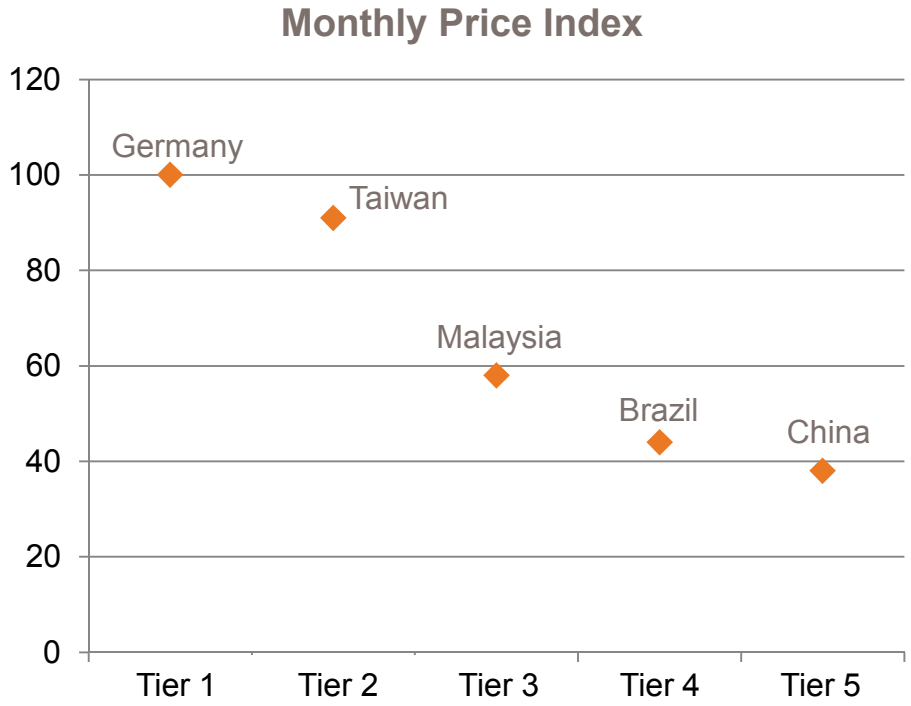
Patient Access & Global Reach

Tiered pricing based on GNI & payers' willingness/ability to pay

Global patient reach



Illustrative case study



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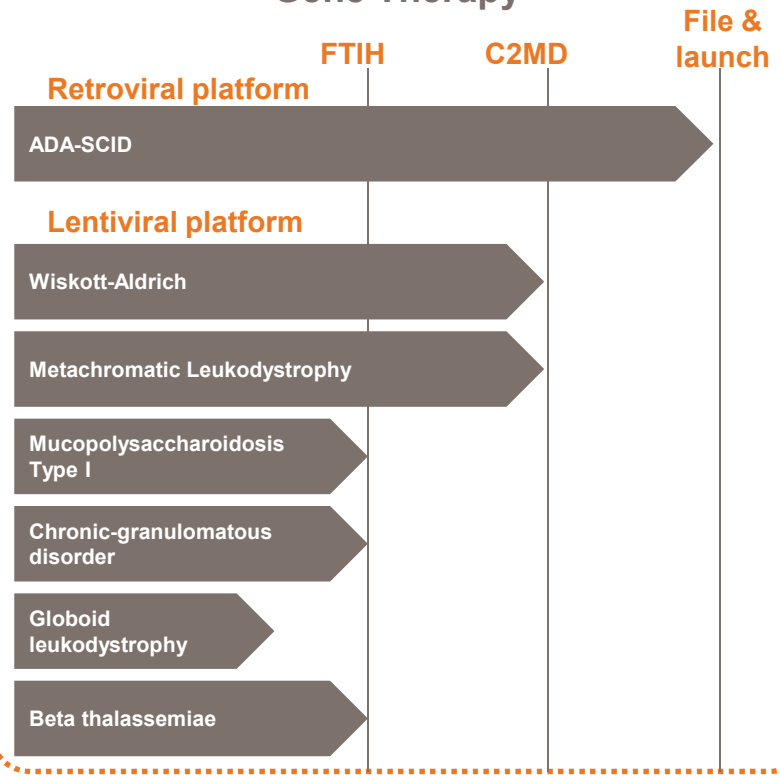
Rare Diseases Investment Dynamics the Importance of Franchises

Technology Franchises

Gene Therapy



Synergies

- Development
- Regulatory
- Access
- Advocacy
- Commercial

Diseases Franchises

Duchenne Muscular Dystrophy

DMD EXON 51
GSK 968

DMD EXON 44

DMD EXON 45 & 53

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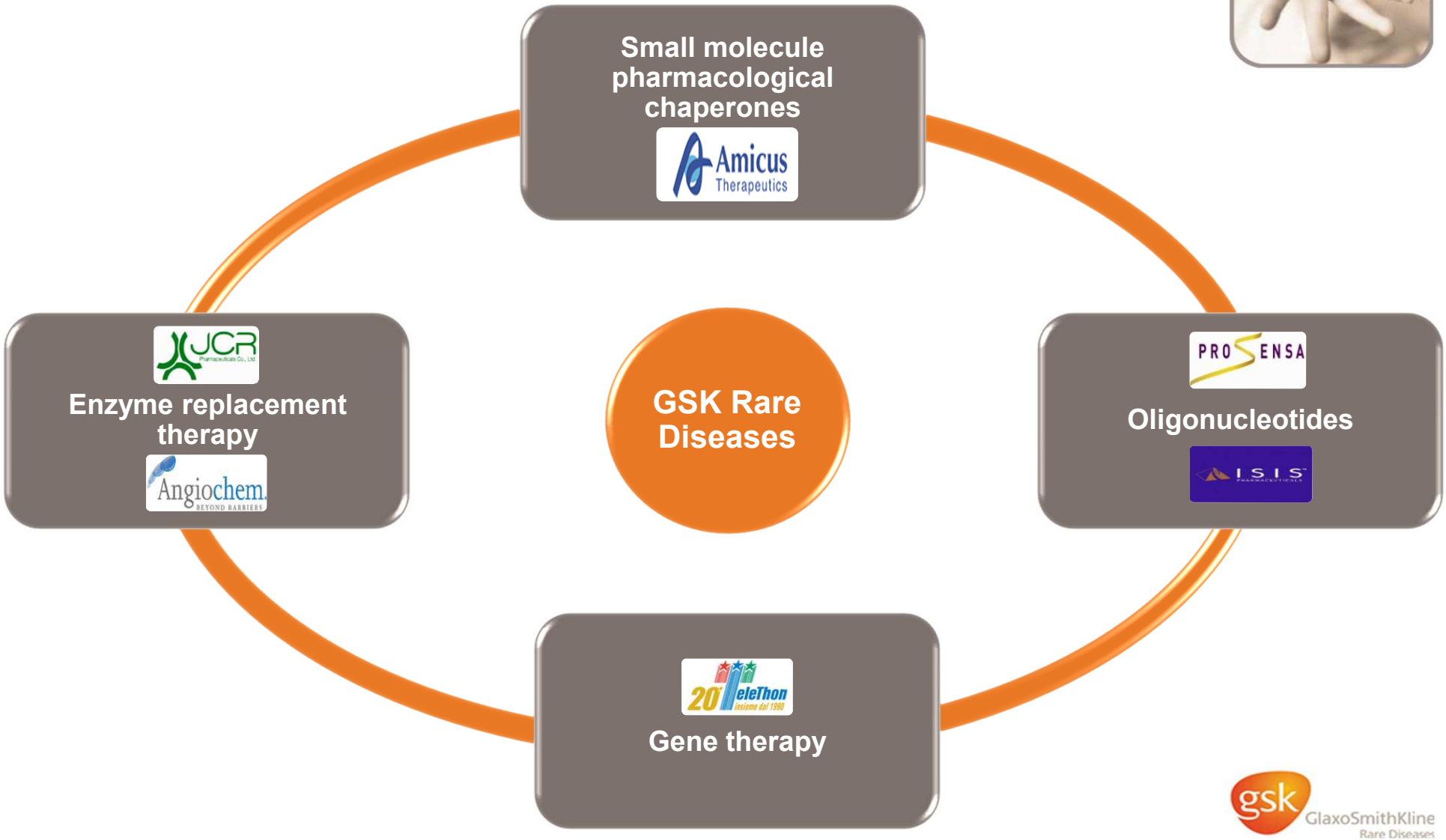
Rare Diseases Investment Dynamics
Alliances & Partnerships



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A Sustainable Model is Possible

- Rare diseases treatments societal value recognition
- Development / market access process should be seen as a continuum
- Global reach & innovative Holistic pricing approaches can be considered to address affordability
- Role of patient disease registries & post approval studies
- importance of early & constant dialogue between sponsor-regulator-payers-patient groups

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Rare Diseases Competition: A Sustainable Model for the Pharmaceutical Industry
http://www.gsk.com/rare-diseases
Thank you
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