Niemann-Pick
DISEASE GROUP (UK)
Registered charity No. 1144406

Orphazyme Clinical Trial Announcement
Summary Information produced by NPDG (UK)

The notes below provide a summary of the information available from Orphazyme and are provided in order to assist with an overview of the proposed trials.

Who is Orphazyme?

Orphazyme, a biotech company based in Denmark, develops new therapies for the treatment of rare and genetic diseases. Their core program is developing heat shock protein based therapies for the treatment of diseases caused by defects in the function and/or metabolism of proteins, with a focus on severe and often fatal diseases with a very high unmet need. The therapies in development also have the potential to address the neurodegenerative aspects of these devastating diseases.

What is HSP70?

Heat shock proteins (HSP) are a class of functionally related proteins involved in the folding and unfolding of other proteins and are named according to their molecular weight. Proteins with similar structure exist in virtually all living organisms.

Production of high levels of HSPs can be triggered by exposure to different kinds of environmental stress conditions, such as infection, inflammation or exercise. They also occur under non-stressful conditions, acting as “monitors” for the cell's proteins, by carrying old proteins to the cell's "recycling bin" (proteasome) and helping newly synthesised proteins to fold properly. These activities are part of a cell's own repair system, called the "cellular stress response" or the "heat-shock response".

HSP70 chaperones are required for key cellular processes. A chaperone is a protein that assists folding/unfolding in molecular biology. The HSP70s are an important part of the cell's machinery for protein folding, and help to protect cells from stress. HSP70 also aids in trans-membrane transport of proteins, by stabilizing them in a partially folded state.

Orphazyme has developed rhHSP70, a recombinant (meaning produced by genetic engineering) version of human HSP70, as a potential therapy for NPC. rhHSP70 has the capacity to cross the blood brain barrier and may potentially address neurological involvement found in many lysosomal storage diseases, such as NPC.

Proposed Clinical Trial of rhHSP70 for NPC

In recent years, Orphazyme has worked closely with leading experts in the field of heat shock proteins and lysosomal storage diseases. They have held regulatory meetings in Denmark and in the UK, and in the near future they will undertake meetings with the European Medicine’s Agency (EMA) and the US Food and Drug Administration (FDA). All of this is necessary to gain the required approval to undertake a clinical trial.

Where Will the Trial Take Place?

It is proposed that a Phase 1 trial (safety, observation and dose escalation) will be carried out in Europe with the later stages (Phase 2 onwards), including additional patients, being rolled out to additional centres outside Europe. The actual sites for the studies have still to be agreed; the UK will be considered along with other European countries for Phase 1.

Proposed Clinical Trial Protocol (subject to change and approval)

Patients will first be enrolled on to an observational study. In an observational study, investigators assess health outcomes in groups of participants according to a protocol or research plan. Participants will follow there their usual routine medical care, and investigators will observe in order to learn more about the individual patient. In this trial, investigators will use the observational study to develop individualised biomarkers for each participant.

Following this, a dose escalation study will commence, involving those who have participated in the observational study. In this step, the amount of the drug is periodically increased to determine the most effective dose in people.

There will then be a follow up period, where participants will be monitored, prior to the commencement of Phase 2 (subject to outcome of Phase 1).

When Will the Trial Start?

It is proposed that the observational study will start in late 2013.

Proposed Inclusion Criteria

For Phase 1, Orphazyme will be looking to recruit 17 patients who meet the following criteria:

- Have a confirmed diagnosis of NPC
- Are aged between 2 and 12 years
- Have a stable disease state, without seizures (this will be confirmed through a screening programme)
- Are able to participate in and complete the Observational Study

Further information:

Orphazyme

Website: http://www.orphazyme.com/

NPDG (UK):

Email: niemann-pick@zetnet.co.uk

Telephone: 0191 415 0693

Website: www.niemannpick.org.uk