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Bringing Patients and Researchers Together

The Ectodermal Dysplasia International Registry is hosted by the National Foundation for Ectodermal Dysplasia (NFED) in America and supported by Edimer Pharmaceuticals (www.edimerpharma.com). Edimer have been working on a potential replacement therapy for X-Linked Hypohidrotic Ectodermal Dysplasia (XLHED) for many years and are now moving to clinical trials. The following is my understanding of the Registry, the replacement therapy, the Edimer XLHED Patient Network (www.XLHED.com) and how they are related but distinct. Included is a little history of XLHED research.

The International Registry

The NFED launched the first ever Ectodermal Dysplasias International Registry in March 2010. The Registry is a central, online database for individuals with any Ectodermal Dysplasia syndrome. In the past the ED support groups around the world have tried to collate information on the different symptoms as best they could, but now, with recent advances in technology, ED individuals have the opportunity to create an efficient and accurate central information base. This pooled information will assist all medical professionals involved in treating and supporting ED patients to recognise and understand the range of symptoms caused by the Ectodermal Dysplasias. A database of clinical features and symptoms covering all ED syndromes, from the very rare to the more common, will be a huge advance in enabling researchers to understand which signs and symptoms of ED are related to specific ED syndromes.

The NFED is committed and obligated to ensure the privacy of all individuals who participate in the Registry. The United States has extremely stringent laws in place to protect the privacy of identifiable health information for all individuals. The Web-based software program used for the Patient

Registry, Innolyst, is compliant with The Health Insurance Portability and Accountability Act of 1996 (HIPAA).

Researchers who are interested in studying the Ectodermal Dysplasias will be able to apply for access to particular areas within the Registry but will not at any time be able to access any personal information which would identify anyone who has registered. Researchers will be looking for specific information relating to their project and would be given access to that part of the Registry only. Should Researchers request contact with families to obtain specific information or to ascertain interest in participation in a research study or clinical trial, they will have to have Institutional Review Board approval from their Institution and be approved by a Scientific Review Board. Once written approval has been given, the relevant families will be contacted by the NFED Registry Program Director or Co-ordinator with the research information; individuals or families can then decide if they want to contact the researcher for more information and choose whether to participate in the project; the Researcher will not have direct contact with individuals or families without their express permission.

The NFED and International ED Support organisations need every person affected by any kind of Ectodermal Dysplasia in every country to participate in the Registry for it to be as successful as possible. Please visit www.nfed.org to register.

Edimer Pharmaceutical

Within this document is an explanation of the history of the replacement therapy; however I would like to explain my understanding of Edimer's involvement. Edimer do not have direct access to the International Registry. Edimer have set up an XLHED Patient Network which is completely separate from the Registry. Edimer are working with a company called BBK Healthcare who help pharmaceutical companies with patient outreach; using an outside organisation restricts Edimer's access to the Network and prevents direct access to any personal details. Edimer will never have direct access to any personal information. They may ask BBK for reports on the Network's members but these reports will not list your name or any identifiers. The reports will be completely anonymous. BBK will send out all of the Network updates and communications so that Edimer will not have access to any of your contact information.

informed of Edimer's progress for future generations. Please visit their website - www.edimerpharma.com - for more information on Edimer and EDI200 and to register for the XLHED Patient Network today.

Diana Perry
Executive Director
14/02/11

A company in Switzerland called Apoxis licensed the drug from the University of Lausanne, and in 2007 it was acquired by a Danish company, TopoTarget, which was primarily interested in other Apoxis products. Essentially, the research stalled at this point. Christopher Maier and Stephane Demotz, originally from Apoxis, formed Edimer Biotech SA in 2008 to focus on the development of EDI200. They travelled all over the world searching for funding to continue the research. Their search ended successfully in late 2008 when they connected with Philip Reilly, M.D. J.D. and Third Rock Ventures, a venture capital firm in Boston. Third Rock Ventures was interested in rare disorders and specifically XLHED and launched Edimer Pharmaceuticals, Inc. – a U.S.-based company – on July 1, 2009.

According to Dr. Kirby, "As the focus of development moves to the United States, Edimer have been particularly concerned about maintaining continuity with the key people who have played important roles with EDI200. As such, Dr. Schneider and Dr. Gaide are working closely with Edimer as advisors and are performing many key experiments in their labs to understand more about the EDAR/EDA1 pathway and how EDI200 works. Christopher Maier and Stephane Demotz will also play important roles as EDI200 moves into the clinical phase".

The EDI200 is not gene therapy, it is the administration of a protein at the right time for the right period that then corrects this disorder, (Edimer believe), forever, and data in the dogs suggests that a very short course of therapy early in life corrects these dogs for the rest of their lives.

Having learnt more about the disease from the biological perspective, it is now important for Edimer to learn more about the disease from the perspective of the patients and their families as they move forward to clinical trials.

Edimer is committed to developing a treatment for XLHED, and to improving the health and quality of life of future generations living with XLHED. They have created the XLHED Patient Network (www.XLHED.com) for patients, family members and healthcare professionals who would like to stay informed and stay connected to their efforts. Joining the Network does not mean you have to join clinical trials, but will ensure you are kept

As the Network is separate from the Registry, Edimer would like all XLHED individuals to join the Network. The focus is quite different from the Registry and is specifically for individuals who have X-Linked Hypohidrotic Ectodermal Dysplasia whereas the Registry is for all ED syndromes. The Network was launched early 2010 and a website set up to enable individuals to join and also to learn more about Edimer – www.XLHED.com

If you participate in the Network, you will enable Edimer to collect some basic information on individuals affected by XLHED, on carriers, friends and relatives of affected individuals, and on health care providers. Edimer will give regular updates to members of the Network on progress, regulatory status, what they are doing with the FDA and EMEA and what their plans are for clinical trials. It is very important that research-interested individuals with XLHED join the Patient Network. By joining the Network, you provide Edimer with a means to stay in touch with you and a way for you to stay informed of Edimer's progress and plans moving forward.

With such a Network in place, Edimer would be able to inform its members of plans for upcoming clinical trials. It would enable Edimer to get more information out to the medical profession, particularly doctors globally to make sure they know about Edimer's work by sending letters, fact sheets and through the website. In fact, Edimer has already sent 42,000 emails through BBKs Network to give doctors information about XLHED, the EDA1 gene and the EDI200 protein (see included information sheets).

The ED Society hope that with this new understanding you will register with the NFED Registry and join the Edimer XLHED Patient Network (www.XLHED.com) so that, as a global group, we can help achieve the goals of individuals, ED organisations, researchers, the medical profession etc., in bringing more awareness and the largest goal of all, a cure for Ectodermal Dysplasias.

Diana Perry
Executive Director
14/02/11

Stay Informed. Stay Connected.
The XLHED Network.

Edimer and EDI200 Replacement Therapy

At an International ED Group Leaders meeting in October 2010, Dr Neil Kirby, President and CEO of Edimer Pharmaceutical, presented their vision to improve the health and quality of life of future generations affected by X-linked HED (XLHED). Their goal is to make EDI200 (a protein replacement therapy) available to all families affected by XLHED. Dr. Kirby explained EDI200 and its development as a therapy to eliminate the symptoms of XLHED.

In 1996, a team of international researchers identified the first genes responsible for hypohidrotic Ectodermal Dysplasia (HED), the EDA1 (Ectodysplasin-A) gene and the EDAR (ectodysplasin-A Receptor) gene, which are located on the X chromosome. Mutations in the EDA1 and EDAR genes result in the most common form of the condition, X-Linked Hypohidrotic Ectodermal Dysplasia.

The EDA1 gene provides instructions for producing many slightly different versions of ectodysplasin-A. One version, ectodysplasin-A1, interacts with a protein called the ectodysplasin-A receptor (produced from the EDAR gene); these proteins work together during the embryonic development to form part of a signalling pathway that is critical for the interaction between two cell layers, the ectoderm and the mesoderm. In the early embryo, these cell layers form the basis for many of the body's organs and tissues. Ectoderm-mesoderm interactions are essential for the formation of several structures that arise from the ectoderm, including the skin, hair, nails, teeth, and sweat glands.

It may help to think of EDA1 as the key and of EDAR as the lock. For those not affected by XLHED, both molecules exist and work together as part of the formation of important appendages in the body, such as sweat glands, teeth, hair and certain other glands in the body. For those affected by XLHED the lock and key molecules do not work together and therefore the formation of important appendages is defective.

Through the work of research teams in Finland, USA, UK and elsewhere, we now know a lot about the pathway through which the EDA1 protein is involved in organ development, mainly because there are multiple animal models of the disorder; not only do people get affected by ED but multiple animal models do too. A tabby mouse or a dog which is deficient in EDA1 has many of the phenotypic changes (the way something looks) that are also found in affected persons in respect of hair, teeth, etc. They also suffer with XLHED.

By 2003, Dr. Pascal Schneider and Dr. Olivier Gaide at the University of Lausanne characterized the protein produced from the EDA1 gene, the EDA1 protein. They designed a therapeutic molecule, which is now called EDI200. It is a “fusion protein” which combines a portion of the EDA1 protein (which, in XLHED patients, is not produced correctly) with a portion of a particular class of antibody molecule. This allows it to be pumped across into a foetus from the mother’s side of the placenta.

Drs. Scheider and Gaide successfully tested EDI200 in a mouse affected by XLHED. It worked as a therapy in mice where the naturally produced EDA1 molecule was missing. Using the dog as a model for the human condition, Dr. Margaret Casal at the University of Pennsylvania examined the treatment of XLHED using the same therapy. In both studies, by injecting this engineered form of the missing protein, the mice and dogs developed ‘more or less’ normal teeth, sweat glands and hair. Before using the EDI200 drug in humans, however, Edimer need to know as much as possible about both the condition in humans and also in these animal models, so the mice and dogs with XLHED are important for developing treatments for our friends and families.

Interestingly, the affected dogs and mice have many of the same issues as people with XLHED. Maggie Casal has found that, if dogs are left untreated they get a lot of respiratory tract (chest) infections; Maggie estimates that in their first year of life 40% of dogs die because of respiratory infections which are difficult to treat.