Industry Expectations:

Discovery, Research, Development ,

Access to medicines

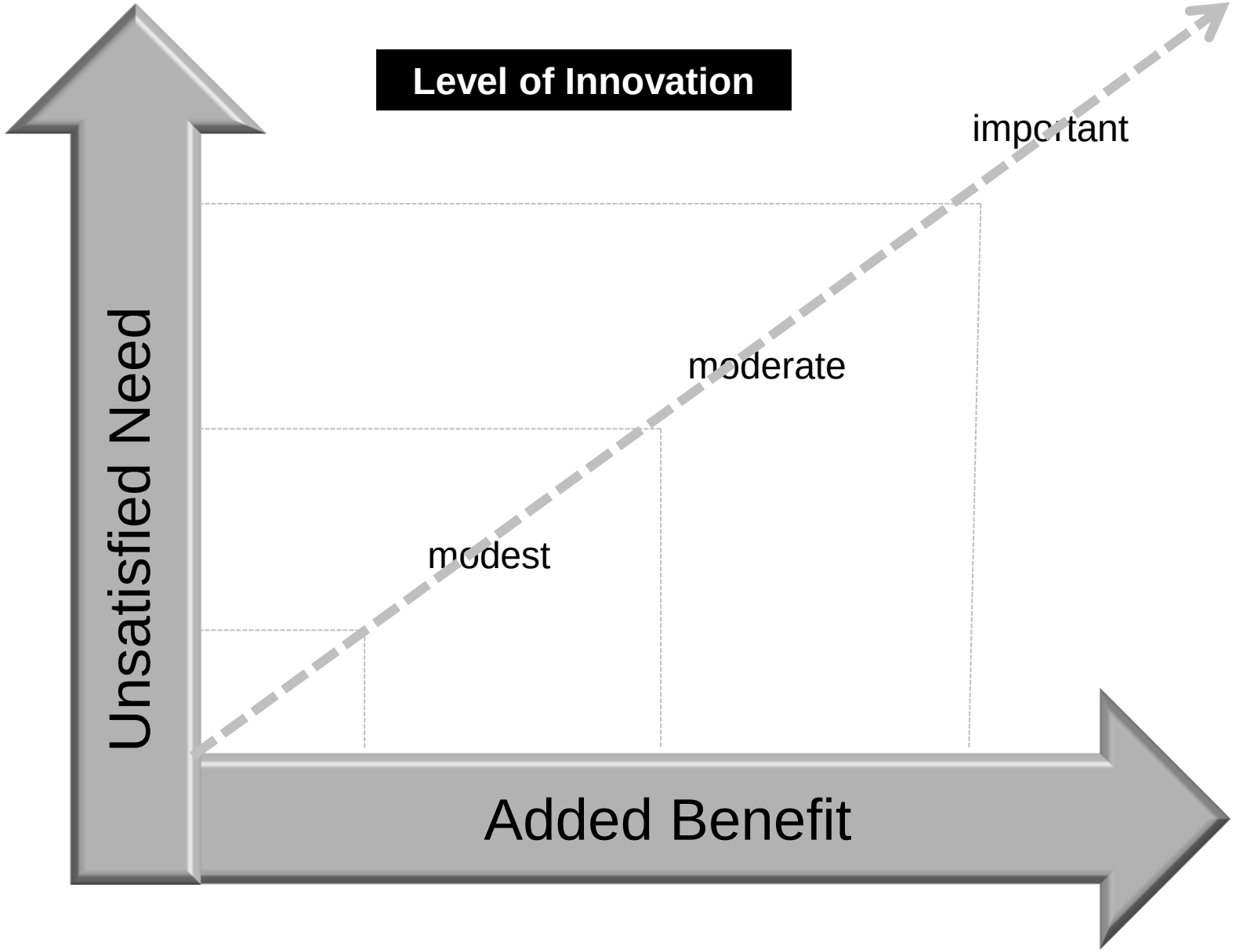
Mihaela Ianosev – European Medical Director CDBU

Pharmaceutical R&D Ecosystem – radical changes

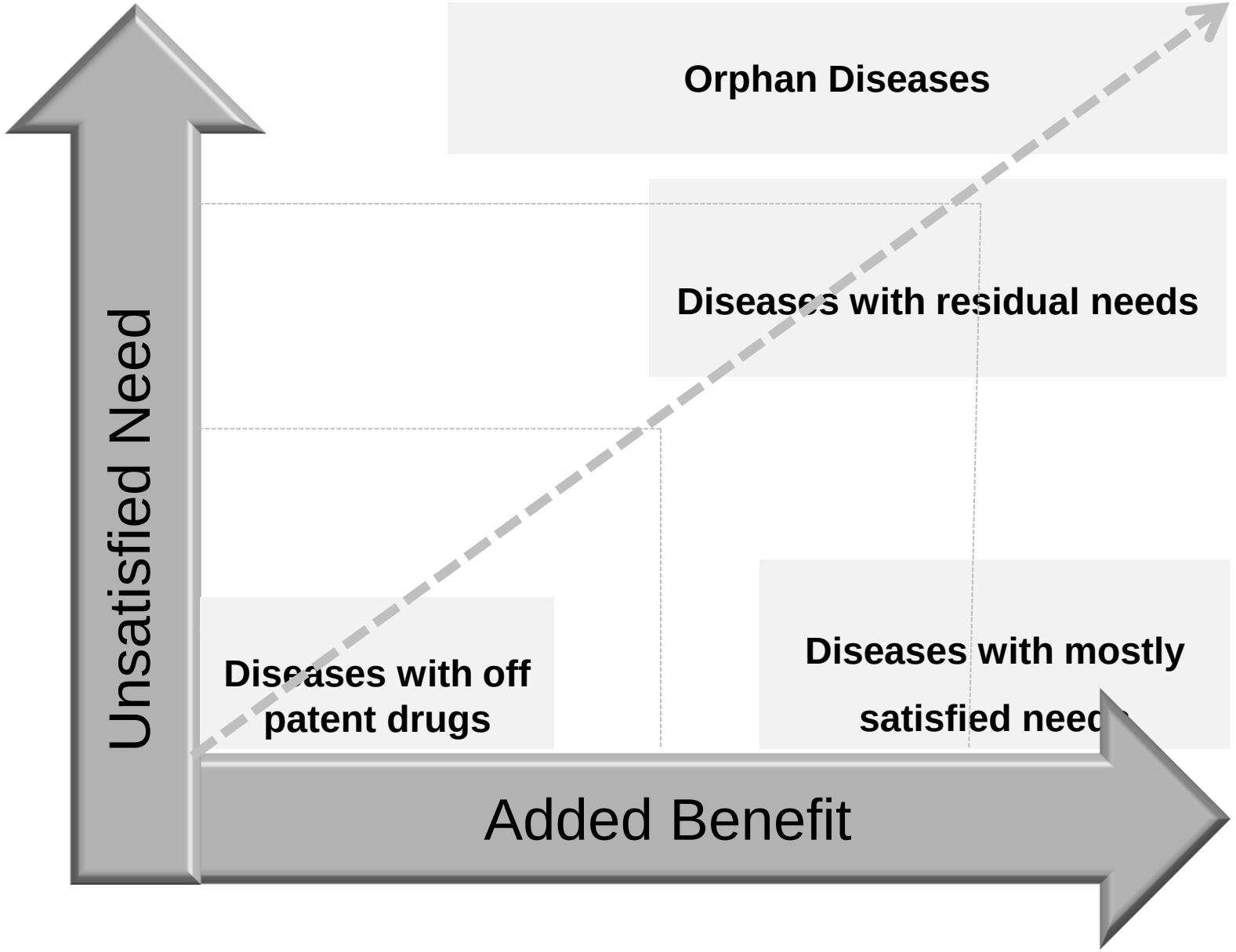
- Change in demographics
- R&D productivity
- Rapid escalation
- Higher risks of fail
- Global tightening
- Diminishing advar
- Changes in social
- Patent expiration
- Science & Techno
- Economical crisis
- HTA, pricing & reimbursement

1. **Priorities for Research**
2. **Value based development and access to medicines**
3. **Modalities of Discovery**

Priorities of Research



Priorities of Research



Priorities of Research

RuiPing Dong explains Merck's Chinese R&D expansion p100

The neuropathic pain market p101

New drug approved for myelofibrosis p103

2011 FDA drug approvals

The US FDA approved 30 new therapeutics last year, including 11 first-in-class agents.

Asher Mullard

Last year the US Food and Drug Administration (FDA)'s Center for Drug Evaluation and Research (CDER) gave the green light to 24 new molecular entities and 6 new biologics. The approval of 30 new therapeutics is the most since 2004, which saw 36 products approved. The relative bumper crop, moreover, includes a substantial number of novel drugs that address major unmet medical needs, hit new targets and leverage the promise of genetic approaches to understanding disease.

"It is a really exciting list," says Chris Milne, Associate Director of the Tufts Center for the Study of Drug Development, in Boston, Massachusetts, USA. Andrew Jones, an analyst at Ernst & Young, agrees. "The thing to focus on is the level of innovation within the [illegible] of approvals," he says. [illegible] stand-out statistics, he [illegible] approval of 11 first-in-[illegible]

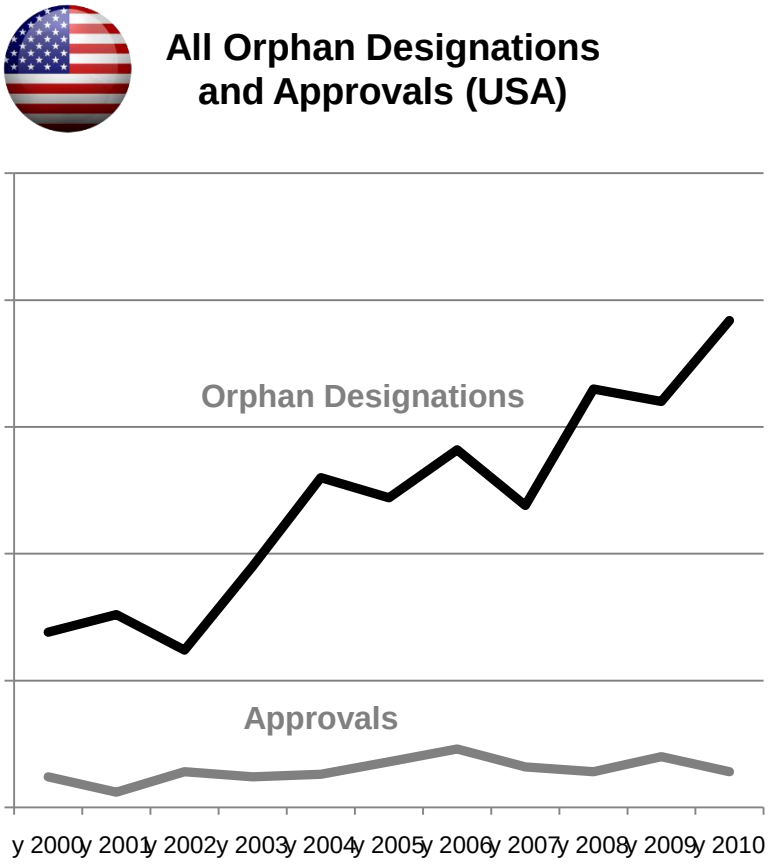
Big winners among [illegible] companies involved in [illegible] GlaxoSmithKline and [illegible] Johnson, which, with [illegible] both brought three new [illegible] the market.

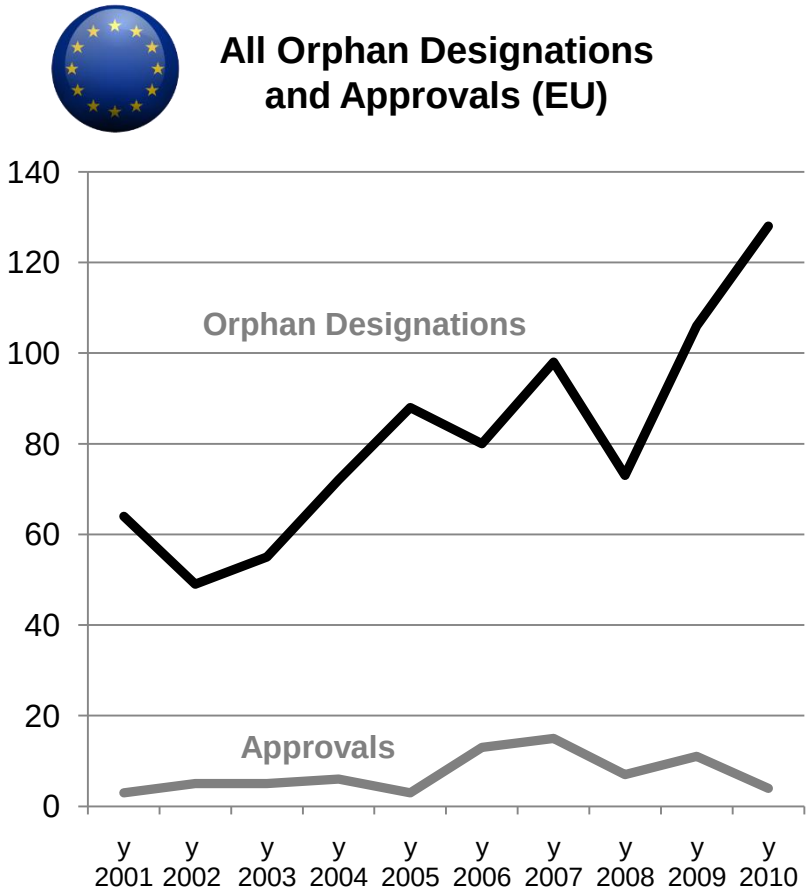
"In terms of approv[illegible] the FDA did its job," ad[illegible] Schmidt, an analyst at [illegible] Cowen. "The agency w[illegible] in reviewing their drugs, in general they hit their timelines, and for the most part the decisions were not too surprising." Nineteen of the approvals were granted to drugs in

Orphan and cancer overlap

One of the clearest trends evident within the list was the preponderance of orphan products, which accounted for 11 out of 30 approvals (TABLE 1). This focus reflects a decade-long shift by drug developers towards potential niche busters — often targeted at focused patient populations for which the disease biology is relatively well understood or for which there are few or no good existing treatments. "Overall, we've found that around 25% of new agents over the past half decade or so have been orphan drugs," says Milne. Unlike previous years, however, these orphan designations were

Rate of Orphan Product Approvals Remain Flat





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
  - Regulatory expectations established primarily for more common diseases => big, long clinical studies

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

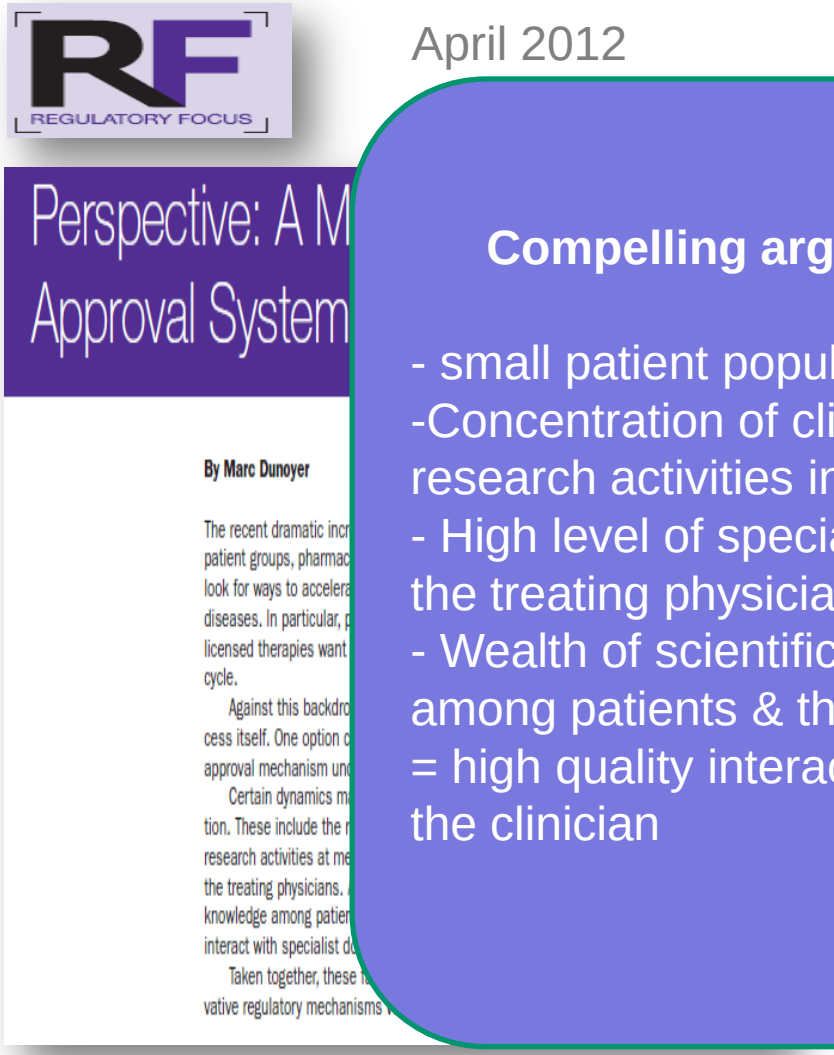
Marc Dunoyer

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

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



April 2012

Compelling arguments:

- small patient population
-Concentration of clinical research activities in CoE
- High level of specialization of the treating physician
- Wealth of scientific knowledge among patients & their families
= high quality interaction with the clinician

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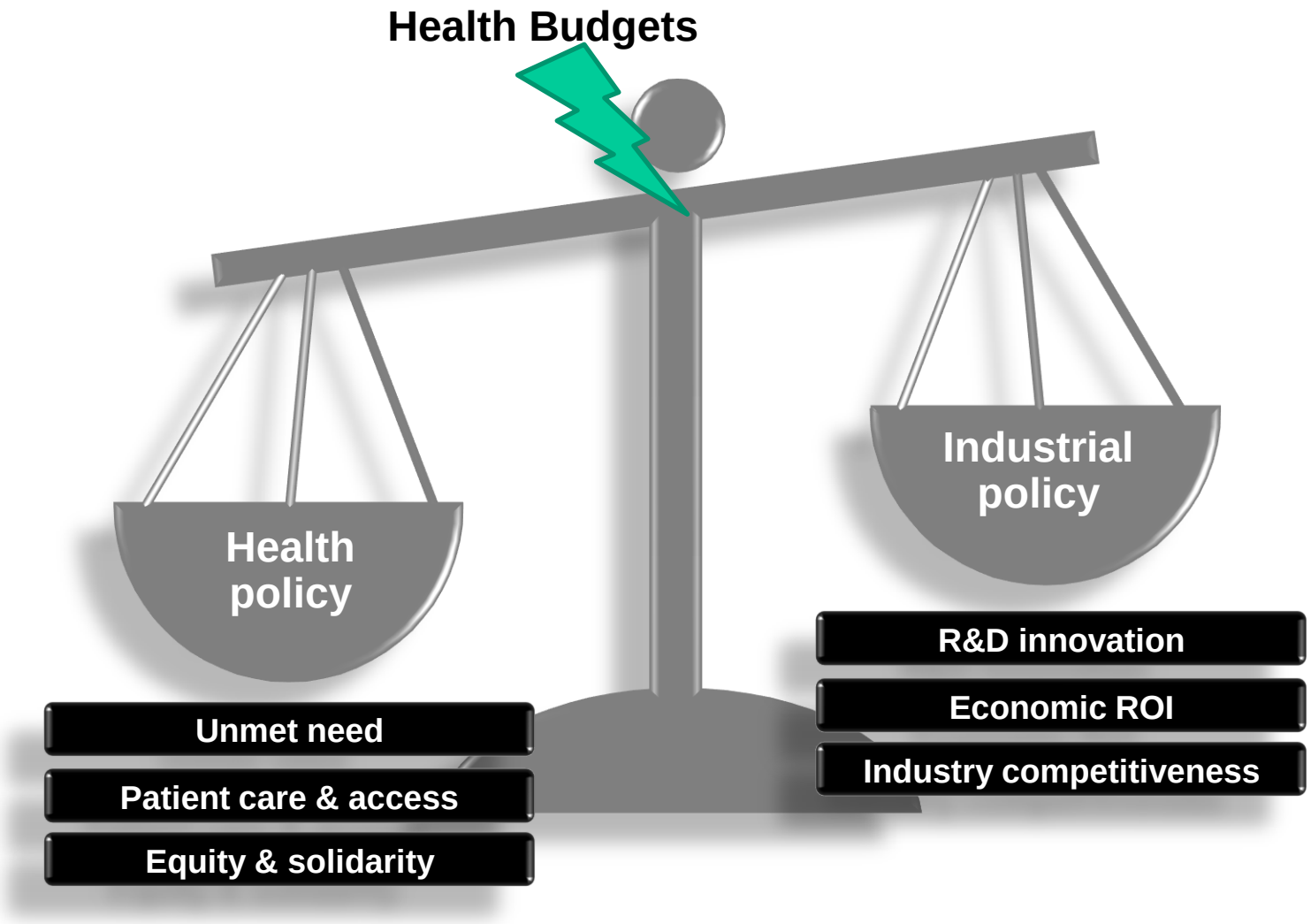
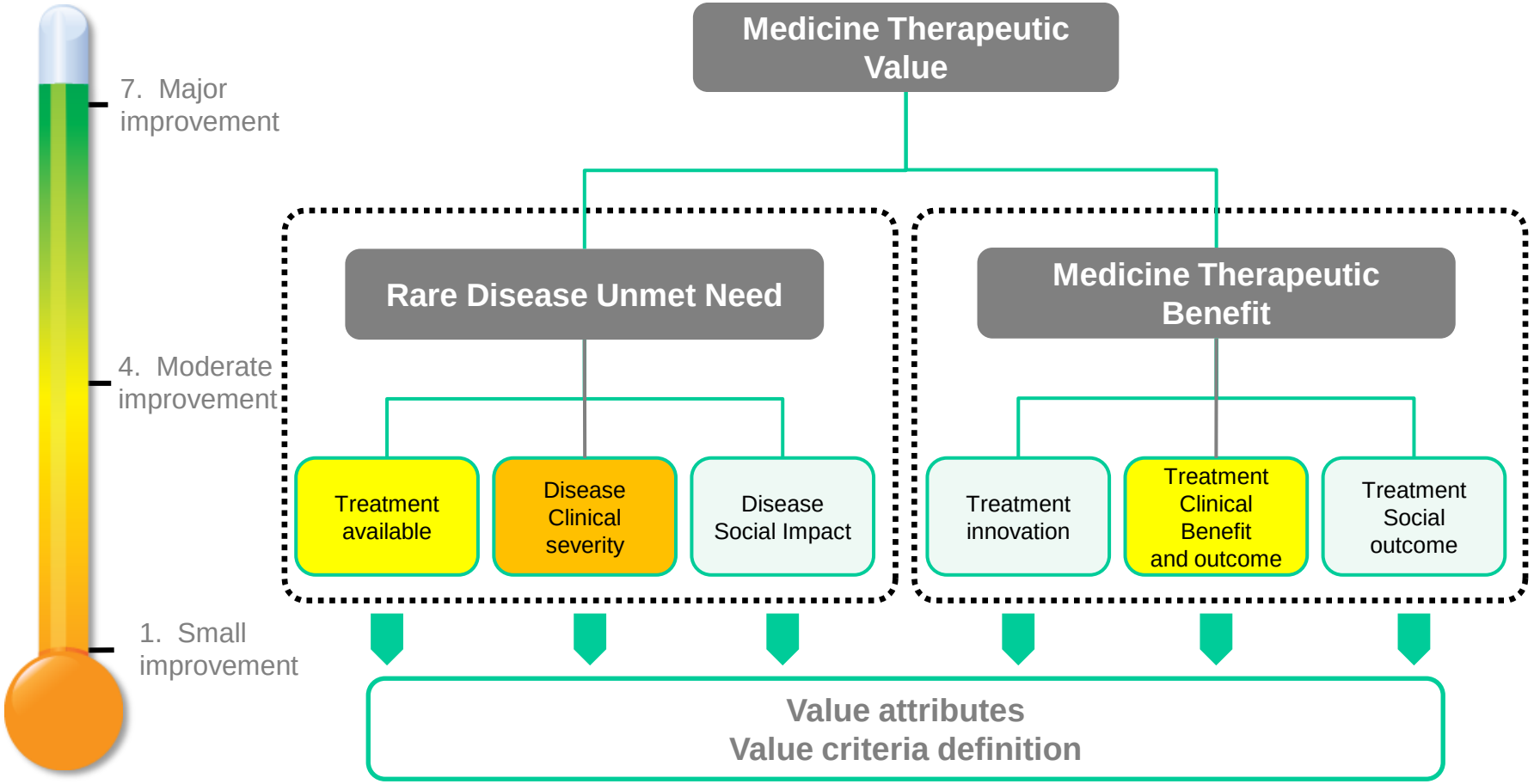
Value & Specificity of the Rare Diseases
Model the Policy Equation



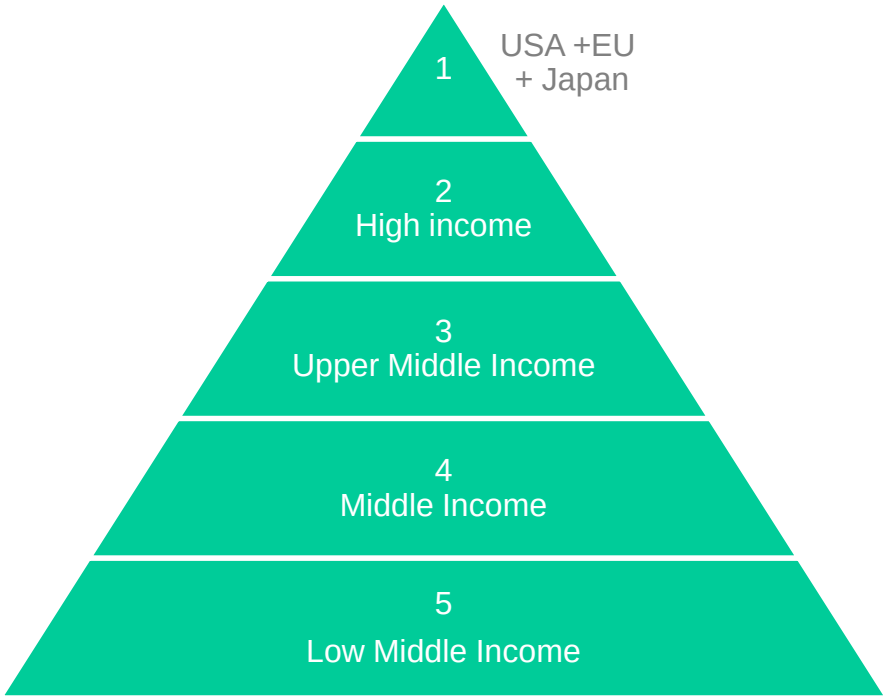
Define Medicine Therapeutic Value



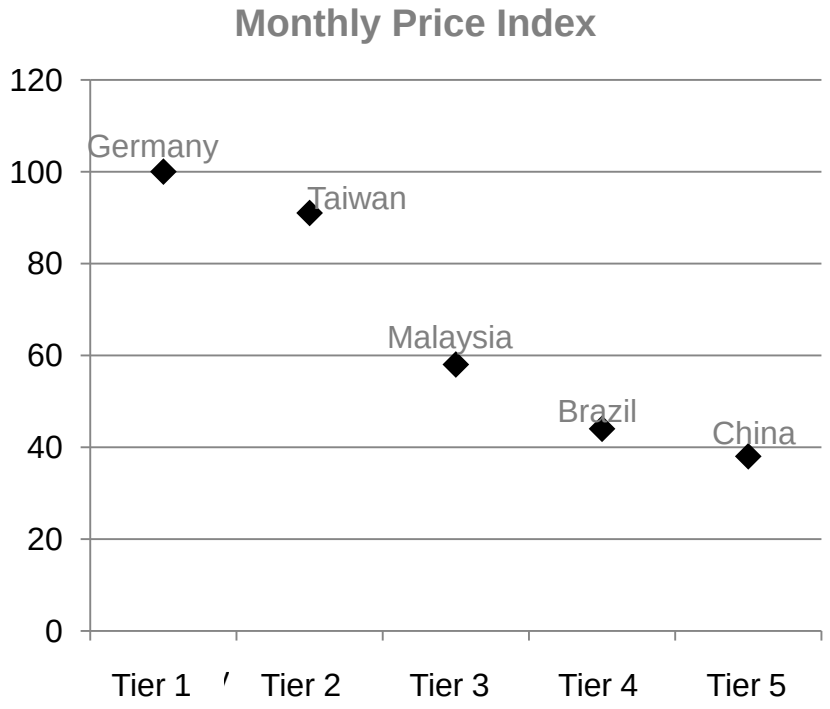
Patient Access & Global Reach

Tiered pricing based on payers' willingness/ability to pay

Global patient reach



Illustrative case study



Modalities of Discovery

nature publishing group

PERSPECTIVES

POINT/COUNTERPOINT

The Future Is Much Closer Collaboration Between the Pharmaceutical Industry and Academic Medical Centers

P Vallance[1], P Williams[1] and C Dollery[1]

A reader of newspaper articles and editorials in some medical journals might conclude that relationships between pharmaceutical companies and academic clinical investigators are dominated by mistrust and the desire of academics to keep industry at a distance from the high moral ground of academia. Fortunately, that is not a correct analysis of a complex situation, but even the perception is an impediment to the pressing need for the parties to work very closely together with a shared desire to improve human health by disc
the un
popula

physiological control mechanisms in living animals and humans, and this in turn led to the emergence of flourishing academic departments of pharmacology and clinical pharmacology. James Black developed β-adrenergic blocking drugs with the treatment of angina in mind, but the opportunity provided by these agents found applications in clinical situations as varied as tremor and heart failure. Many academic scientists became advisers to the pharmaceutical companies, but the information about new approaches to

among the first to discover these, but the information did not readily translate into useful new medicines. A basic limitation was the lack of knowledge of the physiological role of the new targets and their relationship, if any, to the etiology of a disease process. A company might have a handful of biologists working on a new target, but once the information was in the public domain, it was likely to be investigated by hundreds of academic scientists, resulting in much more rapid expansion of knowledge. However, the

Enhancing ties between academia and industry to improve health

S Claiborne Johnston[1, 2], Stephen L Hauser[1] & Susan Desmond-Hellmann[3]

Concerns about conflicts of interest have driven a wedge between academia and the pharmaceutical and devices industries. Although elevated concern for bias is justified, particularly when academics may affect drug sales, partnerships between industry and academia are essential to achieve the full promise of health improvement from the public investment in biomedical research. New models for such partnerships are developing and should be encouraged.

Rancor over conflicts of interest in health care and biomedical research has steadily increased in recent years. Instances of undisclosed financial ties between faculty at aca-

of individual physicians. In research, unstated sources of potential conflicts of interest also have been revealed, raising questions about the reliability of published findings. The need for greater transparency and control of potential conflicts is obvious.

Academic institutions have responded to revelations of conflicts of interest by setting more explicit policies. These policies include requiring full public disclosure of all financial ties, limiting campus access of pharmaceutical company employees and setting strict limits on the types of ties and amounts of compensation. However, in the heat of apprehension and sometimes embarrassment, such policies may have unintended negative consequences, driving a wedge between academia and industry. The atmosphere of inquisition

ing contacts with industry in fear of being called out as corrupt. The press has fueled this concern. We have seen many prominent experts appear on the pages of *The New York Times* for reasons other than glorious discoveries. An article in the *BMJ* listed 100 physicians not 'on the take', implying that others not similarly vetted should be avoided for commentary[3].

Although it is clear that new attitudes and policies about conflicts of interest are necessary, the importance of academic-industry collaboration in improving health cannot be denied. Academic researchers judge their relationships with industry to be very meaningful[4], and nonfinancial relationships may be as important as financial ones[5]. There are many examples of discoveries made and pat-

Drug discovery: new models for industry–academic partnerships

Cathy J. Tralau-Stewart, Colin A. Wyatt, Dominique E. Kleyn and Alex Ayad

covery Centre and Business Development, Imperial College London SW7 2AZ, UK

-focusing of pharmaceutical industry research away from early discovery activities is stimulating velopment of novel models of drug discovery, notably involving academia as a 'front end'. In this the authors explore the drivers of change, the role of new entrants (universities with specialised acilities) and novel partnership models. If they are to be sustainable and deliver, these new models be flexible and properly funded by industry or public funding, rewarding all partners for butions. The introduction of an industry-like process and experienced management teams signals lution in discovery that benefits society by improving the value gained from publicly funded ch.

CORRESPONDENCE

LINK TO ORIGINAL ARTICLE

Nature Reviews Drug Discovery | AOP, published online 30 March 2012; doi:10.1038/nrd3078

Measuring the value of public–private partnerships in the pharmaceutical sciences

Tom. R. Denee, Arnold Sneekes, Pieter Stolk, Antoine Juliens, Jan A. M. Raaijmakers, Michel Goldman, Daan J. A. Crommelin and Jorg W. Janssen

The declining productivity of drug research and development (R&D) analysed in an article by Paul and colleagues (How to improve R&D productivity: the pharmaceutical industry's grand challenge. *Nature Rev. Drug Discov.* 9, 203–214 (2010))[1] is of major concern for private and public stakeholders in the pharmaceutical industry, and in health care more broadly. One strategy to tackle this challenge that has gained momentum in recent years is the establishment of precompetitive public–private partnerships (PPPs) to focus on issues that are too large for single organizations to effectively address alone, such as the development of biomarkers of drug toxicity[2]. Examples of such partnerships include the Innovative Medicines Initiative in the

propose a framework and list of indicators for measuring the value of PPPs in the pharmaceutical sector, based on a literature study and two international stakeholder workshops involving over 50 leaders from industry, academia, government and PPPs, in which the proposed indicators were discussed (see Supplementary information S1 (box)).

The framework resulting from these discussions, which has four stages and four domains for value creation, is shown in FIG. 1, which also includes examples of measurable indicators. The four stages are: input, process, output and outcome. For the 'input' stage, indicators measure the ability of the PPP to bring together the people, funds and

The four domains for value creation address the incentives for participation in a PPP. These domains are: 'networks' (how the public–private platform serves as a bridge between various stakeholders), 'know-how' (access to new techniques, proprietary knowledge and sharing of knowledge), 'human capital' (the training of a new generation of biomedical researchers) and 'financials and operations' (measuring the multipliers gained for partners, the efficiency of the PPP operations and the eventual (economic) benefits resulting from the PPP).

However, defining a set of indicators is just the first step. To fully implement performance measurement in a PPP, three conditions have to be met: first, support from all partners; second, a clearly defined method for data collection; and third, a well-equipped mediating body. Furthermore, when using such frameworks it is important to consider that value measurement should reflect the stage of maturity of the PPP. For example, given the lengthy timelines that are characteristic of the pharmaceutical industry, the emphasis for a PPP may lie on the 'input' and 'process' indicators for the first 5 years. Five years later, 'output' indicators would have a more important role, and in the long term (10 years or more) 'outcome' indicators will become relevant.

Coopetion & Collaboration

1. **Among Companies**
   - Pre-competitive research
2. **Knowledge Chain**
   - Universities, Charities, Foundations, No profit
   - Start Up, Micropharma

Coopetion & Collaboration

Ten Pharmaceutical Companies Unite to Accelerate Development of New Medicines

New Non-Profit Organization to Speed Pharmaceutical R&D

PHILADELPHIA, Sept. 19, 2012 /PRNewswire/ -- Ten leading biopharmaceutical companies announced today that they have formed a non-profit organization to accelerate the development of new medicines. Abbott, AstraZeneca, Boehringer Ingelheim, Bristol-Myers Squibb, Eli Lilly and Company, GlaxoSmithKline, Johnson & Johnson, Pfizer, Genentech a member of the Roche Group, and Sanofi launched ***TransCelerate BioPharma Inc. ("TransCelerate")***, the largest ever initiative of its kind, to identify and solve common drug development challenges with the end goals of improving the quality of clinical studies and bringing new medicines to patients faster.

Through participation in ***TransCelerate***, each of the ten founding companies will combine financial and other resources, including personnel, to solve industry-wide challenges in a collaborative environment. Together, member companies have agreed to specific outcome-oriented objectives and established guidelines for sharing meaningful information and expertise to advance collaboration.

"There is widespread alignment among the heads of R&D at major pharmaceutical companies that there is a critical need to substantially increase the number of innovative new medicines, while eliminating inefficiencies that drive up R&D costs," said newly appointed acting CEO of ***TransCelerate BioPharma***, Garry Neil , MD, Partner at Apple Tree Partners and formerly Corporate Vice President, Science & Technology, Johnson & Johnson. "Our mission at ***TransCelerate BioPharma*** is to work together across the global research and development community and share research and solutions that will simplify and accelerate the delivery of exciting new medicines for patients."

Members of ***TransCelerate*** have identified clinical study execution as the initiative's initial area of focus. Five projects have been selected by the group for funding and development, including: development of a shared user interface for investigator site portals, mutual recognition of study site qualification and training, development of risk-based site monitoring approach and standards, development of clinical data standards, and establishment of a comparator drug supply model.

TransCelerate BioPharma Inc.

Scope: identify and solve common drug development challenges with the end goals of improving the quality of clinical studies and bringing new medicines to patients faster

Initial area of focus = clinical study execution

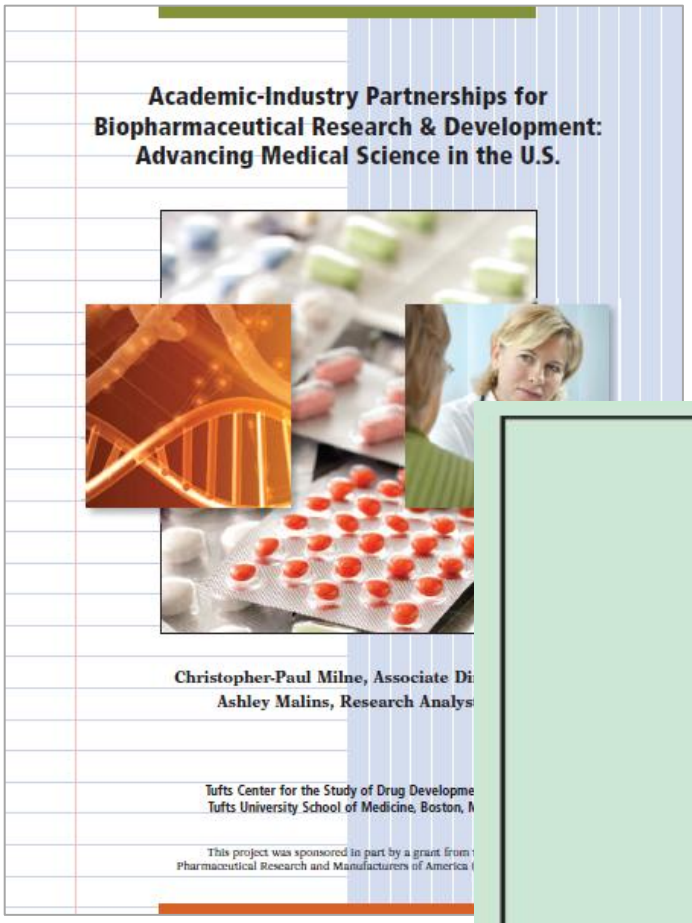
1. development of a shared user interface for investigator site portals
2. Mutual recognition of study site qualification and training
3. Development of risk-based site monitoring approach and standards
4. Development of clinical data standards
5. Establishment of a comparator drug supply model

As shared solutions will be developed – will involve industry alliances (ex. Clinical Data Interchange Consortium, Critical Path Institute, Clinical trials Transformation Initiative), regulatory bodies (FDA, EMA) and CROs.

Coopetion & Collaboration

1. **Among Companies**
   - Pre-competitive research
2. **Knowledge Chain**
   - Academia, Charities, Foundations
   - Start Up, Micropharma

Modalities of Discovery – The "How"



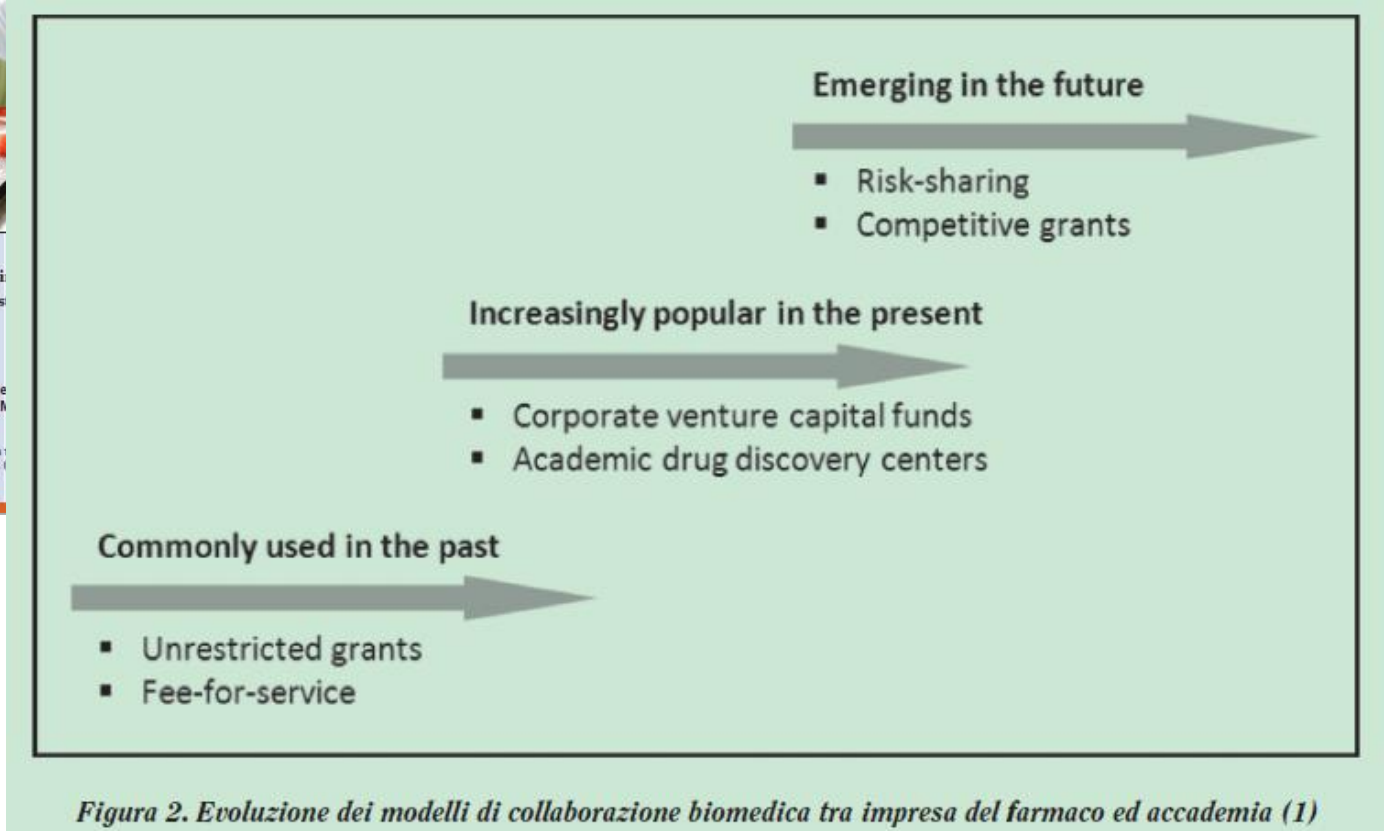


Figura 2. Evoluzione dei modelli di collaborazione biomedica tra impresa del farmaco ed accademia (1)

Preliminary Experience

THE TIMES

Date 19 October 2010
Page 48
Circulation 600000
Scale 100%
Cm² 144
Article AVE £2592

Giant takes up fight against rare diseases

Catherine Boyle

Britain's biggest drugs company has created a division to deal specifically with rare diseases, such as Huntington's, Duchenne muscular dystrophy and hard-to-treat cancers.

The decision by GlaxoSmithKline marks an evolution in attitude by the world's largest drugs groups. Many have ignored diseases that affect hundreds or thousands of patients a year, as they can be difficult to treat and based Sanofi-Aventis is bidding $18.5 billion (£11.6 billion) for Genzyme, the world's most successful developer of rare disease drugs, which charges more than $200,000 a year for Cerezyme, its Gaucher disease treatment.

Marc Dunoyer, global head of GSK Rare Diseases, said: "There is a very tight-knit community within rare diseases; there are small numbers of patients affected by these diseases and they are very often experts on their

Gsk, Telethon e San Raffaele per la terapia genica

di Anna Lisa Bonfranceschi | Pubblicato il 28 Ottobre 2010 09:04

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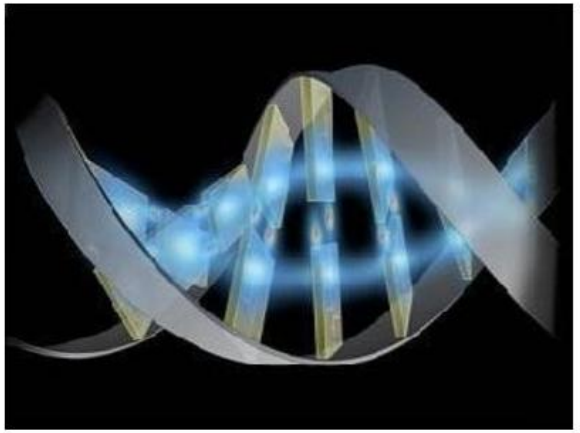
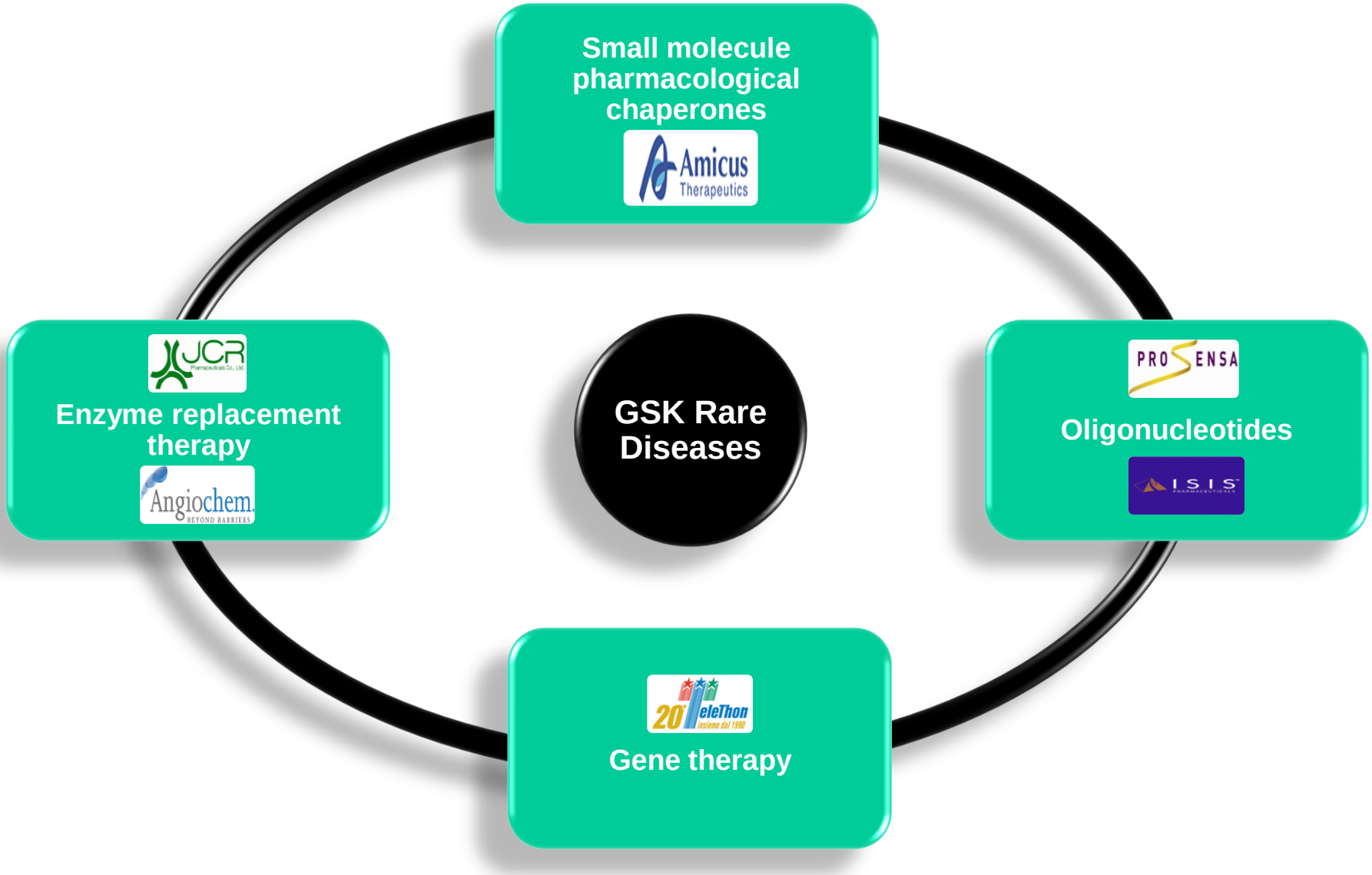


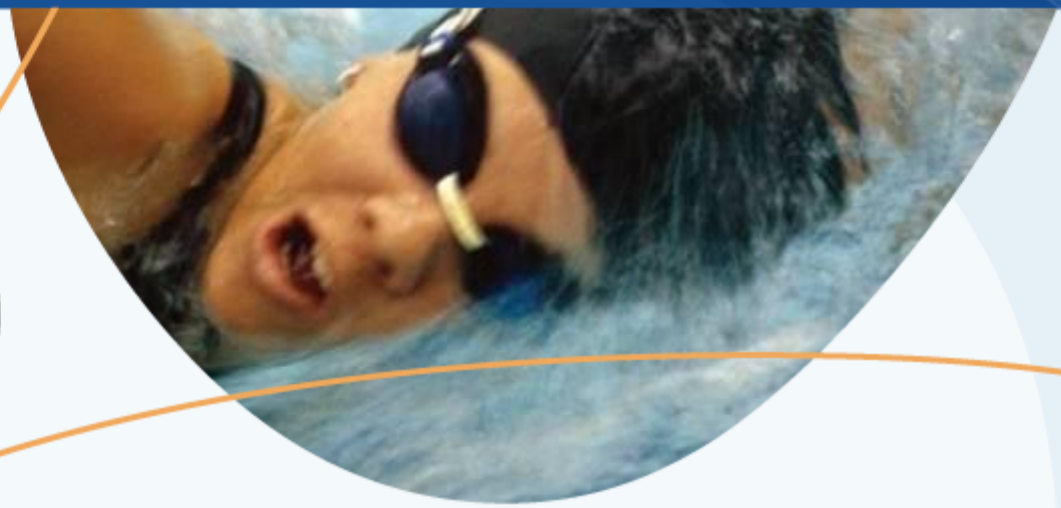
Dieci milioni di euro per sostenere la terapia genica in Italia. È il contributo promesso dal colosso farmaceutico GlaxoSmithKline (Gsk) nell'accordo siglato con la Fondazione Telethon e l'Istituto Scientifico San Raffaele di Milano (Hsr-Tiget). "Un'alleanza di portata storica", ha affermato il presidente di Tehethon Luca Di Montezemolo.

La collaborazione tra Telethon, il San Raffaele e GSK riguarda la messa a punto di protocolli di terapia genica che utilizzano le cellule staminali autologhe, ovvero ricavate dal midollo osseo del malato. Nello specifico la tecnica prevede diverse fasi. La prima è il prelievo dal paziente delle cellule portatrici della variante genetica dannosa. Seguono poi l' "eliminazione" del difetto genetico presente tramite l'utilizzo di "vettori virali"- virus completamente innocui utilizzati solo per veicolare i geni funzionanti -, e la reintroduzione delle stesse cellule, ormai "corrette", nel paziente.

Rare Diseases Investment Dynamics
Alliances & Partnerships



Our mission



To improve the quality of human life

by enabling people to

do more

feel better

live longer