

## welcome

Welcome to the 63rd newsletter from TREAT-NMD.

A week ago a broad group of DMD experts gathered at the offices of the European Medicines Agency (EMA) in London to begin dialogue on the regulatory issues surrounding antisense oligonucleotide therapies for genetic conditions like DMD. A report on this important meeting and its outcomes is included this week.

Poster abstracts for our November conference are now available online on our [conference website](#). Note that you that we are still encouraging all our readers to pose a question to one of our expert panels to be considered during the conference.

This week's newsletter also features a short online survey for DMD preclinical researchers that we would ask anyone making use of mdx or GRMD models to complete, plus news of Duchenne Foundation Australia's Sydney conference in February 2010, the deadline for abstracts for which is Friday 16th October, and a meeting report from the IDMC-7 myotonic dystrophy conference that took place in Würzburg, Germany, in September.

Also included are details of a future job opportunity here at Newcastle for clinical researchers interested in translational medicine in the neuromuscular field.

As always, if you have anything to be considered for inclusion in future editions of the newsletter please contact the coordination office with your suggestions.

Best wishes from Katie, Volker, Hanns, Steve, Emma, Rachel, Samantha and Michael, the Newcastle TREAT-NMD team

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at a glance...

05-06 Oct 2009 6th UK SMA  
Research Conference, Edinburgh,  
UK



### Press Release: TREAT-NMD, EMA and Patient Group Workshop on AO Therapies in DMD.

On 25 September 2009 a broad group of 98 DMD experts assembled by TREAT-NMD – including clinicians involved in current clinical trials, patient/parent groups and pharmaceutical companies working on Duchenne therapies – met at the London offices of EMA, the European Medicines Agency, to begin a dialogue on the regulatory issues surrounding the unprecedented level of personalization inherent in antisense oligonucleotide therapies for genetic conditions like DMD. EMA representatives included the chairs and members of the committees for Human Medicinal Products (CHMP), Paediatrics (PDCO), Advanced Therapies (CAT), Orphan Drugs (COMP) as well as members of the Scientific Advice Working Party (SAWP) and senior members of the EMA secretariat. Furthermore, representatives from the Standing Committee for European Doctors (CPME) and EMA eligible patient organizations such as the European Genetic Alliances' Network (EGAN) and the International Alliance of Patients' Organizations (IAPO) participated in the workshop. Input from Duchenne patient groups and experts worldwide ensured that there was global representation at the meeting, which also included a representative of the US Food and Drug Administration (FDA).



Recent promising preclinical and clinical trial results of antisense oligonucleotides (AOs) as a therapy for boys affected by DMD suggest that this novel approach could provide a therapeutic option for the majority of affected individuals. Studies that will hopefully lead to the registration of the first of these compounds, which are designed to skip exon 51 of the DMD gene, will start in the near future. Although more than 80% of Duchenne boys could potentially benefit from the "exon skipping" approach, each exon targeted requires a unique AO, and thus treating all the different mutations known to cause DMD requires the development of large numbers of AOs, each treating only a small subset of the patient population. This represents a personalized approach to therapy that is currently without precedent for a genetic disease. It is the concern of advocacy groups and scientists in the field that if the standard regulatory and product development path of taking new drugs into the clinic has to be followed for each individual AO, this will threaten the viability of this promising approach.

The meeting with EMA therefore sought to take steps to identify a pathway that will allow the safe and efficient progress of these drugs through the approval process. Extensive preparatory work prior to the meeting ensured that the DMD expert scientist and advocacy groups were able to present a united voice to the regulatory authorities, clearly identifying the areas of concern whilst seeking to partner with EMA to guide future developments. This is the second time that TREAT-NMD has convened a broad, strategic meeting with the regulatory authorities, and the approach has been welcomed as a unique forum for discussion that benefits both sides.

"The usual procedure is for pharmaceutical companies to apply for marketing authorization for each drug individually, but it was clear that for some of these new therapies a far broader discussion was needed to establish the overarching strategies and find out how the regulatory authorities would view applications for these highly similar compounds," said TREAT-NMD partner and workshop chair Francesco Muntoni. "We are delighted that EMA have been so willing to interact with the Duchenne community and are confident that by dealing with these issues openly and constructively now we can help smooth the pathway of all these therapies towards approval without compromising on safety or efficacy."

Following the meeting Pat Furlong, Founding president & CEO of Parent Project Muscular Dystrophy noted the landmark status of this meeting for the field. "It was brilliant. To be honest, as we crossed the Thames in the ferry, I realized it was quite symbolic. Thank you for including me in this historic meeting".

The regulatory experts also underlined the success of the workshop and Dr. Agnes Saint Raymond, Head of Sector for Scientific Advice, Orphan Drugs and Paediatric Medicinal Products at the EMA, added "the EMA and its Committees welcome the opportunity to continue the dialogue with

[23-24 Oct 2009 Action Duchenne International Conference Holiday Inn Bloomsbury London](#)

[14-18 Nov 2009 Mechanisms Involved in Muscle Atrophy and Hypertrophy, Carmona, Spain.](#)

[17-19 Nov 2009 TREAT-NMD / NIH International Conference](#)

[27 Nov 2009 King's College London Neuromuscular Symposium](#)

[26-27 Feb 2010 Towards a Brighter Future - Sydney, Australia.](#)

TREAT-NMD as part of their exchanges with Patients' organisations and Health professionals. These are promising times for children and adults with Duchenne and Regulatory authorities strongly encourage early collaboration in drug development to maximise the chances of success at approval time."

#### Meeting Outcomes

During the workshop, EMEA representatives indicated that they would be willing to be flexible; with the help of the tools and procedures they have in place, and are prepared to be engaged in more detailed discussion regarding the development of a regulatory pathway for approval of future exons. The regulatory experts stressed that they are willing to discuss alternative ways forward for very small populations. Furthermore it was noted that even though each exon may have to be approved individually it may not be necessary to do separate studies for each of them as many data can be shared and/or data can be extrapolated. However it was pointed out that regulators will always need sufficient data to evaluate the medicinal product and conclude on the benefit-risk balance. To ensure that adequate data for approval of the medicinal products are collected the regulatory experts strongly recommended that sponsors discuss early with the SAWP and the PDCO and agree on the trials before they are conducted. Moreover there are fast regulatory procedures of approval for medicinal products especially if they are life saving and there is an unmet medical need. The EMEA invited the community to approach them early in the drug development and emphasised that collaboration of the community is key, complimenting the community on its harmonisation.

Following the meeting TREAT-NMD will produce a workshop report for publication and maintain dialogue with EMEA to help respond to the needs of the community. Further information is available to interested parties via the TREAT-NMD coordination office.

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### 7th International Myotonic Dystrophy Consortium meeting highlights science with translational potential

The International Myotonic Dystrophy Consortium (IDMC) hosts conferences every two years focusing on the latest developments in myotonic dystrophy research. Since the last meeting (IDMC-6) in Milan in September 2007, several pivotal discoveries have been made, and expectations were therefore high when more than 250 scientists and 200 patients from 40 countries convened in Würzburg, Germany from 9-12 September 2009 for IDMC-7. The meeting also marked the 100th anniversary of the description of myotonic dystrophy as a distinct clinical entity by Hans Steinert at a hospital in Leipzig, Germany. Over four days, 75 oral presentations and 96 poster presentations covered basic research, clinical aspects, current therapy, translational research, rehabilitation and psychosocial issues of myotonic dystrophy. Open dialogue with patients, family members and patient organizations in both English and German was a highlight of the program.



Recently published studies in mouse models of myotonic dystrophy were appreciated as major steps towards the development of future therapies. Experiments in a transgenic mouse model of DM1 carried out by Dr Thornton's group in Rochester showed that sequestration of the MBNL1 protein may be reversible by morpholino antisense oligonucleotides (Wheeler TM et al; Science. 2009;325:336-9). Another mouse model developed by Dr Cooper's group in Houston recapitulates muscle wasting as seen in myotonic dystrophy and links increased steady-state levels of CUGBP1 to PKC-mediated hyperphosphorylation (Orengo JP et al; Proc Natl Acad Sci USA 2008;105:2646-51. Kuyumcu-Martinez NM et al. Mol Cell. 2007;28:68-78).

To translate these exciting findings from animal studies into therapies for patients with myotonic dystrophy, well-designed clinical trials need to be conducted over the coming years. TREAT-NMD will partner with the myotonic dystrophy community to build appropriate infrastructures for such trials. Agreement was reached and presented to establish an international TREAT-NMD patient registry for myotonic dystrophy, based on the coordinated collaboration of existing and new national patient registries.

The 2011 IDMC-8 meeting will be held in the USA (place and date to be announced shortly). The chairs of IDMC-7, Drs Krahe, Grimm and Schoser, would like to thank all participants, patient organizations and sponsors for a stimulating and successful meeting.

Report by [Benedikt Schoser](#), Munich

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### Wanted: DMD preclinical researchers' feedback

Anyone involved in preclinical research using animal models for Duchenne muscular dystrophy is invited to complete a short research study to enquire on and improve the services that TREAT-NMD offers researchers in the field of DMD. The survey is in the form of a short online questionnaire that will take about 5 minutes to complete. Your responses are





important to us and will help evaluate the success of the TREAT-NMD initiatives in harmonizing and accelerating preclinical treatment development for DMD. The results of the survey will help improve the tools that TREAT-NMD offers to scientists.

Please feel free to forward the link to anyone you think may be interested in participating. Thank you in advance for your collaboration.

[Complete our questionnaire](#)

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## Job Opportunity in Newcastle

An exciting opportunity for training in translational medicine will be available soon in the Newcastle Muscle Centre. Via an award scheme funded by the Wellcome Trust, we are able to offer a four year training programme including a year of taught courses around the many issues of drug development and trial design, followed by a three year PhD project.



Industry and academic leads deliver the courses and the PhD programmes also have industry components, providing a broad education in the field of drug development and translational medicine.

The successful applicant will be based in the Newcastle muscle team, and will be able to take part in clinical, research and TREAT-NMD activities within the centre. This is an attractive full-time salaried position on a Clinical Research Associate salary scale (currently £27,523 - £46,426, although more senior candidates could be appointed to a higher scale). The scheme is competitive, and applicants will need to be eligible for General Medical Council registration in the UK as well as being able to fulfil residency requirements. It is likely that successful applicants will be on or have just finished a training pathway in Neurology, Paediatric Neurology, Genetics or other specialties relevant to neuromuscular diseases.

Interested candidates are welcome to contact :

[Kate Bushby](#)  
[Volker Straub](#) or  
[Hanns Lochmüller](#)

for more details before the official announcement.

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## Call for Abstracts - Towards a Brighter Future Conference - Sydney 2010

Friday 16th October is the deadline for abstract submission to the Sydney 2010 Duchenne Foundation Australia Conference - Towards a Brighter Future. The organisers welcome submissions (under either basic science or clinical research streams) that showcase solutions to common problems, patient/practice management techniques, innovative uses of technology and research related to the conference theme. All poster proposals should describe specific case studies, programs, innovations or research to pursue quality and quantity of life for those affected by a neuromuscular disorder.



Director of Duchenne Foundation Australia Deborah Robins writes, "We aim to provide sound medical and scientific information to reassure parents that whilst there is no "one size fits all" miracle cure for each disorder, the future is going to be much better for many of our children. We know that world standards of care are changing every year via new drug therapies, practices and research findings and it is critical that we keep abreast of new information.

Conference aims:

- To bring families affected by Duchenne and other common neuromuscular disorders together to update world standards of care and research progress - firsthand, rather than in a diluted or technical written form
- To focus on the most common without neglecting other major neuromuscular diseases
- To encourage Australian medical specialists, doctors and therapists to grow in their proactive approach to the diagnosis and treatment of persons affected by neuromuscular diseases reducing surgical interventions and hospitalizations.
- Increased awareness of the positive outcomes of such pro-activity should eventually encourage more specialists and therapists into the field and it is not uncommon to register a number of medical & allied health students seeking accreditation.
- To address family, cognitive, social, psychological and palliative care issues to reinforce that quality of life is more important than quantity of life

- Greater overall quantity and quality of life for all."

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### TREAT-NMD International Conference Abstracts

The TREAT-NMD conference website now features a [section](#) listing titles of all the successful abstracts and their authors. Registration for the conference is still open and we encourage anyone who has not yet registered to do so soon!

Don't forget you can also [submit a question](#) to be considered by our expert panels during the conference. We strongly encourage all our readers to help us make the conference an interactive event that reflects the current issues in the field.



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