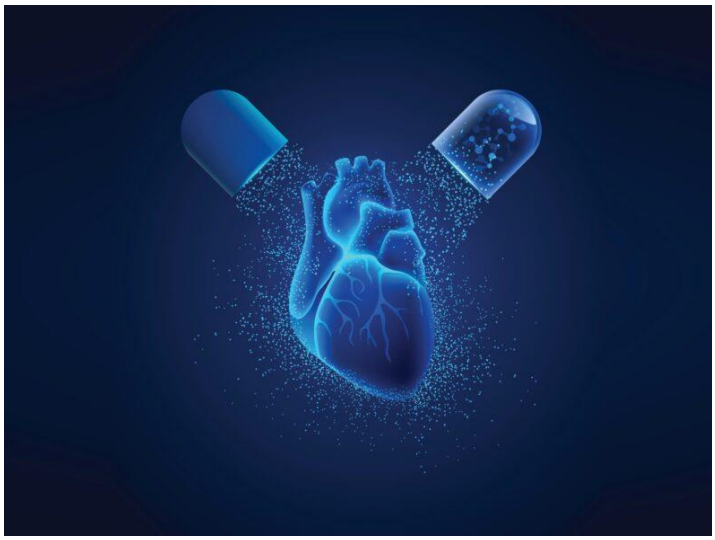
VUMC NEWS

Pediatrics
March 12, 2025

Potential therapeutic for Duchenne muscular dystrophy takes step forward

Positive findings from a clinical trial support further study of the investigational drug ifetroban to treat cardiac complications, the leading cause of death in patients with DMD.



By: Leigh MacMillan

A drug with connections to Vanderbilt University Medical Center improved heart function in patients with Duchenne muscular dystrophy (DMD), the company Cumberland Pharmaceuticals recently reported.

DMD is a rare inherited disorder that causes progressive muscle weakness. Children with DMD gradually lose muscle function — and their ability to walk, stand and even breathe on their own. Heart failure is the leading cause of death in DMD patients, but there are no approved therapies that specifically target DMD-related heart disease.

The positive findings from the Phase 2 FIGHT DMD trial support further study of the investigational drug ifetroban to treat cardiac complications of DMD.

The link between VUMC and ifetroban goes back almost 20 years. The drug was developed by the biopharmaceutical company Bristol Myers Squibb for various cardiovascular indications. It blocks signaling by thromboxane A2 and prostaglandin H receptors, which prevents platelet activation, clotting and blood vessel constriction, among other actions.

Bristol Myers Squibb discontinued development of ifetroban, and because of connections to the late John Oates, MD, who founded the Division of Clinical Pharmacology at Vanderbilt University and was a renowned researcher in the field of thromboxane and prostaglandin biology, the company donated the ifetroban program to Vanderbilt in 2006. Vanderbilt licensed ifetroban to Cumberland Pharmaceuticals, a specialty pharmaceutical company based in Nashville.

Researchers at VUMC and Vanderbilt continued to study ifetroban in cell and animal models, discovering other potential indications for the drug.

Notably, James West, PhD, professor of Medicine in the Division of Allergy, Pulmonary and Critical Care Medicine, and colleagues showed that ifetroban treatment improved cardiac output and survival, and reduced cardiac fibrosis (scarring), in animal models of muscular dystrophy. Their findings, reported in the *Journal of the American Heart Association* in October 2019, suggested that

ifetroban and other thromboxane receptor blockers could be novel therapeutics for treating heart disease in patients with muscular dystrophy.
In the FIGHT DMD trial, researchers at 10 locations, including Monroe Carell Jr. Children's Hospital at Vanderbilt, tested oral ifetroban in patients with DMD. The double-blind, randomized trial enrolled 41 DMD patients who received ifetroban (low or high dose) or a placebo. The trial measured the heart's left ventricular ejection fraction, a measurement of how much blood the left ventricle pumps out with each contraction, as a primary endpoint.

Larry Markham, MD, division chief of Pediatric Cardiology at Riley Hospital for Children in Indianapolis, is the principal investigator of the FIGHT DMD trial, which was supported by the Food and Drug Administration Office of Orphan Products Development.

Both doses of ifetroban were well tolerated, Cumberland Pharmaceuticals reported in a news release, with the patients receiving high-dose ifetroban having an overall 3.3% improvement in left ventricular ejection fraction.

"The cardiac imaging data from this trial is compelling," pediatric cardiologist Jonathan Soslow, MD, co-director of the DMD Clinic at Monroe Carell, noted in the release.

"The preservation and even improvement in cardiac function seen with ifetroban treatment stands in stark contrast to the expected decline we typically observe in untreated DMD patients," added Soslow, who holds the Dr. William R. Long Directorship in Pediatric Research.

The study findings represent a step forward to developing a treatment that specifically targets cardiac complications in DMD.

“Drug development can be a long road for small pharmaceutical companies,” said Kenneth Holroyd, MD, MBA, Vice President for Tech Transfer at VUMC and director of the Brock Family Center for Applied Innovation. “The positive trial results reflect Cumberland Pharmaceutical’s perseverance and belief in the science, along with a careful and well-executed clinical trial design.

“Hopefully, there is great impact to come for patients with DMD thanks to the long-standing VUMC-Cumberland Pharmaceuticals partnership and collaboration.”