Challenges of New Drug Development: From Laboratory to Clinic to Hollywood

(Extraordinary Measures, The Story Behind the Scenes)

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Abstract

Pompe disease is an autosomal recessive disorder of glycogen metabolism caused by a deficiency of the lysosomal enzyme acid alpha-glucosidase (GAA). Patients present differentially with variable rates of progression ranging from a rapidly progressive course, often fatal by 1 year of age, to a slower, but nevertheless relentlessly progressive course. Prior to 2006, therapy for Pompe disease remained essentially palliative and the natural history of infantile onset Pompe disease was uniformly poor with death occurring usually by age 1 year from cardiomyopathy or respiratory failure. Research on the development of enzyme replacement therapy (ERT) started in the early 70's but not until mid 90's that the *in vivo* efficacy of ERT was first demonstrated in the animal model of Pompe disease. Subsequently, pilot human phase I/II studies of recombinant human GAA began in 1999, followed by phase II clinical trials and pivotal trials which eventually leads to market approval of the Myozyme® (alglucosidase alfa, Genzyme, Cambridge, MA, USA) in 2006 and more recently Lumizyme® in 2010 for late-onset patients. The story of a father searching for a life-saving drug for his two children with Pompe disease and the development of this new drug has been adapted to a Hollywood movie entitled ***"Extraordinary Measures"*** featured Harrison Ford and Brendan Fraser. The story behind the scenes of the movie and the challenges of new drug development will be discussed.