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BC EXTRA | PRECLINICAL NEWS

EXONICS SHOWS CRISPR TREATS DMD IN DOGS

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Exonics Therapeutics Inc. (Boston, Mass) is one step closer to bringing its SingleCut CRISPR gene editing Duchenne muscular dystrophy treatment to the clinic after preclinical data showed the therapy led to dystrophin restoration of up to 92% in a canine model of the disease. The company published the **results** in *Science* along with researchers from University of Texas Southwestern Medical Center, from whom Exonics licensed the gene editing technology.

Exonics CEO John Ripple told BioCentury the paper "is one of the important milestones on our path toward the clinic" but declined to disclose a development timeline.

Lead author Eric Olson told BioCentury the study is the first demonstration of systemic distribution of CRISPR to muscles and heart of a large mammal for dystrophin restoration. Olson is also a founder and chief science adviser at Exonics.

In the paper, the team used adeno-associated viral (AAV) vector-mediated delivery of Cas9 and single guide RNA to target exon 51 of the dystrophin gene to correct the dystrophin reading frame in a canine model of DMD.

In two canines, systemic IV delivery of the therapy restored dystrophin expression to up to 25-70% of normal levels in skeletal muscle after 8 weeks, and led to a 92% restoration of dystrophin in cardiac muscle and 58% in the diaphragm.

The authors said longer-term studies are required to establish whether the expression of dystrophin and maintenance of muscle integrity are sustained, but the one-time treatment may have benefits over exon skipping therapies, which require continuous treatment.

The study builds on Olson's previous work in smaller animal models. In a 2016 *Science* paper, the group showed CRISPR gene editing restored dystrophin protein expression to varying degrees and enhanced skeletal muscle function in a mouse model of DMD (see **"Snipping Vs. Skipping for DMD"**).

Exonics launched in 2017 based on CRISPR technology from Olson's lab with $5 million in seed funding from CureDuchenne, and raised $40 million in a November 2017 series A from The Column Group (see **"Extending Exonics"**).