What's the next step for exon skipping therapies to treat duchenne muscular dystrophy?

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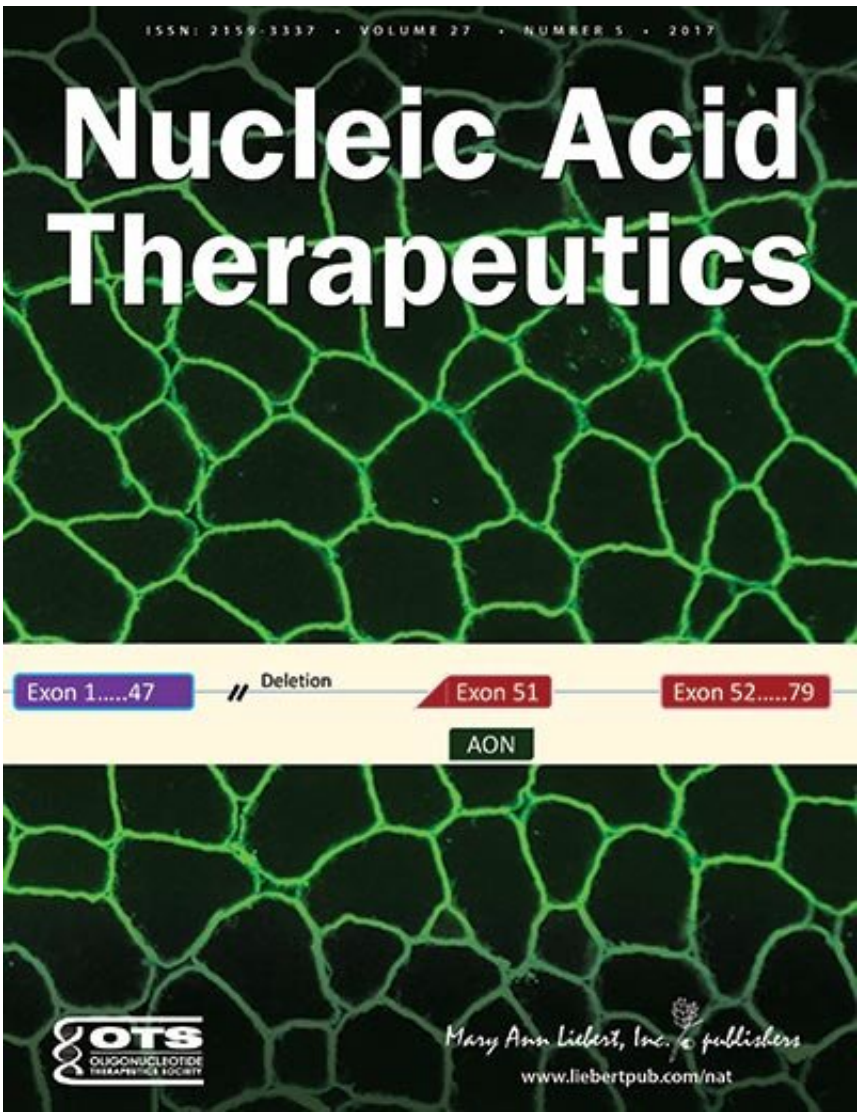

Credit: Mary Ann Liebert, Inc., publishers

A team of leading European clinicians and scientists presents a unique perspective on how to move forward in the development of exon skipping therapies to treat the severe muscle-wasting disease Duchenne Muscular Dystrophy (DMD). Following recent approval by the U.S. regulatory authorities of the first such drug for DMD, the team of authors representing key European regulatory agencies, academic medical centers, industry, and patient groups discusses the main challenges and opportunities for the development and regulatory approval of these therapeutic agents going forward, in an article published in *Nucleic Acid Therapeutics*.

The article entitled "Development of Exon Skipping Therapies for Duchenne Muscular Dystrophy: A Critical Review and a Perspective on the Outstanding Issues," was coauthored by Annemieke Aartsma-Rus, PhD, Co-Editor-in-Chief of Nucleic Acid Therapeutics, Pavel Balabanov, MD, PhD, and colleagues from Leiden University Medical Center (The Netherlands), Newcastle University (Newcastle upon Tyne, U.K.), Medicines and Healthcare Product Regulatory Agency (London, U.K.), European Medicines Agency, Bundesinstitut für Arzneimittle und Medizinprodukte (Bonn, Germany), Medicines Evaluation Board (Utrecht, The Netherlands), Catholic University and Centro Clinico Nemo (Rome, Italy), UCL Great Ormond Street Institute of Child Health (London, U.K.), Universidade de Lisboa, Faculdade de Farmácia (Portugal), and United Parent Project Muscular Dystrophy (Amsterdam, The Netherlands).

The authors review the mechanism of action, effectiveness, and limitations of the first-in-class antisense oligonucleotide (AON) drug eteplirsen, which targets exon 51 in patients with DMD. Only 13-14% of patients with DMD have a mutation in exon 51 and would benefit from this treatment, with other small patient clusters requiring distinct AON

drugs that each target a different exon. Based on the most recent scientific and medical evidence in the field and the views expressed by European regulators, the authors offer their perspective on the most efficient strategy for developing future exon skipping drugs for DMD, which would deliver effective treatments to patients as quickly as possible. The discussion includes the use of biomarkers in AON drug development, approaches for developing AONS for very small groups of patients, regulatory tools and incentives in the EU, and the potential for obtaining "class" or "platform" approval for AON drugs.

"This paper exemplifies the journal's commitment to advancing the field through consensus, or where necessary, healthy debate among all stakeholders. The piece can also be seen as a call for more candid dialogue with regulatory agencies," says Executive Editor Graham C. Parker, PhD, The Carman and Ann Adams Department of Pediatrics, Wayne State University School of Medicine, Children's Hospital of Michigan, Detroit, MI.

More information: Annemieke Aartsma-Rus et al, Development of Exon Skipping Therapies for Duchenne Muscular Dystrophy: A Critical Review and a Perspective on the Outstanding Issues, *Nucleic Acid Therapeutics* (2017). DOI: 10.1089/nat.2017.0682