Gene therapy product for Acute Intermittent Porphyria: Phase I Clinical trial

- **Adenoassociated viral** (AAV) **vectors** are very promising tools for therapeutic gene delivery, since they are safe and they induce an efficient and long-term transduction.
- In collaboration with **uniQure** a gene therapy product for the treatment of Acute Intermittent Porphyria has been developed and is currently being evaluated in **phase I clinical trial**.
- A **new AAV expression system** has been developed and an **AAV production system** has been optimized.
  - AAV tetracycline-inducible system
  - liver and brain specific expression.

AAV vectors

- Safe, with no or only limited toxicity.
- Induce an efficient and long-term transduction in quiescent cells, a very important point to be effective in adult tissues.
- Genes carried by rAAV vectors have been efficiently transduced in skeletal muscle, heart, brain, joints, eyes and liver leading to stable expression at therapeutic levels.

AAV-PBGD: gene therapy product for Acute Intermittent Porphyria (licensed to UniQure)

- In collaboration with the Dutch company uniQure, a gene therapy product for the treatment of Acute Interment Porphyria has been developed.
- Orphan designation approved.
- Grant from the EU's FP7 program (AIPGENE consortium) to bring this product forward to completion of a Phase I/II study in humans.
- The product is currently being evaluated in **phase I clinical trial** at the Clínica Universidad de Navarra and Hospital 12 de Octubre.
- Phase II clinical trial will be started in the near future.
- References:

Unzu C et al. Helper-dependent adenoviral liver gene therapy protects against induced attacks and corrects protein folding stress in acute intermittent porphyria mice. *Hum Mol Genet*. 2013 Jul 15;22(14):2929-40.

Unzu C et al. Sustained enzymatic correction by rAAV-mediated liver gene therapy protects against induced motor neuropathy in acute porphyria mice. *Mol Ther*. 2011 Feb;19(2):243-50.

AAV Platform

- A new AAV tetracycline-inducible system for liver and brain specific expression has been developed.
- Recombinant AAV viruses to express cytokines, shRNAs, antibodies and many other different genes have been constructed and produced for the treatment of infectious diseases, malignancies or hereditary metabolic disorders.
- Gene therapy products for rare diseases, hyperoxaluria and Wilson disease are under development.
- AAV vectors for different research groups at CIMA, Universidad de la Laguna, Universidad Complutense de Madrid, Centre Esther Koplovitz (CEK), San Raffaele Scientific Institute have been designed and produced.
- **Competitive Advantage:** Developed tools that allow designing therapeutic vectors according to the characteristics of the disease, such as tissue specificity or controlled expression.

Intellectual Property

- PCT/NL2009/050584. Porphobilinogen deaminase gene therapy. (*Shared ownership Proyecto Biomedicina CIMA SL and UniQure).*
- PCT/ES2010/070715. Regulated expression systems.

References

Vanrell L et al. Development of a liver-specific Tet-on inducible system for AAV vectors and its application in the treatment of liver cancer. *Mol Ther*. 2011 Jul;19(7):1245-53.

Pañeda MA et al. Safety and liver transduction efficacy of rAAV5-cohPBGD in non-human primates: A potential therapy for Acute Intermitent Porphyria. *Hum Gene Ther*. 2013 Sep 26.

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