Meeting summary
Hamburg, October 2013

The EVERREST project had a very successful 3rd consortium meeting in Hamburg, hosted by the clinical team at the Universitätsklinikum Hamburg-Eppendorf. The meeting focused on progress in the bioethics study and design of the clinical trial in the light of feedback from independent experts. The interventional radiologists, who will administer the investigational maternal growth factor gene therapy in the clinical trial, also had the opportunity for an in depth discussion of their protocol.

The EVERREST Team (left to right): Mirja Pagenkemper, John Martin, Jocelyn Brookes, Petra Arck, Gerhard Adam, Jane Ogilvie, Sara Sleigh, Anna David, Kurt Hecher, Anna Morka, Donald Peebles, Jana Brodszki, Rebecca Spencer, Ryoko Mehnert, Tommi Heikura, Anke Diemert, Karel Marsal, Angela Huertas-Ceballos, Thilo Diehl, Marta Burrel, Francesc Figueras, and Martin Malina

Richard Ashcroft, Professor of Bioethics at Queen Mary and Westfield College, London, was the first to present. He provided the team with a progress report on their study of the bioethics of maternal growth factor gene therapy. He completed a literature review earlier in the year, and his post-doctoral fellow, Dr Maria Sheppard, has now conducted a series of more than 20 interviews with professional groups, non-governmental organisations, parental support groups and charities in the field of obstetrics and fetal medicine. She has worked with groups in all of the partner countries – UK, Germany, Spain and Sweden – and with umbrella groups representing countries across the EU. The groups largely gave positive responses, as they believe that fetal growth restriction (FGR) is an important disease that is difficult to treat and they are willing to support a project that could help to improve outcomes. The few negative responses were around the very idea of gene therapy and possible difficulties of obtaining informed consent from women and their partners for the intervention. The team noted that the latter concern is not specific to the use of maternal growth factor gene therapy but is relevant to any trial of an intervention carried out in pregnancy.

Richard reported that Maria will complete the interviews with stakeholders and, after submission of the report to the EC, she will focus on preparing an application for

ethical approval to conduct a similar interview study in parents with personal experience of FGR.

Anna David, Consultant in Obstetrics and Maternal/Fetal Medicine at UCL and the project's coordinator, summarised feedback from two important independent groups: the Ethics Advisory Committee (EAC) and the Data Safety Monitoring Board (DSMB). Both groups met for the first time in September.

The EAC were unanimous in their view that there were no fundamental ethical contraindications to giving a treatment to a mother for the benefit of the fetus. They made the suggestion that information on participant experience be collected during the trial, and they raised the concern that being offered the opportunity to participate in the trial may affect a woman's decision to terminate the pregnancy. Both issues were discussed at length. Of the four partner countries, termination of pregnancy is not usually offered in Sweden as an option to parents whose fetus has severe FGR. It was also thought unlikely to be taken up by parents as an option in Spain, Germany or the UK.

The DSMB discussed the choice of gene therapy vector and the design of the clinical trial. They recommended that the project team seek further advice and feedback from experts with experience of Phase 1 clinical trials with gene therapies as well as the UK Medicines and Healthcare Regulatory Agency. Both of these recommendations were agreed and are being actioned.

In the afternoon Dr Rebecca Spencer, Clinical Research Fellow at UCL, reported that UCL had received ethical approval for conduct of the prospective data collection study. This study will collate information on biomarkers and the outcomes of pregnancies affected by severe FGR, including extensive information on maternal health and neonatal follow up, at the four participating clinical centres. Discussion focused on preparation for ethical approval for the study at the other centres, the database for the study, and the laboratory and ultrasound manuals.

Finally, John Martin, Professor of Cardiovascular Medicine at UCL, presented ideas for dissemination of information about the project and commercial exploitation of project results.

The next meeting will be held in May 2014 at the University of Lund, Sweden.