

# A Cure For Wolfram

## Three Steps 5.0

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***REGROW*** vital tissues

- *MANF*

***REPLACE*** pathogenic genes

- *Gene editing*
- *Virus expressing healthy WFS1*

***STOP*** progression

- *ER calcium stabilizers (dantrolene & new)*
- *Molecular Prosthetics*

**Mutant WFS1 gene**



**Mutant WFS1 protein**



**ER calcium leakage**



**ER stress**



**Clinical Manifestations**

## **Gene Therapy**

- Deliver healthy WFS1
- Correct mutant WFS1
- Deliver a regenerative gene

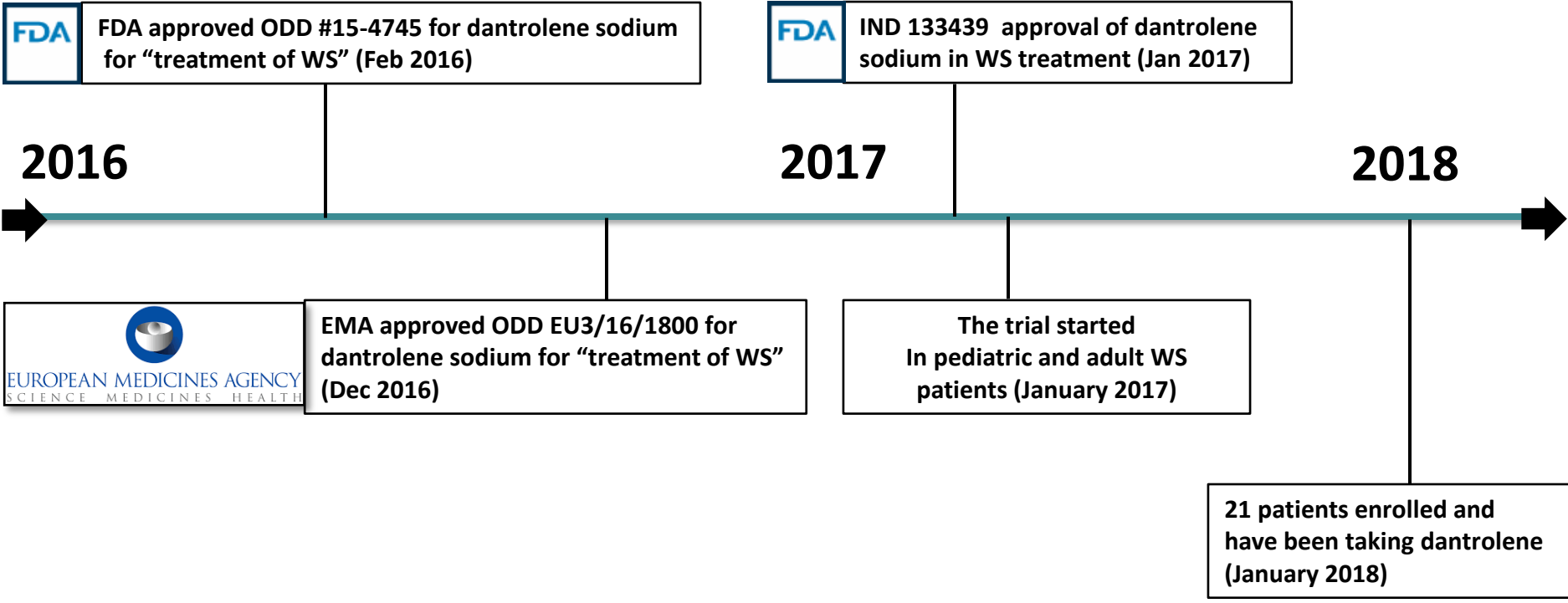
## **Molecular Prosthetics**

- Correct mutant WFS1 structure

## **ER Calcium Stabilizers**

- Dantrolene sodium (drug repurposing)
- 2<sup>nd</sup> generation ER calcium stabilizers

# Dantrolene Clinical Trial Progress



# Ongoing Proof-of-Concept Clinical Trial

ClinicalTrials.gov Identifier: NCT02829268

- **Adult and Paediatric Patients**
- **All the patients take dantrolene sodium**
- **To assess the safety, tolerability, and efficacy of dantrolene administered orally for 6-24 months.**
- **Endpoints**
  - **Safety and Tolerability (Liver enzymes, Muscle Strength)**
  - **Remaining Beta cell function (amount of insulin produced from participants' pancreas)**
  - **Best Corrected Visual Acuity**
  - **Neurological Functions (balance, bladder, and etc)**
  - **Quality of Life**

# Ongoing Proof-of-Concept Clinical Trial

ClinicalTrials.gov Identifier: NCT02829268

- **Adult and Paediatric Patients: 6-31 yo**
- **Appropriate Dose: 50 mg BID (1 mg/kg BID in children)**
- **Common side effects**
  - Diarrhea
  - Fatigue
- **Efficacy**
  - **Improved Remaining Beta cell function (cannot conclude this is due to dantrolene sodium as this is an open-label study)**
  - **Best Corrected Visual Acuity: No change**

# Gene Therapy – Three Options

2. Correct pathogenic  
WFS1 **GENE EDITING**

3. Deliver a regenerative gene  
**MANF**

1. Deliver healthy WFS1  
**VIRAL VECTORS**

