TREAT-NMD Workshop on
The Development of Antisense Oligonucleotide Therapies for Duchenne Muscular Dystrophy
at European Medicines Agency, London, UK
25th September 2009

***Morning Chair**: Francesco Muntoni (TREAT-NMD, University College London)*

8:30 Arrival and Registration

9:00 Welcome and Introduction
Agnes Saint-Raymond (EMEA)
FDA Representative
Volker Straub (TREAT-NMD, Newcastle University)

9:15 Aims of the meeting and questions for the regulatory authorities
Francesco Muntoni (TREAT-NMD, University College London)

9:25 Parental / Patient Perspective
Elizabeth Vroom (United Parent Project Muscular Dystrophy)

Session I: Clinical overview of Duchenne Muscular Dystrophy and Exon Skipping

***EMEA co-chair**: Kerstin Westermark (COMP)*

9:40 Presentation 1- General Overview: What is Duchenne Muscular Dystrophy Natural History and Standards of Care
Genetic Basis of Duchenne and Becker Muscular Dystrophies
Standards of Care for DMD
Kate Bushby (TREAT-NMD, Newcastle University)

10:05 Presentation 2- Outcome measures for clinical trials in DMD
Outcome Measures currently used in ambulant DMD boys
Outcome measures in non ambulant DMD boys
Outcome measures in young boys
Julaine Florence (Washington University School of Medicine, St. Louis)

10:30 Presentation 3- The Specific Issues of Personalised Medicine in Duchenne Muscular Dystrophy
What is exon skipping in Duchenne Muscular Dystrophy?
How does it work?
How many exons should be targeted?
How long it would take to develop AOs approach for the first 10 exon to skip using current procedures?
Are additional tests required for double exon skipping?

Annemieke Aartsma-Rus (TREAT-NMD, Leiden University Medical Center)

10:55 Coffee

Session II – Clinical Applications of Antisense Oligonucleotides

EMEA co-chair: Cristina Sampaio (CHMP)

11:15 Presentation 4 - Overview of experience with different AON chemistries in clinical trials to date

A historical perspective on antisense technologies: successes and disappointments

Efficacy / equivalency dose

What is an appropriate toxicology package for AON

Art Levin (Levin Biosciences and Santaris Pharma, Hørsholm)

12:00 Discussion and consolidation (*led by Dominic Wells***)**

12:30 Lunch break

Afternoon Chair: Volker Straub (TREAT-NMD Coordinator, Newcastle University)

Session III – Clinical Applications of Antisense Oligonucleotides –II Part

EMEA co-chair: Gopalan Narayanan (CAT)

13:30 Presentation 5- Toxicological issues in development of AOs as a medicinal product

Long term toxicity

Toxicology package for combinations of AOs

Pathway for subsequent AOs to be taken to clinic

Art Levin (Levin Biosciences and Santaris Pharma, Hørsholm) and Dominic Wells (Imperial College London)

14:00 Industry Presentation 1: Prosensa *(Giles Campion)*

14:10 Industry Presentation 2: AVI *(Steve Shrewsbury)*

14:20 Industry Presentation 3: ISIS *(tbc)*

14:30 Discussion and consolidation (*Led by Art Levin***)**

Session IV – Ethical Aspects

EMEA co-chairs: Agnes Saint-Raymond (EMEA), Michael Wilks (Standing Committee of European Doctors

15:30 Presentation 6 – Ethical considerations for trials in DMD

Funding for trials
Personalised medicine
Fragmentation of the patient community based on 'have and have not's' of specific exons.
Recruitment of patients into sequential trials
Quality of life and burden of disease
Improvement vs stabilisation of condition for regulatory approval?
Simon Woods (TREAT-NMD/ PEALS, Newcastle University)

16:00 Discussion and consolidation (*led by Simon Woods and Elizabeth Vroom***)**

Session V – Summary Discussion

Session Chair: Edward Connor (Children's National Medical Center)

EMEA co-chairs: Daniel Brasseur (PDCO) and Spiros Vamvakas (EMEA)

16:15 EMEA / FDA Feedback and suggestions to the community

17:00 Summary and Discussion

Francesco Muntoni (TREAT-NMD)
Kate Bushby (TREAT-NMD)
Industry Representative
Patient Organisation Representative
Daniel Brasseur and Spiros Vamvakas (EMEA)
FDA Representative

17:15 Concluding Remarks

Daniel Brasseur and Spiros Vamvakas (EMEA),
FDA representative,
Francesco Muntoni and Kate Bushby (TREAT-NMD)

17:30 End of meeting

Steering Committee:

1. **Francesco Muntoni** (TREAT-NMD DMD Network in Action WP Leader, Institute of Child Health, University College London)
2. Emma Heslop (TREAT-NMD Coordination Office / DMD Network in Action WP, University College London)
3. Janbernd Kirshner (TREAT-NMD Clinical Trial Coordination Centre, Freiburg)
4. Kate Bushby (TREAT-NMD Coordinator, Newcastle University)
5. Volker Straub (TREAT-NMD Coordinator, Newcastle University)
6. Annemieke Aartsma-Rus (TREAT-NMD, Optimisation and Delivery of Therapeutics, Leiden University Medical Center)
7. Nathalie Kayadjanian (TREAT-NMD / AFM / DRCI)
8. Serge Braun (TREAT-NMD/ AFM /DRCI)
9. Nathalie Goemans (TREAT-NMD, Universite Catholique de Louvain)
10. Elizabeth Vroom (UPPMD / DPP / DRCI)
11. Pat Furlong (PPMD / DRCI)
12. Valerie Cwick (MDA / DRCI)
13. Dominic Wells (MDEX Consortium, Imperial College London)
14. Eric Hoffman (Children's National Medical Center)
15. John Porter (NIH / NINDS)
16. Robert Griggs (University of Rochester and Muscle Study Group Executive Committee)
17. Art Levin (Independent Consultant, Levin Biosciences and Santaris Pharma, Hørsholm, DK)
18. Divyesh Popat (Lawyer/ Action Duchenne)
19. Luis Garcia / Thomas Voit (TREAT-NMD Institut de Myologie)
20. Edward Connor (Children's National Medical Center)

The organizers would like to thank the following organizations for their financial support of this workshop

AFM Association Française contre les Myopathies

MDA Helping Jerry's Kids

Parent Project Muscular Dystrophy
LEADING THE FIGHT TO END DUCHENNE

Duchenne Parent Project

The elements originating during the discussion will not constitute a formal specific advice on a particular product or class of products. The positions expressed by the Experts and the EMEA during this workshop will not be regarded as binding in relationship to any aspect of subsequent institutional work before to be endorsed by the CHMP and/or the PDCO.