TREAT-NMD
Neuromuscular Network

16th May 2008 · Newsletter No. 33

Welcome to the latest newsletter. This edition features information from two pharmaceutical companies about their drug development programmes, an update on the German patient registries for DMD and SMA and a "partner focus" on the University of Basel.

Please forward any items that you would like to be included in future editions to info@treat-nmd.eu.

Best wishes,

Katie, Volker, Stephen, Emma, Rachel, Brigitta and Neville – the TREAT-NMD coordination team

Newsletter contents

*****IMPORTANT MESSAGE TO ALL OUR READERS*****

We'd like to remind readers that receiving this newsletter does not automatically make you a member of TREAT-NMD. If you have not completed our membership application form, you are not a member! If you are interested in developing closer links with us, we encourage you to read our Members' Charter and complete the membership application form. These documents can be found on our web site at the address below.

Become a Member of TREAT-NMD

If you are interested in becoming a member of the TREAT-NMD Network please visit our web site to download our membership charter. An application form is also available for download. The web link to our Members' section is: http://www.treat-nmd.eu/news/item/?members_charter We look forward to welcoming new members!

About this newsletter

This is a fortnightly newsletter sent to all members of TREAT-NMD's "Club of Interest" worldwide. Earlier editions of the newsletter can be found online at www.treat-nmd.eu/news/newsletter/index.htm. If you would like to subscribe directly, please visit our website at www.treat-nmd.eu/ where you will find a subscription form at the bottom of the homepage. You can also use the same form if you no longer wish to receive this newsletter – just select the unsubscribe button.

Working with us

TREAT-NMD aims to be an inclusive rather than an exclusive network, and you do not have to be based in Europe or be a partner to be involved. International collaboration with experts from all over the world is already taking place, and new links are being developed.

If you are involved in any of TREAT-NMD's areas of interest and have something you'd like to say or a suggestion of where we could work together, we encourage you to get in touch by writing to us at info@treat-nmd.eu. The coordination team in Newcastle will be happy to put you in touch with the person most relevant to your particular interest.

Summit reports progress of Duchenne muscular dystrophy programme

- Drug candidate SMT C1100 boosts muscle strength and function in preclinical studies
- Third independent verification of Summit's therapeutic approach

TREAT-NMD partner Summit, a UK biotech company, reported on the progress of its DMD programme at the recent New Directions in Muscle Biology and Diseases conference in New Orleans. Summit's molecule SMT C1100 was shown to significantly increase the strength of muscles when compared to no treatment in a series of tests on the *mdx* mouse model for DMD. In addition, when SMT C1100 was combined with steroid treatment (prednisolone), a synergistic benefit in reducing muscle fatigue during exercise (ability to walk longer distances) was seen. Steroids are currently the only frontline therapy for DMD.

Importantly, this study demonstrating a reduction in muscle fatigue during exercise is a surrogate for the agreed primary clinical endpoint in human clinical trials, and is designed to demonstrate that patients' muscle function is improved by measuring the increase in distance they can walk.

This latest data was presented to leading research scientists and companies in the field of neuromuscular diseases at the New Directions in Muscle Biology and Diseases conference, held in New Orleans, USA (27-30 April). A copy of the presentation is available on request from investors@summitplc.com.

The study was undertaken at the University of Bari, Italy, by Professor Annamaria De Luca and is the third independent verification of the potential of this drug in the treatment of DMD. Summit's plan is to conclude preclinical development work by the end of 2008 and begin Phase I clinical trials shortly afterwards.

Owing to an inherited genetic defect, DMD patients lack an important protein called dystrophin, which is crucial to maintaining muscle integrity. The absence of dystrophin results in extensive muscle wasting that severely restricts the mobility of DMD patients by their teen years and is ultimately fatal in their twenties. There is no cure for the disease and steroid treatment only acts to delay the patients' requirement of a wheelchair.

Summit has identified SMT C1100, a proprietary small molecule that acts to replace the missing dystrophin by increasing levels of a functionally similar protein called utrophin. Summit believes the major advantages of this approach is that their product is an oral drug and has the potential to be effective in the treatment of all DMD patients, whereas other current treatments in development are expected to be limited to specific groups of patients.

Further information about Summit is available at www.summitplc.com

Prosensa announces the start of an international multi-center phase I/II clinical study with 'smart drug' PRO051 in patients with Duchenne Muscular Dystrophy

On May 5th, 2008, Prosensa announced that it had started a phase I/II study to explore the effect, safety and tolerability of systemic injections of PRO051 in Duchenne Muscular Dystrophy (DMD) patients. This trial is performed in collaboration with several TREAT-NMD partner institutions including UZ Leuven (Belgium), and the LUMC (the Netherlands) as well as the Queen Silvia Children's hospital (Sweden). The UZ Leuven and the Queen Silvia Children's hospital have already started to enrol patients. In this study, an important parameter will be the presence of dystrophin in muscle biopsies, the protein missing in patients with Duchenne Muscular Dystrophy (DMD). This clinical trial in patients with DMD uses an antisense oligoribonucleotide, a 'smart drug' removing an unwanted segment of the faulty DMD gene product, and represents a novel approach to combat genetic diseases like DMD. TREAT-NMD partner Dr. Nathalie Goemans, the coordinating and principle investigator in Leuven says: "I am excited that, based on the encouraging proof of concept data from the previous clinical study, we can now proceed with this next important step in the investigations that are required to determine whether this highly promising approach can be developed into an effective and safe treatment for patients with this devastating disease. "

Cont ..."We are proud that quickly after completion and publication of the first trial we are able to conduct this study. We expect to provide further information on the developments later this year. In this study, we extend our recent success proving the concept of local dystrophin production to a study with systemic application to achieve widespread dystrophin expression in muscles. ", says Gerard Platenburg, Prosensa's CEO.

TREAT-NMD Partners involved in WP6.1 will meet with Prosensa in June to discuss how the network tools can facilitate this and future trials.

Successful launch of the German DMD and SMA registries for TREAT-NMD

The German Muscular Dystrophy Network MD-NET, a partner of TREAT-NMD, has set up the German national registries for patients with Duchenne/Becker Muscular dystrophy and Spinal Muscular Atrophy. The registries are based at the Friedrich-Baur-Institute, Department of Neurology at the University of Munich, and are led by Dr. Maggie C. Walter and Dr. Sarah Baumeister. Data from the German registries will be transferred to the global TREAT-NMD database at the University of Montpellier to facilitate planning of multi-national clinical trials, improve patient recruitment for research studies and clinical trials, and to provide up-to-date information to patients and families.

The registries were launched on April 16th. Within the first three weeks, close to 100 patients registered online (www.dmd-register.de or www.sma-register.de) by completing the TREAT-NMD self-report questionnaire. To ensure accuracy of the genetic data, patients are asked to send in their genetic report, together with the signed informed consent form. Registration is easy and can be completed in less than 1 hour. Simone Thiele, curator for the German DMD and SMA registries is happy to support families in the registration process (for contacts please see www.treat-nmd.de). The registry software has been developed by Marcel Kiel, an IT specialist working at the Friedrich-Baur-Institute. Future open-source versions of the software will be released publicly and may enable other organizations to set up registries in their own countries.

The launch of the registries was a major focus of the annual meetings of the German patient organisations "action benni & co" (German Duchenne parents project) and "Initiative SMA" of the Deutsche Gesellschaft für Muskelkranke (SMA patients group within the German muscular dystrophy organization) which were held on May 2nd and 3rd. Both organisations are co-sponsoring the registries and encourage their members to promote the registries. The meetings and the launch of the registries received wide media attention in Germany.

Andreas Hornkamp, father of a Duchenne boy and chairman of "action benni & co" emphasises "This patient registry is an important mile stone on the way towards a cure for our children". Inge Schwersenz of "Initiative SMA" states "We are very happy that this project, which is of high importance to patients as well as scientists, is starting now"

For questions regarding the German DMD and SMA registries, please contact register@treat-nmd.de

From left to right: Maggie Walter, Sarah Baumeister, Marcel Kiel, Simone Thiele

TREAT-NMD work package 8.2 meeting - Exon Skipping

On May 10th 13 participants met in the Institute of Child Health (London, UK) for the first TREAT-NMD WP8.2 "exon skip" meeting, organized by Francesco Muntoni, Emma Heslop and Annemieke Aartsma-Rus. Participants were representatives of partners involved in WP8.2, WP6.1 and/or members of the MDEX consortium. The aim of this meeting was not so much to discuss the differences between approaches (e.g. AON chemistries and delivery methods), but to compare results and identify common problems, to coordinate experiments done in parallel and to identify possibilities to help each other. A confidentiality agreement was signed to allow discussion of unpublished data. In the morning session, participants gave an overview of available cell and animal models and experimental procedures in their lab. In the afternoon recent (unpublished) results were discussed and compared. It was concluded that much progress has been made for the systemic application of exon skipping during the last two years. However, there is also a lot of work to be done before exon skipping is clinically applicable. All participants agreed that the meeting was useful and were in favor of having such meetings regularly. In addition, it was suggested that a TREAT-NMD Material Transfer Agreement (MTA) would be a convenient tool, involving the TREAT-NMD Biobank, to accelerate the exchange of materials between TREAT-NMD partners/collaborators. It was also agreed to use the TREAT-NMD website and secure portal to share TREAT-NMD approved Standard Operating Procedures, links to AON analysis software programs and develop collaborations with other research projects to further enhance collaboration and develop an integrated plan for exon skipping research across Europe.

The next meeting will be hosted in Leiden (LUMC) in 6-8 months time. A full report of the meeting is in progress and due to the sensitive nature of the data this will be distributed only to meeting participants and partners involved in WP8.2.

Participants: Annemieke Aartsma-Rus (LUMC), Serge Braun (AFM/ MDEX), Patrick Dreyfus (INSERM), Alessandra Ferlini (University of Ferrara), Ian Graham (Royal Holloway, London / MDEX), Emma Heslop (Newcastle University / UCL / MDEX), Kanagasabai Ganeshaguru (UCL ICH/ MDEX), Jenny Morgan (UCL ICH/ MDEX), Francesco Muntoni (UCL ICH/ MDEX), Volker Straub (Newcastle University / MDEX), Jenny Versnel (MDEX), Dominic Wells (Imperial College London / MDEX), Matthew Woods (Oxford University / MDEX)

Research Approaches for a Therapy of Duchenne Muscular Dystrophy.

The latest of *Günter Scheuerbrandt*'s research reports is now available to download from the TREAT-NMD website. The reports are written for the boys, young men and families affected by Duchenne, who wish to know how the work of scientists and clinicians in many research laboratories across the world is progressing towards effective therapies for Duchenne muscular dystrophy.

Click on the link below to download the report:

http://www.treat-nmd.eu/news/documents/ResearchApproachesforDMD2008.pdf

Focus on University of Basel (UNIBAS)

Biozentrum, University of Basel
Klingelbergstrasse 50/70
CH - 4056 Basel
Switzerland

http://www.biozentrum.unibas.ch/rueegg/index.html

The University of Basel has a long history of excellence in Life Sciences. In particular, the Biozentrum, founded in 1971, was among the first institutions world-wide dedicated to molecular biology and is currently an interdisciplinary institute working in fields from fundamental to applied research. It is the founding institute for MyoContract (now Santhera Pharmaceuticals Ltd) and hosted the company at its early stages (until 2002).

Work on neuromuscular junction and neuromuscular diseases has a long tradition at the University of Basel, the University Hospital and nearby institutes of NGO. Research focuses on the mechanisms important for neuromuscular function with a particular emphasis on mouse models. Some groups are concerned with mechanisms important for muscular dystrophies and for neuron degeneration. In particular, the laboratory of Markus A. Ruegg is engaged in developing therapeutic approaches for the treatment of congenital muscular dystrophy. Important achievements in his group related to muscular dystrophy are "proof-of-concept" studies in mice that might open new possibilities for the treatment of congential muscular dystrophies.

The Biozentrum is the leader of Workpackage 7.2 (Select appropriate mammalian animal models). The main objective of WP 7.2 is to help overcome the fragmentation currently hindering preclinical drug therapy tests. Pre-clinical research is the first step in the identification and development of new therapeuticals. These have to be tested in animal models that reflect the human disease as closely as possible before they can be tested in patients (clinical trials) and finally become approved for general medical use. However, several species with different genotypes are currently in use and these animal models do not always show the exact same symptoms of disease and responses to therapy as humans. The goal of this workpackage is to select those mammalian models that best represent the human disease and that are most promising for the identification of effective therapies, thereby setting a first step in the harmonization and comparability of pre-clinical results.

People Involved in WP 7.2

Prof. Markus A. Ruegg has a track record as researcher in basic research addressing the development and function of the neuromuscular junction and mechanisms of neuromuscular diseases. He has authored more than 60 publications in major journals such as Nature, Nat. Cell Biol., Neuron, J. Cell Biol., EMBO J. and is inventor on 4 patents. Invited speaker to EMBO and ENMC Workshops, Gordon Research Conferences, to the World Muscle Society and several additional major meetings in the field. Co-founder of MyoContract. He is the scientific representative of the University of Basel on the TREAT-NMD Governing Board.

markus-a.ruegg@unibas.ch

Dr. Raffaella Willmann studied Biology in Italy and obtained her PhD in Biochemistry in Konstanz (Germany). After a first post-doc position in muscle physiology in Konstanz, she joined the group of Prof. Fuhrer at the University of Zürich in 2000. There, she worked on a project on the formation and stabilization of the neuromuscular junction. She joined TREAT-NMD on March 1st, 2007 as a scientific writer and Activity coordinator.
raffaella.willmann@unibas.ch

Dr. Shuo Lin has a long-standing interest in muscular dystrophies. He worked previously with Prof. J.-M- Burgunder (Berne, Switzerland) on the function of utrophin and is currently involved in generating mouse models to test treatment options for Duchenne muscular dystrophy. He has authored more than 20 publications.
shuo.lin@unibas.ch

Dr. Sarina Meinen main project concerns the development and realization of treatment options for MDC1A. She is currently involved in the testing of anti-apoptosis and replacement therapies for the treatment of MDC1A. In addition, she will evaluate whether losartan, an angiotensin II type 1 receptor antagonist that is widely used in clinics to treat hypertension, offers a new interesting entry point for the treatment of MDC1A patients. These studies are mainly done in mouse models for the disease.
sarina.meinen@unibas.ch

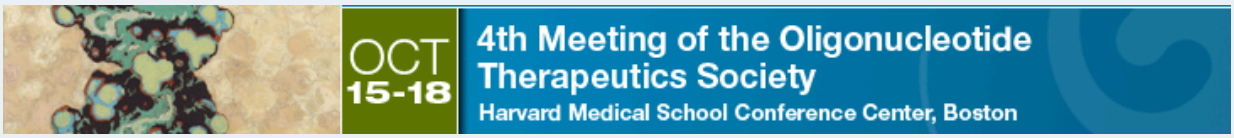
Conrad Florian Bentzinger started his studies in the laboratory of Markus Rüegg in 2003 as a master student. In his PhD, he is interested in the molecular regulation of skeletal muscle mass with the goal to identify new approaches for the treatment of muscle diseases. He is currently investigating the mTOR signalling pathway in skeletal muscle.
cf.bentzinger@unibas.ch

Claudia Escher works as a PhD student on protein-based diagnostic methods. She currently establishes an analytical method to find surrogate markers in primary human muscle cells with the aim to facilitate diagnosis of DMD/BMD on a microarray platform. This work is done in collaboration with the University of Applied Sciences in Northwestern Switzerland.
claudia.escher@fhnw.ch

Marcin Maj studied Biology in Krakow, Poland. He works as a PhD student on agrin/MuSK signalling at the neuromuscular junction. His main interests include signalling at the neuromuscular junction as well as in diseases affecting these signalling pathways (myasthenia gravis and myasthenic syndromes).
marcin.maj@unibas.ch

Manuela von Arx is **a** technician and takes care of our mouse colony.
manuela.vonarx@unibas.ch

Meetings and workshops



For further information please visit: http://www.nyas.org/events/eventDetail.asp?eventID=10680&date=10/15/2008).

Job advertisements

ENMC TREAT-NMD Project Coordinator, Baarn, The Netherlands

TREAT-NMD partner the European Neuro Muscular Centre (ENMC) is a small and efficient research support organisation with a prominent international standing in its field. To lead important components of the ENMC activities within TREAT-NMD, the ENMC is seeking candidates for the position of **ENMC Project Coordinator for TREAT-NMD** (20 – 28 hrs per week)

Tasks:

- Reporting – financial and project activities (deliverables, milestones)
- Planning – financial and project activities (develop project plan and description of work for future activities)
- Project management – coordination of ENMC activities within TREAT-NMD, and also co-ordination of workpackages where ENMC is the lead
- Develop the Training and Education Programme within the Network (training courses and European Neuromyology Curriculum) and ensure outreach across Europe
- Increase mobility of scientists and clinicians across Europe
- Coordinate the extension of TREAT-NMD to Eastern European countries
- Disseminate TREAT-NMD information and promote integration of patient groups. One of the means for doing this is a conference to be organised for November 2009

Qualities:

- Fluent English, verbal and written
- Knowledge of academic research, EU funding and preferably also neuromuscular diseases or issues regarding rare diseases
- Pragmatic, pro-active and outcome driven
- University degree, preferably biomedical science or related areas

Salary scale according to CAO Welzijn. The position is based in Baarn, the Netherlands.
Please write to enmc@enmc.org with any enquiries or to send your CV and letter of motivation.
Closing date for submission of CV and letter of motivation is **30 May 2008**.

Partner section

Welcome to Neville!

The Newcastle Coordination Team has been joined by Neville Wilford as IT Coordinator. Neville, who has a background in biochemistry and molecular biology, has worked in IT support at the Institute of Human Genetics for some time and has just come to join the TREAT-NMD team, while Arron Scott has moved to take on other responsibilities within the Institute but can still be contacted at the same email address. Neville is the primary point of contact for the website, portal and other IT issues and can be reached at j.n.wilford@ncl.ac.uk or +44 191 241 8617.

Send us your news and views!

We strongly encourage all partners and supporters to send their own news and updates and we will be happy to include them in future editions of the newsletter. Please send your contributions to emma.heslop@treat-nmd.eu