**INTRODUCTION**

Pyruvate Kinase (PK), catalyzes the last step of Glycolysis

\[ \text{Phosphoenolpyruvate} 
\rightarrow 2 \text{Pyrurate} + \text{ATP} \]

Loss in PK activity impairs the cell metabolism causing Pyruvate Kinase Deficiency (PKD), an autosomal recessive disease caused by mutations in the PKLR gene (Liver and Red Blood Cell isomer).

We have designed a successful preclinical protocol in a PKD mouse model based on autologous transplantation of hematopoietic stem cell (HSC) genetically corrected by a Therapeutic Lentiviral Vector (PGK-coPKLR/Wpre*-LV). This vector has already being designated as Orphan Drug by the European Medicines Agency (EMA) and Food and Drug Administration (FDA).

**AIMS**

Define the minimal proportion of corrected cells required to achieve a therapeutic effect in PKD patients

**EXPERIMENTAL DESIGN**

1° Approach: wt and PKD total bone marrow mice

2° Approach: Transduction of PKD hematopoietic progenitors

**RESULTS**

Phenotype rescue depending on the wt/PKD cell proportion transplanted

Phenotype rescue depending on therapeutic vector MOI used

**CONCLUSIONS**

- PKD correction was found when total bone marrow contained at least 20% of non-deficient cells
- PKD correction by the therapeutic vector was achieved when at least 0.3 copies of the vector were detected among the total peripheral blood cell populations
- Splenomegaly and weight confirmed results obtained in peripheral blood and corroborated the therapeutic properties of the developed clinical vector