Ifetroban

Oral Thromboxane Receptor Antagonist for the treatment of Duchenne muscular dystrophy

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Parent Project Muscular Dystrophy
JOIN THE FIGHT. END DUCHENNE.

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Disclosures

- No direct financial conflicts or disclosures
- PI for the clinical trial (no salary support)

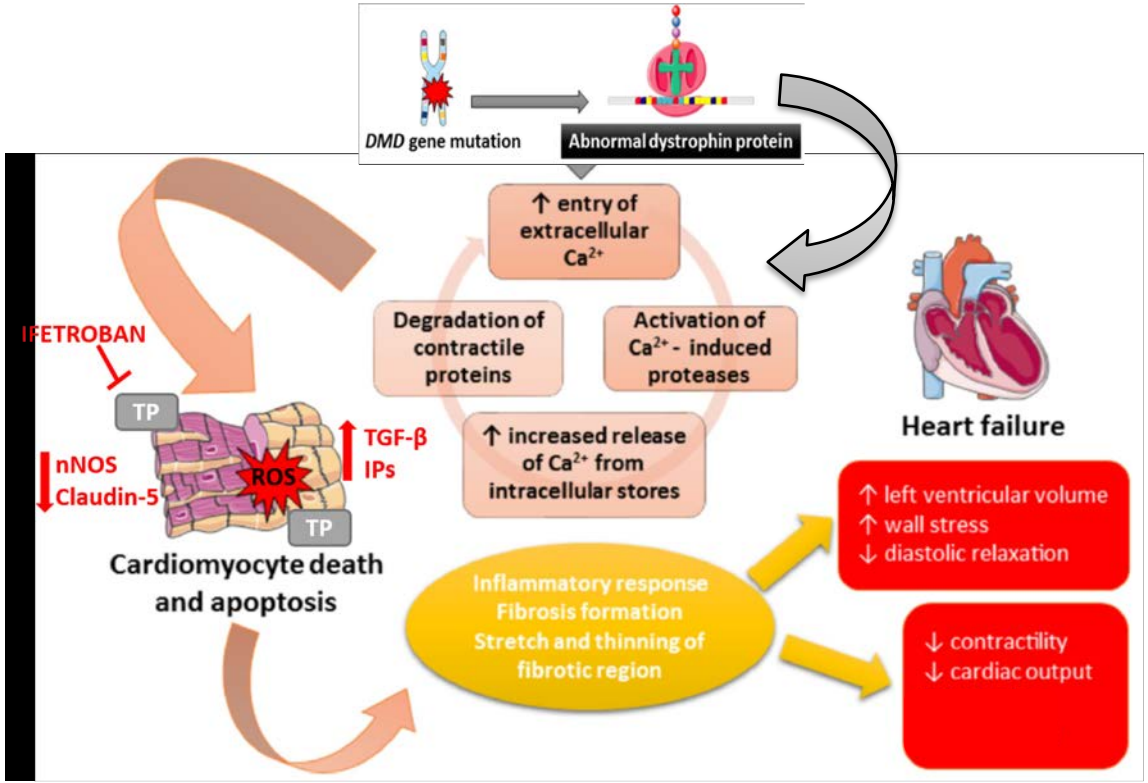
CUMBERLAND® PHARMACEUTICALS

- Specialty pharmaceutical company:
  - Developing products to address unmet medical needs
  - Headquarters in Nashville, TN
- Six marketed products:
  - Acetadote, Caldolor, Kristalose, Omeclamox, Vaprisol, Vibativ
- Ifetroban pipeline:
  - Cumberland is collaborating with multiple research centers to develop ifetroban for various orphan indications
  - Ongoing Phase 2 studies in systemic sclerosis and Samter's triad (allergic disease)
  - 16 Phase 1 & 11 Phase 2 studies completed
    - healthy volunteers or patients with cardiovascular disease, acute renal injury, or portal hypertension

Ifetroban

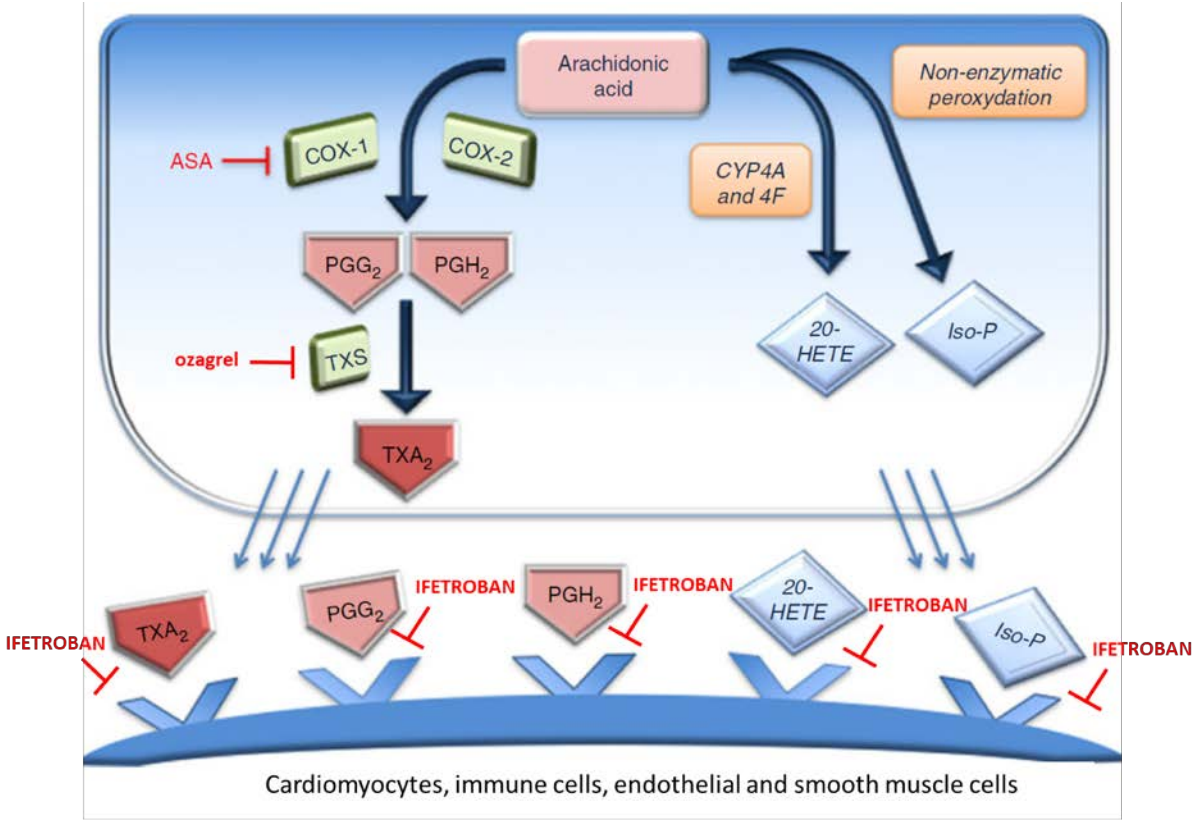
- A potent and selective antagonist of the thromboxane receptor (TPr)
- Ifetroban has or is being studied for unmet medical needs with no safety concerns identified to date
- Safety is well established
  - over 1,300 clinical trial participants
  - dosed in over 26 clinical studies
  - doses up to 1,000 mg without serious adverse events

Ifetroban Blocks Thromboxane Receptor Signaling to Prevent Inflammatory Response & Fibrosis



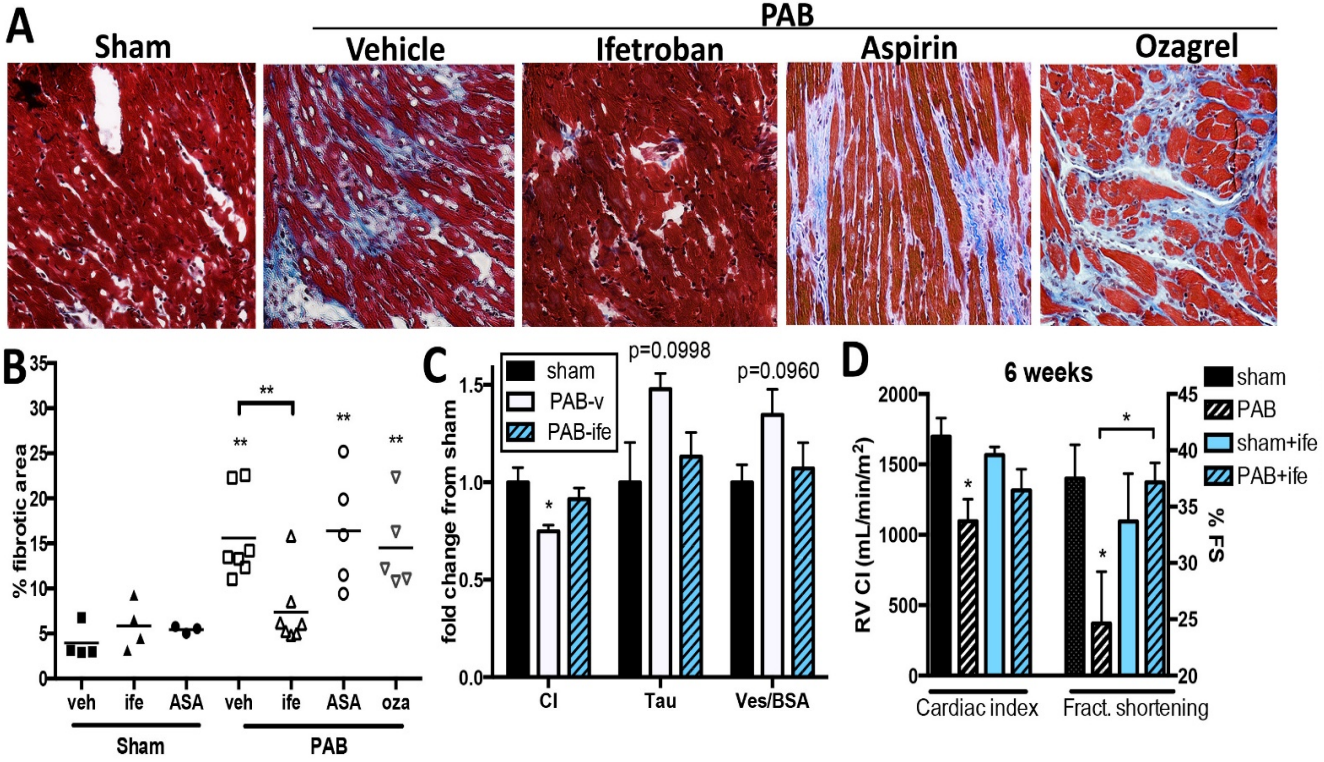
Modified D'Amario et al. 2017

Ifetroban Blocks all Thromboxane Receptor Ligands from Activating Pro-fibrotic Pathways



Ifetroban preclinical cardiac studies

Ifetroban prevents fibrosis & cardiac dysfunction in Pulmonary Artery Banding (PAB) Model of RV overload



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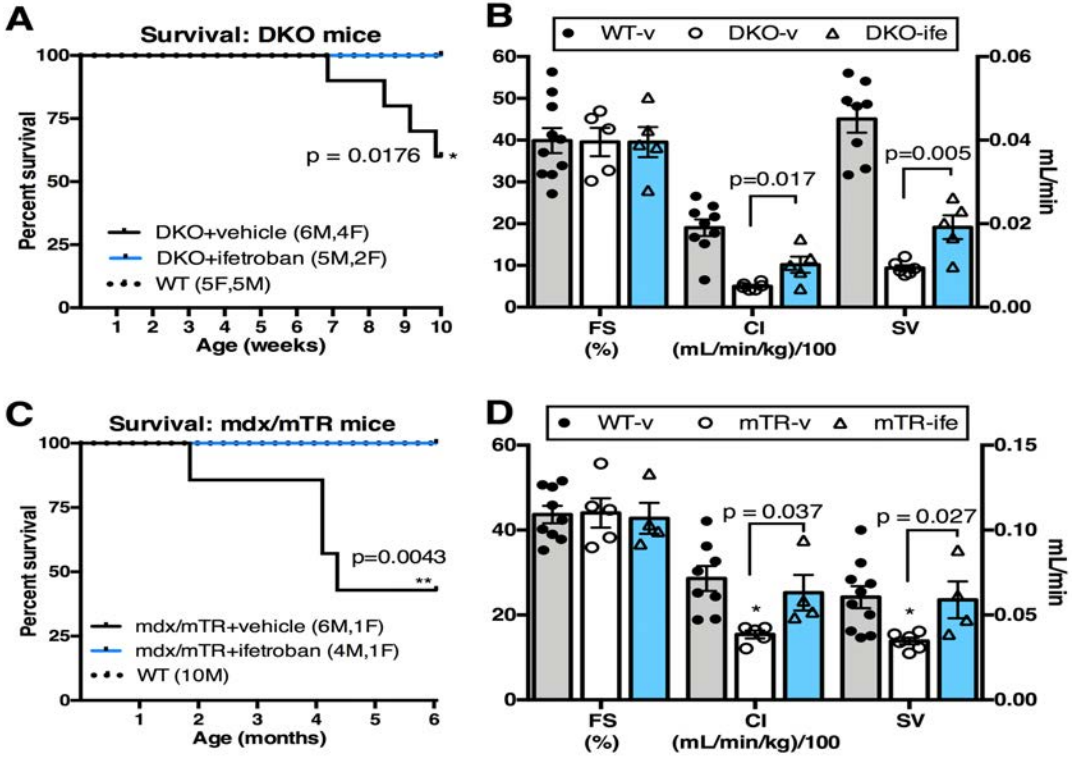
West et al. Pulmonary Circulation 2016

Ifetroban improves cardiac function & survival in two severe DMD mouse Models



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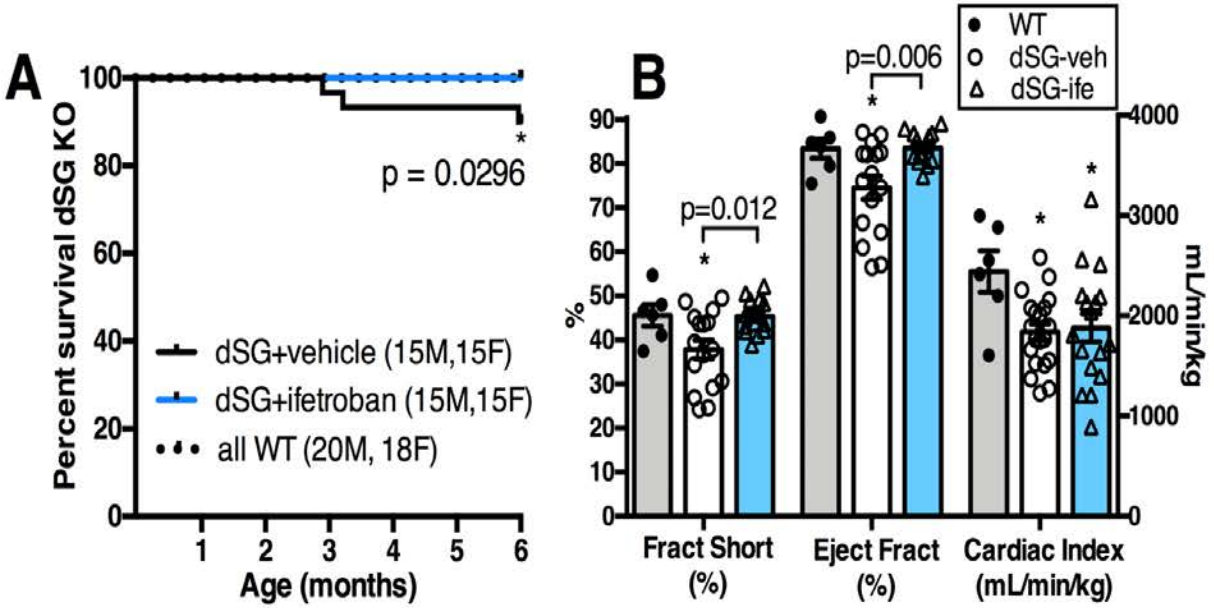
Carrier et al. Submitted unpublished

Ifetroban improves cardiac function & survival in limb-girdle md mouse model



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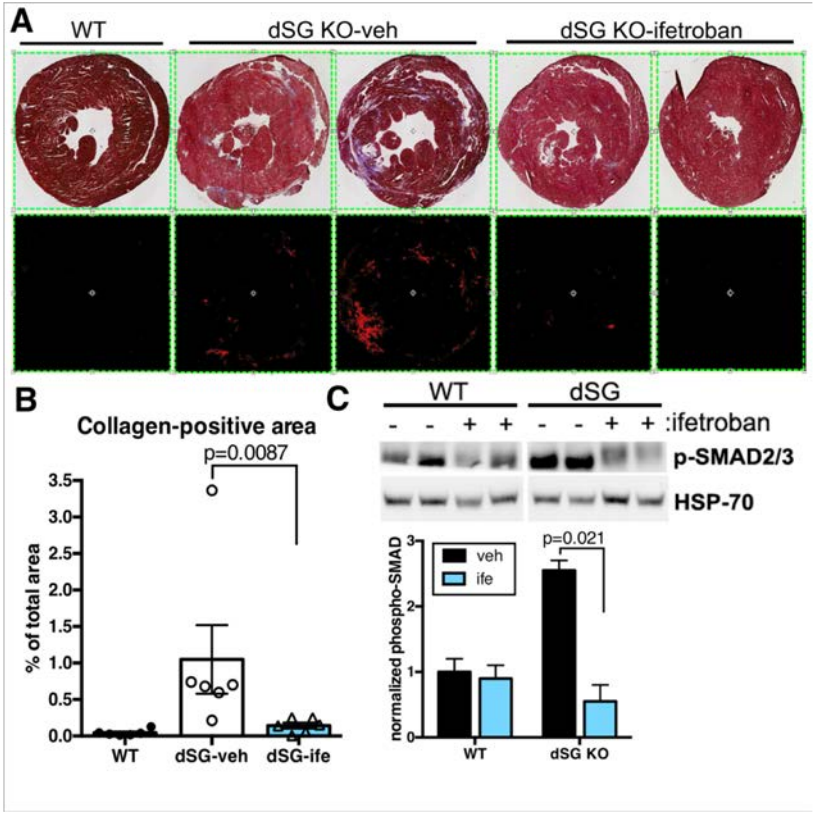
Carrier et al. Submitted unpublished

Ifetroban prevents cardiac fibrosis & blocks the pro-fibrotic TGF-beta pathway in LGMD mouse model



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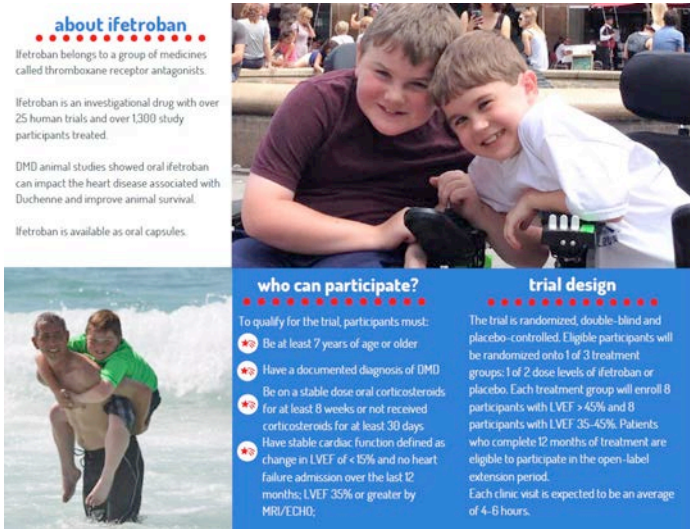
Carrier et al. Submitted unpublished

Ifetroban
Clinical DMD Trial



FIGHT DMD.com

THE FIGHT DMD TRIAL

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Inclusion criteria:

General:

- Males 7+ yo with DMD diagnosis
- Stable dose of oral corticosteroids ≥ 8 weeks or no corticosteroids for ≥ 30 days

Cardiac measures:

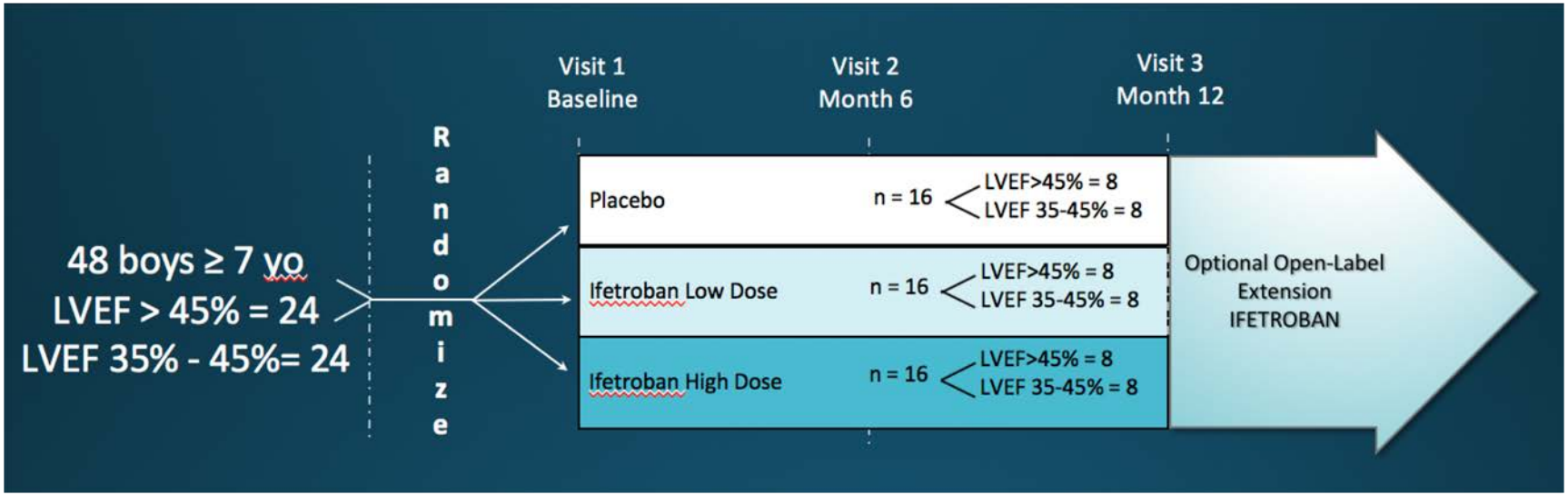
- Stable cardiac function over the last 12 months
  - Defined as change in LVEF of < 15% and no heart failure admission
- LVEF 35% or greater by cine CMR or echo
- Myocardial damage evident by late gadolinium enhancement allowed

Medications:

- ACEI, BB, or ARB therapy allowed (selection dictated by clinical care)
  - Started 3 months or greater from first trial dose
- ARA (spironolactone or eplerenone) allowed
  - Started 12 months or greater from first trial dose

Select Exclusion criteria:

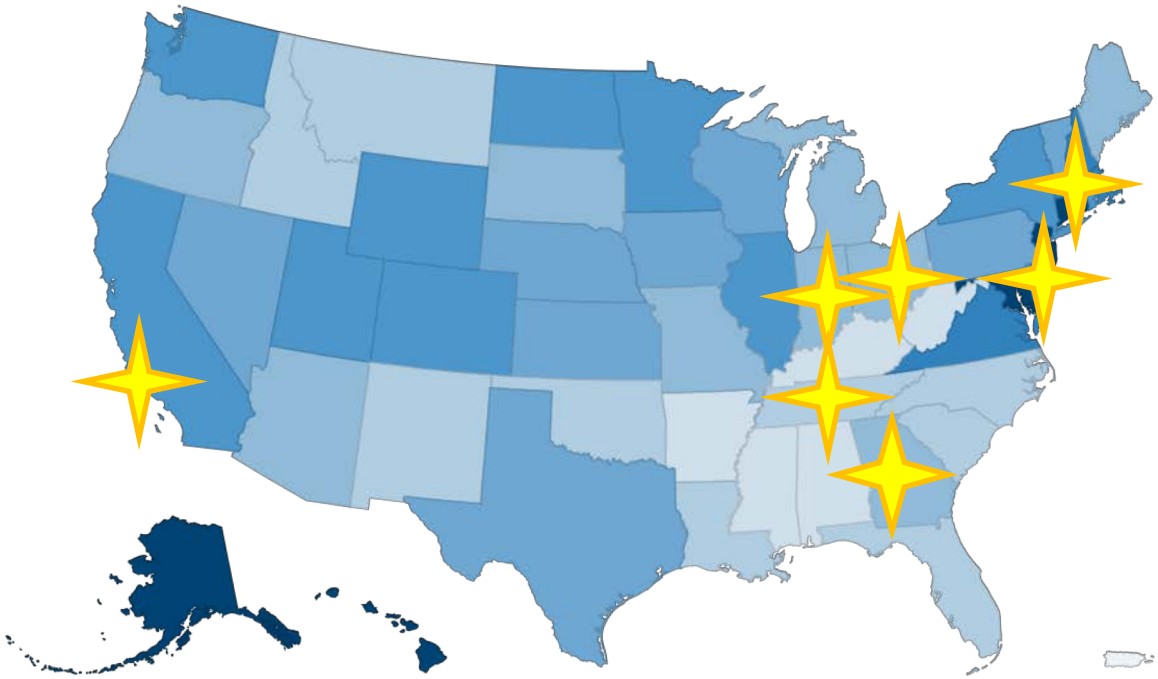
- A LVEF of < 35% by CMR or echocardiography during screening
- Participants in a therapeutic clinical trial in last 30 days or five half-lives (whichever is longer) of study entry
- A known bleeding disorder or has received anticoagulant treatment within 2 weeks of study entry
- Allergy to gadolinium contrast or known renal insufficiency defined as abnormal cystatin C or creatinine above the upper limit of normal for age.
- Non-MR compatible implants (e.g. neurostimulator, automatic implantable cardioverter-defibrillator [AICD])
- Any other active medical condition that could interfere with study participation



- Phase 2 Objective: evaluate efficacy, safety and PK of ifetroban in DMD
- Daily, oral ifetroban/placebo for 12 months; 2/3 of subjects randomized to ifetroban
- 3 visits in 12 months: CMR, PFT, QMT, QoL and 7-day actigraph
- Open-label extension available to all; placebo participants will receive ifetroban

- Key assessments at baseline, Month 6 & Month 12 visits
  - Cardiac MRI, PFT, Muscle Strength, Qualify-of-life surveys, 7-day activity monitoring
  - Day 0 PK completed within 4 hours at site using finger stick; 8-hr and 24-hr post-dose at home
  - Day 7 PK completed at home: pre-dose and 30 minutes post-dose

- Key eligibility and study features
  - All DMD boys ≥ 7 yo regardless of mutation type, ambulation status & steroid use eligible
  - No upper age limit
  - Standard of care meds allowed including eteplirsen
  - No biopsy or 6-minute walk test



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Expected U.S. Locations:

- Riley (IN),
- Vanderbilt (TN),
- Nationwide (OH),
- CNMC (DC),
- Emory (GA),
- UCLA (CA),
- Yale (CT)

For more information: email: research@cumberlandpharma.com
PPMD FAQ site: https://www.parentprojectmd.org/faqs/ifetroban/

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