EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Background to the meeting – Paediatric Investigation Plans for Gaucher.

Presented by: Dr Elin Haf Davies
Scientific Administrator, Paediatrics

Gaucher Disease in the paediatric population

Lysosomal storage disorder

Deficiency of glucocerebrosidase

Accumulation of its substrate glucocerebroside

All three types present in childhood ~ PIPs apply

L 378/20 EN Official Journal of the European Union 27.12.2006

REGULATION (EC) No 1902/2006 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 20 December 2006

amending Regulation 1901/2006 on medicinal products for paediatric use

(Text with EEA relevance)

THE EUROPEAN PARLIAMENT AND THE COUNCIL OF THE EUROPEAN UNION,

HAVE ADOPTED THIS REGULATION:

Having regard to the Treaty establishing the European Community, in particular Article 95 thereof,

Article 1

Background – numerous PIPs submitted

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	Indications + Waiver	Clinical Studies	Completion date / Date Decision signed
Velagulcerase alfa - ERT 000407-08/ 000556-09	Gaucher Disease, Types 1 and 3 Waiver < 2 years Type 2 Waiver < 18 years.	1. Open-label extension study of velaglucerase alfa enzyme replacement therapy in adults and children with Type 1 Gaucher Disease 2. Open-label efficacy and safety study of velaglucerase alfa enzyme replacement therapy in children and adolescents with Type 3 Gaucher Disease	By July 2015. December 2009**
Taliglucerase alfa - ERT 000648-09	Gaucher Disease, (except acute neuronopathic) Waiver < 2 years (acute neuronopathic) Waiver < 18 years.	1. Double-blind, randomised, efficacy and safety study of two doses of taliglucerase alfa enzyme replacement therapy in children and adolescents with Gaucher Disease (non-neuronopathic and chronic neuronopathic). 2. Open-label switchover trial to assess the safety and efficacy of taliglucerase alfa in adult and paediatric patients with Gaucher Disease treated with imiglucerase. 3. Extension trial to assess the long term safety and efficacy of taliglucerase alfa in adult and paediatric patients with Gaucher Disease.	By December 2014. April 2010
Eliglustat - SRT 000461-11	Gaucher Disease, Types 1 and 3 Waiver < 2 years Type 2 Waiver < 18 years	1. Open label, two cohort (with and without imiglucerase), multicentre, historical-controlled study to evaluate pharmacokinetics (PK), safety, and efficacy of eliglustat in paediatric patients with Gaucher disease type 1 (GD1) and type 3 (GD3).	By September 2022. February 2012

**Assessment coincided with Cerezyme shortage.

PDCO Summary of agreed PIPs

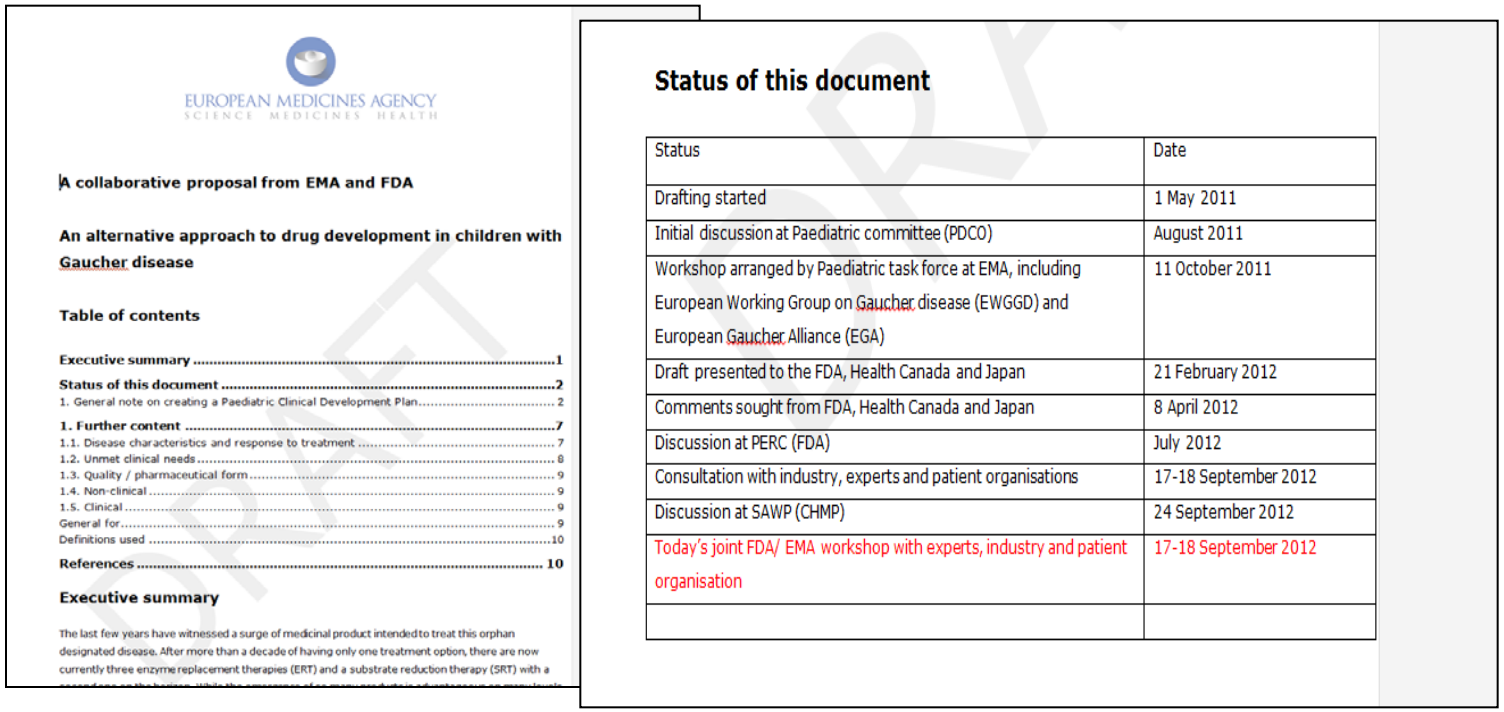
- Target group are **mild disease / stabilised** disease in nearly all studies
- **The current therapeutic needs of severe visceral and CNS disease remains unstudied**

  - Bone
  - Lung
  - Growth
  - Long-term efficacy (dose escalation)
  - Prevention vs symptom management (dose selection)

PDCO Summary of agreed PIPs

- Total paediatric patients to be recruited are between 107 and 120 [with 10 Type III]. This equates to > ½ of the identified paediatric European cohort
- The is likely to lead to **feasibility issues** 
- **Ethical implications** – risk of uncompleted studies
- **Economic implications** – times are tough for all, so why not share the cost

Moving forward



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A collaborative proposal from EMA and FDA

An alternative approach to drug development in children with Gaucher disease

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Executive summary

The last few years have witnessed a surge of medicinal product intended to treat this orphan designated disease. After more than a decade of having only one treatment option, there are now currently three enzyme replacement therapies (ERT) and a substrate reduction therapy (SRT) with a

Status of this document

Status	Date
Drafting started	1 May 2011
Initial discussion at Paediatric committee (PDCO)	August 2011
Workshop arranged by Paediatric task force at EMA, including European Working Group on Gaucher disease (EWGGD) and European Gaucher Alliance (EGA)	11 October 2011
Draft presented to the FDA, Health Canada and Japan	21 February 2012
Comments sought from FDA, Health Canada and Japan	8 April 2012
Discussion at PERC (FDA)	July 2012
Consultation with industry, experts and patient organisations	17-18 September 2012
Discussion at SAWP (CHMP)	24 September 2012
Today's joint FDA/ EMA workshop with experts, industry and patient organisation	17-18 September 2012

The road ahead starts here …

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Paediatric Gaucher disease – exploring a new way forward

Presented by: Dr Elin Haf Davies
Scientific Administrator, Paediatrics

Proposal

- Gaucher disease has led the way in orphan metabolic disorders for drug development
- It can continue to lead the way with innovative ways.
- Such an approach would ensure that study is:
  - in-line with patient needs
  - minimises individual patient burden
  - meeting expectations of experts
  - avoid ‘aggressive’ recruitment strategies
  - identifies necessary data to make an informed choice on drug choice** and dose
  - ** stress that the aim of this is to demonstrate that all are as good as each other

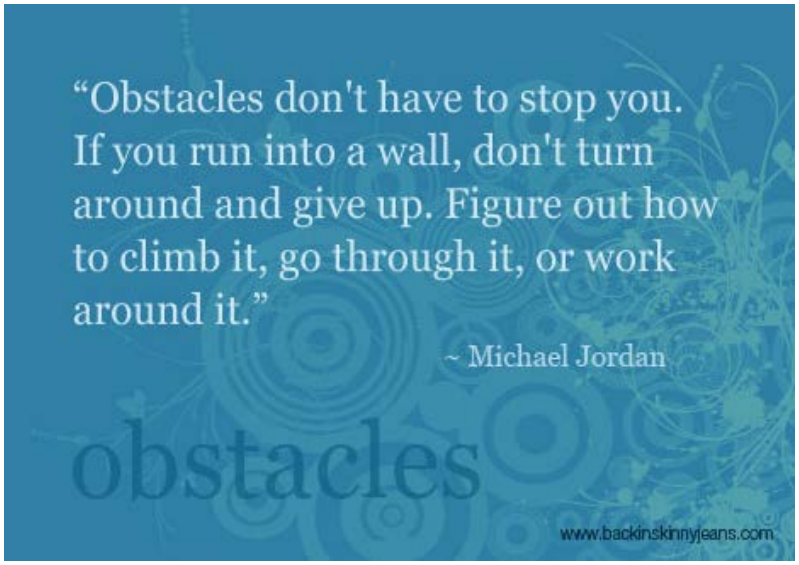
Proposal

- Possibilities for considerations are:
  - A standardised paediatric development plan
  - Extrapolation approach using currently available data
  - A multi-company, multi-product study to evaluate non-inferiority of all products to immiglucerase (based on most amount of data and experience)
  - Other options …

Obstacles

- Engaging a multitude of stakeholders
- Different to the traditional way of working
- Bringing competitors together to engage in collaborative dialogue
- Timing of each individual development
- Many many many more …

Obstacles



Obstacles Are Windows Of Opportunity

"If you can find a path with no obstacles, it probably does not lead anywhere" – Frank A Clark

The NEW ENGLAND JOURNAL of MEDICINE

Perspective

MARCH 3, 2011

Collaborative Clinical Trials

Arthur J. Moss, M.D., Charles W. Francis, M.D., and Daniel Ryan, M.D.

Ongoing improvement in health care require

Advantages of Collaborative Clinical Trials

- Use of a single protocol with uniform eligibility criteria and end points involving the same control or comparison group
- Enhanced patient enrollment, especially when the disease process affects a relatively small subgroup of patients, and shorter time to trial completion
- Reduced competition for patients when similar yet independent trials are conducted
- Comparison of similar yet different drugs or devices that target the same disease process
- Evaluation of the effect of combining different therapies that target diverse pathways or mechanisms in complex medical disorders
- Robust clinical trial results, with identification of patients who do and those who do not benefit from specified therapies
- Reduced expenditures of the individual collaborating entities funding the trial

of death from arrhythmias after myocardial infarction.[1] This landmark study showed that two approved antiarrhythmic agents were associated with excessive mortality, and these findings changed the practice of clinical cardiology. If separate studies had been done, they would have taken much longer to complete, and it's unlikely that such a clear result would have been obtained.

The Sudden Cardiac Death in

A standardised paediatric development plan

Extrapolation approach using currently available data

A multi-company, multi-product study to evaluate non-inferiority of all products

Other options …