

Danish Biotech Company in Phase I/II clinical trial in seriously ill children with MLD

Danish-Swedish researchers in the biotech company Zymenex have developed Metazym, a lysosomal enzyme, for the treatment of the lethal disease Metachromatic Leukodystrophy (MLD). The Danish Medicines Agency and the Independent Ethics Committee approved a Phase I/II clinical trial, which is now being performed in Denmark on patients from around Europe.

Seriously ill children between the ages of 2-5 years, from several European countries are participating in the trial. The children suffer from a rare and until now incurable disease, Metachromatic Leukodystrophy (MLD), which paralyses the nervous system in such a way that the children die.

“The disease is caused by a gene-mutation. The symptoms arise when the children are very young and their motor function development recedes or stops. When the disease is diagnosed there is no available treatment today. The patient families and specialists from around the world are therefore following this field very closely, “ says Dr. Christine i Dali. “Today a number of similar enzyme replacement therapies, for other lysosomal diseases, have been approved. This has greatly improved the quality of life for patients suffering from these diseases.”

The team of medical specialists are, during the next year, conducting and overseeing the trial, which is being performed at the Danish private clinical trial unit PhaseOneTrials A/S, which is responsible for the practicalities with regards to treating the children. Chief investigator for the project is Chief physician Dr. Allan M. Lund, University Hospital Copenhagen, who is the leading specialist in Denmark within rare diseases, such as the lysosomal enzyme deficiencies. Dr. Christine i Dali, who is a specialist in paediatrics, is responsible for testing the enzyme in the patients. She has a broad background within child neurology and is employed at the University Hospital Copenhagen and in a PhD research project.

The clinical trial takes place in Denmark and is conducted by a team of medical specialists from Denmark, Sweden, Germany, United Kingdom, France, and the United States and the Danish biopharmaceutical company Zymenex A/S. The trial comprises a Phase I Safety and Tolerability study and the patients are thereafter rolled over into a Phase II dose-response study.

The children have all been diagnosed by European specialists within child neurology from countries such as Germany, United Kingdom and France. All patients that take part in the trial, participated in a screening, based on the scientific criteria and were evaluated as eligible to participate. The goal of the trial is to fulfil the requirements of the authorities and to achieve a treatment for all MLD patients as fast as possible.

“The patient’s guardians and clinical specialists from all over the world are following the research in this area with great interest” says Dr. Christine i. Dali. “Today we have a number of similar replacement therapies for six of the other lysosomal diseases, which has resulted in an improved quality of life for patients suffering from these diseases”, she explains.

“We have covered a good part of the ground, but we still have a long way to go before we can say we have a breakthrough.” CEO Jens Fogh, Zymenex, has a challenging 2007, with crucial phases for the development of the company’s lead project, the enzyme Metazym. If good progress is made in the experimental treatment of the children, it is already planned to start a parallel clinical trial with the enzyme in the United States.

The enzyme used in the trial is similar to the human enzyme that the MLD patients lack. Studies done in MLD mice have shown that the enzyme removes a sulphatide that can up-concentrate in nerve cells and result in paralysis. Due to the life threatening character of the disease, the clinical trial is performed on affected patients, in order to ascertain a potential effect of the enzyme as quickly as possible.

Therapies for rare diseases called “Orphan Diseases” are regulated by the Orphan Drug Acts in Europe and the United States. Companies developing products for orphan diseases have, according to the Orphan Drug Acts, the possibility for special motivating initiatives, with regards to “fast track approval” and market exclusivity in Europe and the United States.

The Orphan Drug Acts in the United States and Europe have provided breakthroughs for the development of therapies for many rare diseases such as Gaucher, Fabry, MPS-1 and Pompe, which like MLD are lysosomal diseases.

Supplemental information:

Metachromatic Leukodystrophy (MLD), is one of 45 diseases within the family of Lysosomal Storage Diseases.

MLD is caused by an increased concentration of sulphatide in cells and an ensuing breakdown of “myelin”, a substance that protects the nerves in the brain and the rest of the body. The disease occurs due to a lack of the enzyme Arylsulfatase A (ASA), which causes irreparable neurological damage. The disease is lethal and no therapy exists today. Children with MLD are often diagnosed at the age of two years and are quickly bound to a wheelchair and become bedridden until they die within three to four years. The disease is rare and therefore unknown to the general public. The disease can in some ways be compared to Multiple Sclerosis, which also exists in several forms and can have a very quick and lethal progression.

Experimental treatment of subjects in Denmark must, in each case be approved by the authorities. In order to give permission to treat subjects in clinical trials, the authorities require that the trial product be developed using strict quality requirements cGMP and that it has been demonstrated in animal studies that the trial product is safe. Permission must be obtained from the Danish Medicines Agency and the Independent Ethics Committee who, secure that the trial is performed according to applicable regulations and guidelines and ethics requirements.

Zymenex A/S has developed Metazym. The company 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 supported financially by the Danish venture capital investors BankInvest and Vækstfonden.

PhaseOneTrials A/S is an independent Danish contract research clinic with facilities at the University Hospital in Hvidovre. The unit has experience in the performance of Phase 1 and early Phase 2 clinical trials, for companies within biotechnology and the pharmaceutical industry.

Sincerely
Zymenex A/S

Further information:

President, CEO, Jens Fogh, DVM, Zymenex A/S, Hillerød, Denmark, telephone:
+ 45 48 25 00 54, www.zymenex.com

Specialist in Pediatrics, Christine i Dali, MD, University Hospital Copenhagen,
Copenhagen, Denmark, telephone: + 45 25 22 91 55

Chief Physician, Allan Lund, MD, PhD, University Hospital Copenhagen,
Copenhagen, Denmark, telephone: + 45 35 45 38 87

Hillerød, May 2007