

Annual Congress on

# Rare Diseases & Orphan Drugs

October 26-27, 2016 Chicago, USA

## On-going exon 53 skipping clinical trial for Duchenne muscular dystrophy

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Duchenne muscular dystrophy (DMD) is the most common childhood genetic disease, affecting one among 3500-5000 newborn boys, causing progressive muscle weakness, heart and respiratory failure and premature death. This disease is caused by the mutations of the DMD gene and there is no cure exists for this disease but a number of promising new molecular therapies are being intensively studied. Exon skipping by antisense oligonucleotides (AOs) is a novel method to restore the reading frame of the mutated DMD gene and rescue dystrophin expression. We have reported that systemic delivery of AOs targeting exon 6 and 8 of the canine DMD gene to CXMDJ, a dystrophin-deficient canine animal model, efficiently restored functional dystrophin proteins at the sarcolemma of these dogs and improved phenotypes of affected dogs without serious adverse effects. We, then, optimized AO sequences, which allow exon 53 skipping of the human DMD gene, together with Nippon Shinyaku Co. Ltd. After numbers of toxicology study of the AOs, NS-065/NCNP-01, we proposed an early phase clinical trial of exon 53 skipping of DMD patients, which was approved by Japanese Pharmaceutical and Medical Devices Agency (PMDA) and the trial, has been successfully carried as an investigator-initiated trial in NCNP hospital. Following the excellent results of the early phase trial, phase I/II trial in Japan and phase II trial in US are carrying by either Nippon Shinyaku Co. Ltd. or NS Pharma, Inc.

### Biography

Shin'ichi Takeda is currently the Director General of National Institute of Neuroscience in the National Center of Neurology and Psychiatry (NCNP). He initially trained as a Clinical Neurologist and received a PhD degree in Muscle Biology from Shinshu University, Graduate School in 1981 and has a long time laboratory experience including Paris Pasteur Institute (1987-1992). He focused his research on development of molecular therapy of Duchenne muscular dystrophy (DMD), since he came back from France and has gotten the position in NCNP in 1992. He has showed a proof of concept study of exon skipping in the colony of dystrophic dogs that he established and he recently finished the early phase clinical trial of exon 53 skipping of the dystrophin gene among DMD patients in Japan as a PI. He is working as an Associate Editor for review of *J. Neuromuscular Diseases* since 2013 and an Associate Editor of *Am. J. Pathology* since 2014.

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