



People and Ideas for Innovation in healthcare

# The MidPharma and the European Network of Paediatric Research at the EMA

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# “Blombergs” on Chiesi Farmaceutici S.p.A

## *We are part of the MidPharma*

- Chiesi Farmaceutici S.p.A. engages in the research, development, production, and sale of pharmaceutical products.
- It offers products for therapeutic areas, such as respiratory, central nervous system, gastro-nutritional, neonatology, musculo-skeletal, and cardiovascular diseases.
- The company’s products include:
  - Beclometasone dipropionate and formoterol fumarate fixed dose combination pressurised metered dose inhaler for asthma,
  - Tobramycin nebuliser solution
  - Curosurf treatment for neonatal respiratory distress syndrome
  - Peyona for neonatal apnoea
- ❑ The company sells its products through a strategic alliances network of pharmaceutical groups.
- ❑ Chiesi Farmaceutici S.p.A. was founded in 1935 and is based in Parma, Italy.
- ❑ It operates research and development facilities in Italy, France and the United States.
- ❑ The company has operations in Spain, the United Kingdom, Germany, Austria, Bulgaria, the Czech Republic, Hungary, Poland, Romania, Slovenia, the Slovak Republic, the Netherlands, Greece, the Russian Federation, Brazil, Pakistan, Turkey, and China.

**Mid-PHARMA are companies with ~1 billion euros sales**

## Our shared interest, our Patients



# Our shared bleak financial environment where private and public expenditure is rapidly falling

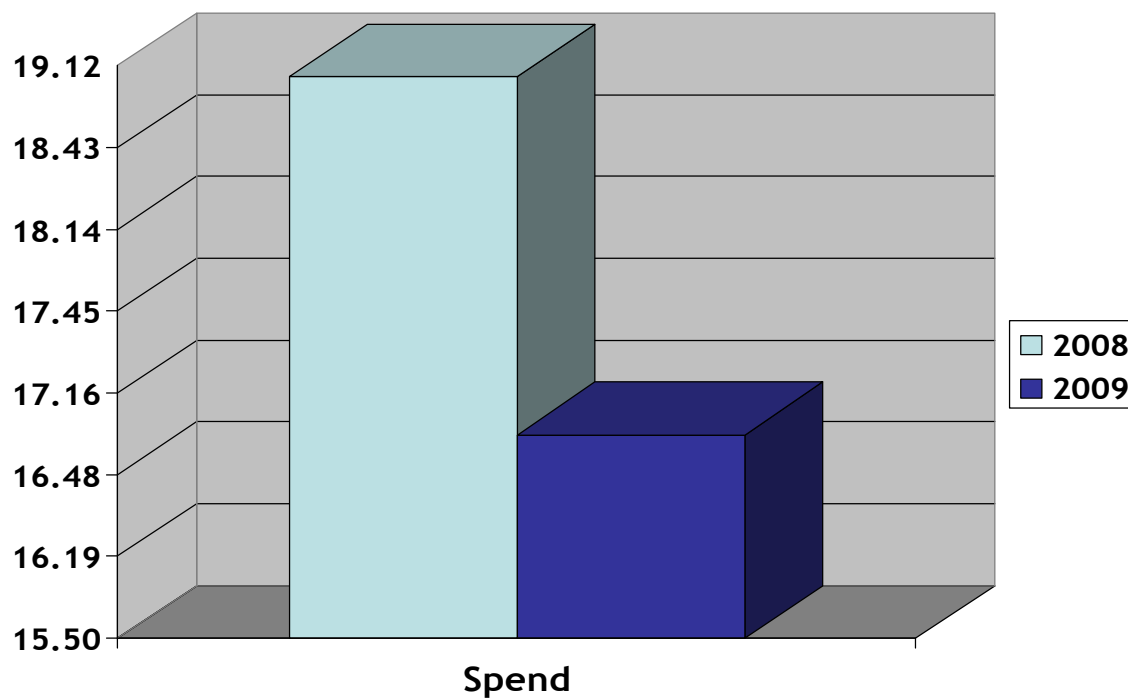


From Fair weather to.....



.....to foul weather

## US Pharmaceutical Company Spending on R&D (billion dollars) is rapidly falling



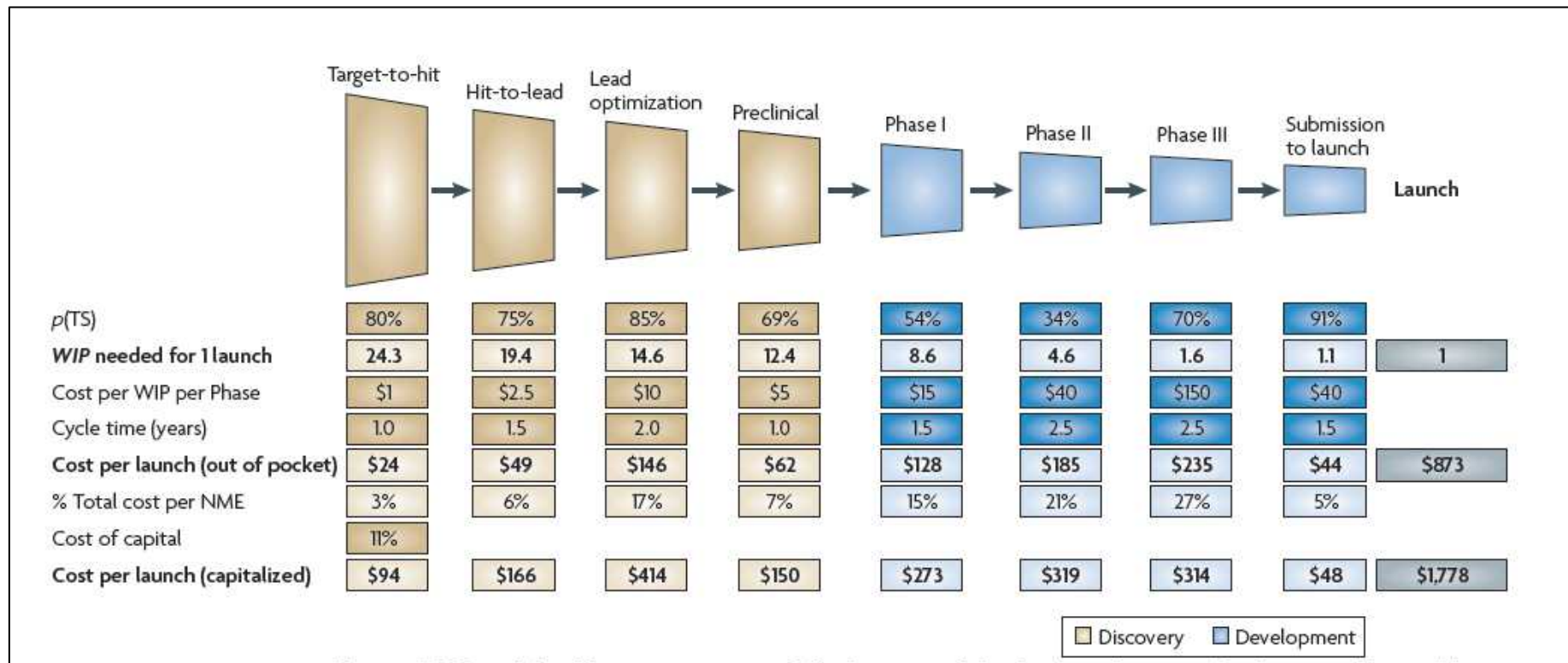
**Worldwide Pharma spending has dropped by 21% in 2009**

# The challenge: drug approvals decrease whilst R&D spend increases



FDA drug approvals and PHARMA spending

# Unit costs are low at the early stage but their accumulative cost is high to deliver into man NMEs



But how do you choose the targets, are they linked to the patient's needs?

You can either reduce costs or reduce attrition or both.....

$$P = \frac{WIP \times p(TS) \times V}{CT \times C}$$

R&D productivity ( $P$ ) can be viewed as a function of the elements comprising the numerator – the amount of scientific and clinical research being conducted simultaneously, designated here as the work in process ( $WIP$ ),

the probability of technical success  $p(TS)$  and the value ( $V$ ) – divided by the elements in the denominator, the cycle time ( $CT$ ) and cost ( $C$ ).

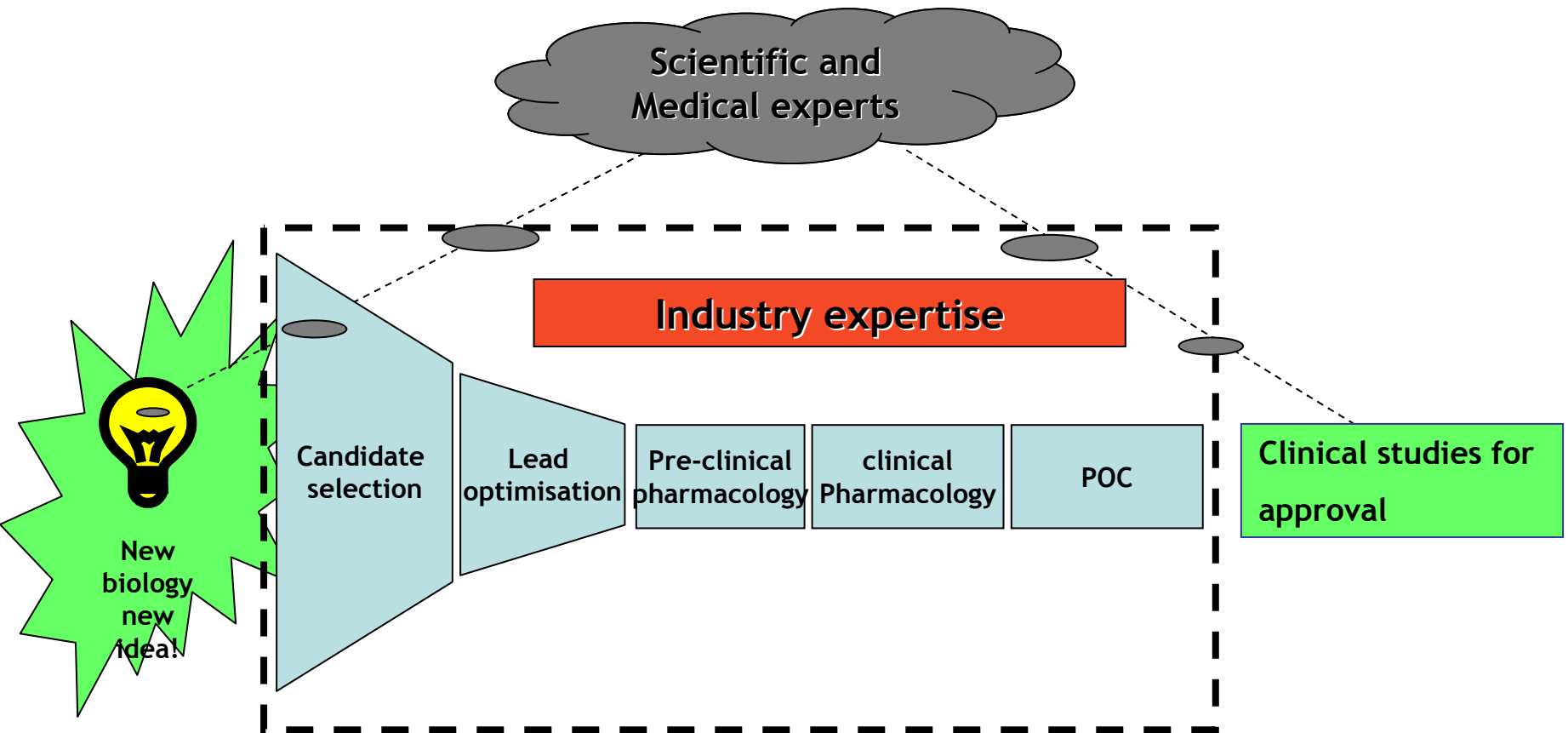
Poor choice of the targets, which were not linked to the patient's needs?

.....But how ~ improve the choice of targets?

### ***“Making the right choices”***

- **Mid pharma** recorded total ethical sales of \$66 billion in 2005, which has grown with a **compound annual growth rate (CAGR) of almost 5%** from 2005 to 2010. In fact, mid pharma growth has outstripped big pharma growth during this period.
- **Externalization** has been their practice, both by in-license and acquisition from smaller companies and outsourcing much of their functions. For a smaller company, dealing with mid pharma may be more appealing than dealing with big pharma.
- The Mid-PHARMA have more bargaining power, which may allow the development company to secure a more financially rewarding agreement. Compared to big pharma, mid pharma companies tend to have a **narrower focus in a particular dimension - often in terms of therapy or geography.**
- But in many Mid-PHARMA companies **keep core drug development activities in house e.g., hit to lead and lead optimization and pre-clinical pharmacology** as Forest, King, Chiesi, Shire and Almirall

# The new paradigm for Medicines Development



- Each year, worldwide more babies are treated for RDS with CUROSURF than any other surfactant.
- Low volume for easy administration
- CUROSURF delivers more surfactant in a smaller overall volume for efficient instillation that may help to minimize complications.<sup>2-6</sup>
- Clinical studies have not established that lower volume results in superior efficacy or safety based on clinically relevant end points.
- Rapid onset of action
- CUROSURF goes to work fast, improving oxygenation within 5 minutes.<sup>7,8</sup>
- Physiological end points (eg, faster reduction in FiO<sub>2</sub>) have not been proven to impact key clinical outcomes such as mortality due to RDS.

**Developed in close collaboration**

**with the Karolinska University and European neonatologists**

## The Peyona story

- Peyona is a solution for infusion (drip into a vein) that contains the active substance caffeine citrate (20 mg/ml). The solution can also be given by mouth.
- Peyona is used to treat primary apnoea in premature newborns. Apnoea in newborns is the cessation of breathing for more than 20 seconds. Primary means that the apnoea has no obvious cause.
- Because the number of patients with primary apnoea of premature newborns is low, the disease is considered 'rare', and Peyona was designated an 'orphan medicine' (a medicine used in rare diseases) on 17 February 2003.
- Approved by the EMA in 2009

**Developed in close collaboration with European neonatologists  
to improve access to this pharmaceutical**

- Vials 300mg 4ml of nebulised Tobramycin
- Two pivotal clinical studies
- One head to head study versus TOBI<sub>(R)</sub>
- Investigator initiated trials with new nebulisers



Considerable help from Paediatric and Adult experts in CF

## Close working collaboration with the ECFS-CTN



- The ECFS-CTN provides:
- Protocol review
- Access and feasibility of clinical research centres
- Itemised cost base
- Balance between academic and pharmaceutical development

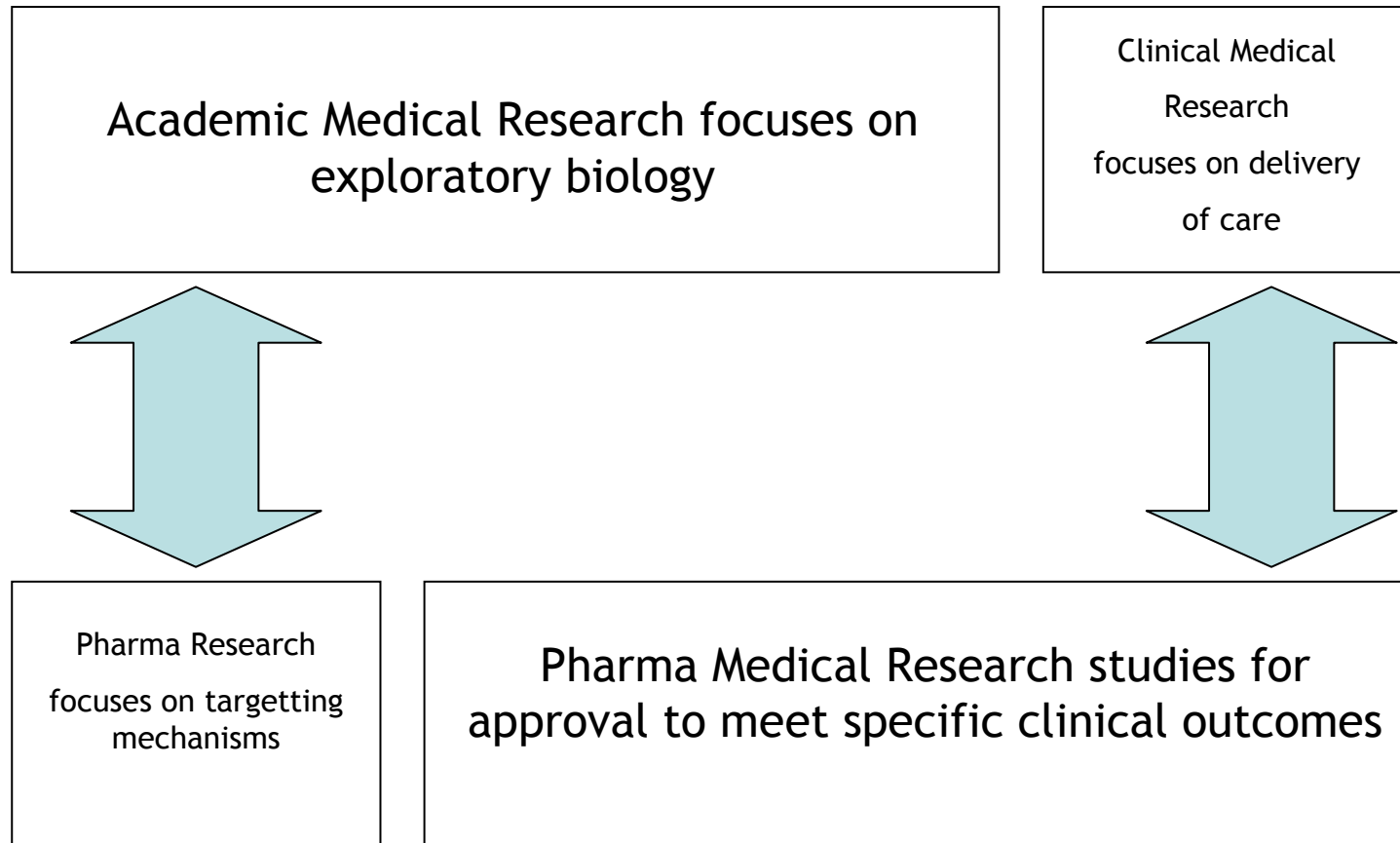
Sole Pharmaceutical sponsor of the Patients registry

# Paediatric Use Marketing Authorization (PUMA)

## Neurosis & Neomero

- **Neurosis** was part of the 3<sup>rd</sup> call 2009 aiming at evaluating budesonide in prevention of Bronchopulmonary Dysplasia
- **Neomero** was part of the 4<sup>th</sup> call 2010 aiming at evaluating meropenem as antibiotic therapy for sepsis and bacterial meningitis
- **Sponsor: Clinicians' Consortia ⇒ Investigators' Initiated Trials**
- **Chiesi** is a partner for drug supply and PUMA preparation and submission
- **Chiesi Neurosis Team:** R. Garzia, C. Baldazzi, L. Fabbri, S. Armani, L. Storari, P. Miloux, GN. Castiglione
- **Chiesi Neomero Team:** R. Garzia, G. Lasagna, L. Fabbri, R. Musa, E. Pani, P. Miloux, GN. Castiglione

# The changing balance between academic and industrial capabilities



A major need to train physicians and scientists in the medicines development

# Innovative Medicines Initiative (IMI) designed to remove bottle necks in medicines development (including training)



**EMTrain and PharmTrain established to train medical scientists in Medicines development**

## National efforts to train .....



The Faculty of Pharmaceutical Medicine

*Advancing the science and practice of pharmaceutical medicine for the benefit of the public*

### Curriculum for the CCT in Pharmaceutical Medicine

#### There are seven Modules of Training:

- Medicines Regulation (can be an internal or external provision)
- Clinical Pharmacology (can be an internal or external provision)
- Statistics and Data-management (can be internally and externally provided)
- Clinical Development (can be internally and externally provided)
- Healthcare market place (can be internally and externally provided)
- Drug Safety Surveillance (can be internally and externally provided)
- Generic Module of interpersonal and management Skills (Internally provided)

Postgraduate Education &  
Training of Pharmaceutical  
Physicians Leading to a  
Certificate of Completion of  
Training (CCT)

*Prof Peter Stonier MPhD  
Director of Education & Training*

214 trainees

**Similar courses in Belgium and Switzerland**

## Take away messages....

- Exploratory biology of disease is *more* successful when led by Medical and Scientific experts
- Design of proof of concept and clinical development needs *major input* for Medical and Scientific experts
- *Pharma skills lie with development of the molecules needed for the treatment*
- Collaborations between Pharma and Paediatric Scientific and Medical experts requires training in the skills for medicines development