

Novel Natural History Study to answer question in Rare Disease

The Natural History Study of the rare lysosomal disease alpha-Mannosidosis will answer the question; why the rare disease develops as it does? The first patients have been included in the first Natural History Study of the disease, being conducted under the HUE-MAN project, a 6th framework, EU grant supported initiative. The study, which is planned to include 38 patients, has recently been approved by the Independent Ethics Committees in Germany, United Kingdom, Czech Republic and Norway and is being performed at four clinical centers: Children's Hospital, University of Mainz, Mainz, Germany; Willink Biochemical Genetics Unit, Royal Manchester Children's Hospital, Manchester, United Kingdom; Department of Pediatrics, Charles University, Prague, Czech Republic; Department of Medicine, University Hospital of Tromsø, Tromsø, Norway and with the Danish biotech company Zymenex as the industrial partner and natural history study coordinator in the project.

The HUE-MAN's project objective is to transfer and expand the knowledge obtained from the 5th framework EU grant supported EURAMAN project studies, which successfully established an enzyme replacement therapy for a mouse model of alpha-Mannosidosis and demonstrated correction of storage in many tissues including brain, after administration of lysosomal acid α -Mannosidase (rhLAMAN). The main objective of the HUE-MAN project is to investigate and establish clinical parameters in the alpha-Mannosidosis mouse model and to perform a natural history study of the human disease in patients in order to define clinical endpoints for the future clinical trials in alpha-Mannosidosis. Furthermore, in parallel, the HUE-MAN partner Zymenex will establish conditions for the large-scale production of rhLaman that can pave the way for a First Clinical Trial in Man.

Alpha-Mannosidosis is a rare inborn disorder caused by the lack of the lysosomal enzyme α -Mannosidase, resulting in mental retardation, skeletal changes, hearing loss, recurrent infections and progression to early death. The children are often born apparently normal, and their conditions worsen progressively, without any possibility to prevent this evolution. In the children that are born healthy, a therapy initiated at an early age could contribute to a normal development. Today, the most promising therapy for lysosomal storage disorders is enzyme replacement therapy (ERT); where the enzyme lacking in the patient is introduced into the blood stream, from where it is internalised by the cells and reaches the lysosomes, acting as the endogeneous enzyme.

The Zymenex pipeline includes the recombinant derived α -Mannosidase enzyme **Lamazym** (rhLaman), for the treatment of the lysosomal disease alpha-Mannosidosis. Lamazym is presently in pre-clinical development.

Supplemental information

The HUE-MAN partnership <http://www.uni-kiel.de/Biochemie/hue-man/> was initiated in April 2006 and is supported by a 3 year, €3.2 million, EU 6th framework grant. The mission is to bring together the critical mass of European scientists to achieve a break through in the quest for understanding and therapy of an inherited disease for



which there is no therapy today, and thereby also contribute to such a progress for other similar and likewise incurable diseases. To reach this ambitious goal the 11 work packages of the project are closely linked and a successful outcome depends upon the close collaboration of the two SME's (Small and Medium Enterprise – non-academic) and eight academic partners. The current project brings together cell and molecular biologists, clinicians with regular patient contact, neuro-pharmacologists with expertise in behavioural analysis, epidemiologists and biochemists with experience in large scale enzyme production and toxicology testing to set up the conditions and knowledge for eventually introducing the rhLaman drug into first clinical trials.

Zymenex A/S is a Scandinavian biopharmaceutical company, founded in 1998, with headquarters in Hillerød north of Copenhagen, Denmark and research laboratories in Stockholm, Sweden. The company is focused on research and development of pharmaceutical products for the treatment of rare, genetic diseases, for which there is no treatment today and which, due to the small patient populations, fall within "Orphan Diseases" and the Orphan Drug Acts. Zymenex is developing several human recombinant enzymes that can be used for therapy within the specific disease areas. Enzyme replacement therapy is a well-known treatment method and there are a number of products on the market today that validates the company concept. Zymenex is supported financially by the Danish venture capital investors BankInvest and Sunstone Capital (formerly Vækstfonden).

Sincerely

Zymenex A/S

July 4, 2007

Further information:

Zymenex A/S, Roskildevej 12C, DK-3400 Hillerød, Denmark (Team leader/Responsible Scientist: CEO, Dr. Jens Fogh, DVM) + 45 48 25 00 54

Children`s Hospital, University of Mainz, 55101 Mainz, Germany (Team leader/Responsible Scientist: Ass. Prof. Dr. Michael Beck, MD)

Willink Biochemical Genetics Unit, Royal Manchester Children`s Hospital, Manchester M27 4HA, United Kingdom (Team leader/Responsible Scientist: Dr. Ed Wraith, MD)

Department of Pediatrics, Charles University, 120 00 Prague 2, Ke Karlovu 2, Czech Republic, (Team leader/Responsible Scientist: Prof. Dr. Jiri Zeman, MD, DrSc)

Department of Medicine, University Hospital of Tromsø, N-9038 Tromsø, Norway (Team leader/Responsible Scientist: Ass. Prof. Dr. Dag Malm, MD, PhD)

Department of Biochemistry, University of Kiel, D-24018 Kiel, Germany (Team leader/Responsible Scientist: Prof. Dr. Paul Saftig, PhD, HUE-MAN project manager)