

# AMO-02-MD-2-001 STUDY: TIDEGLUSIB FOR CONGENITAL AND JUVENILE-ONSET MYOTONIC DYSTROPHY

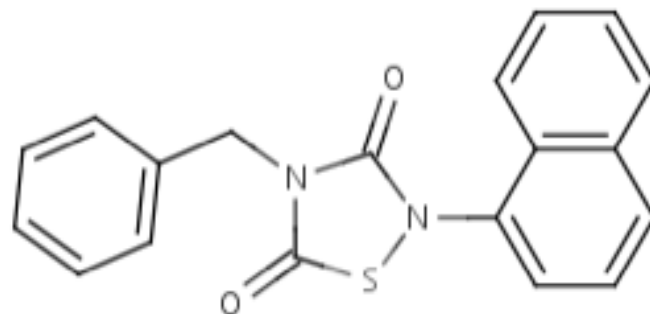
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# BACKGROUND OF COMPANY



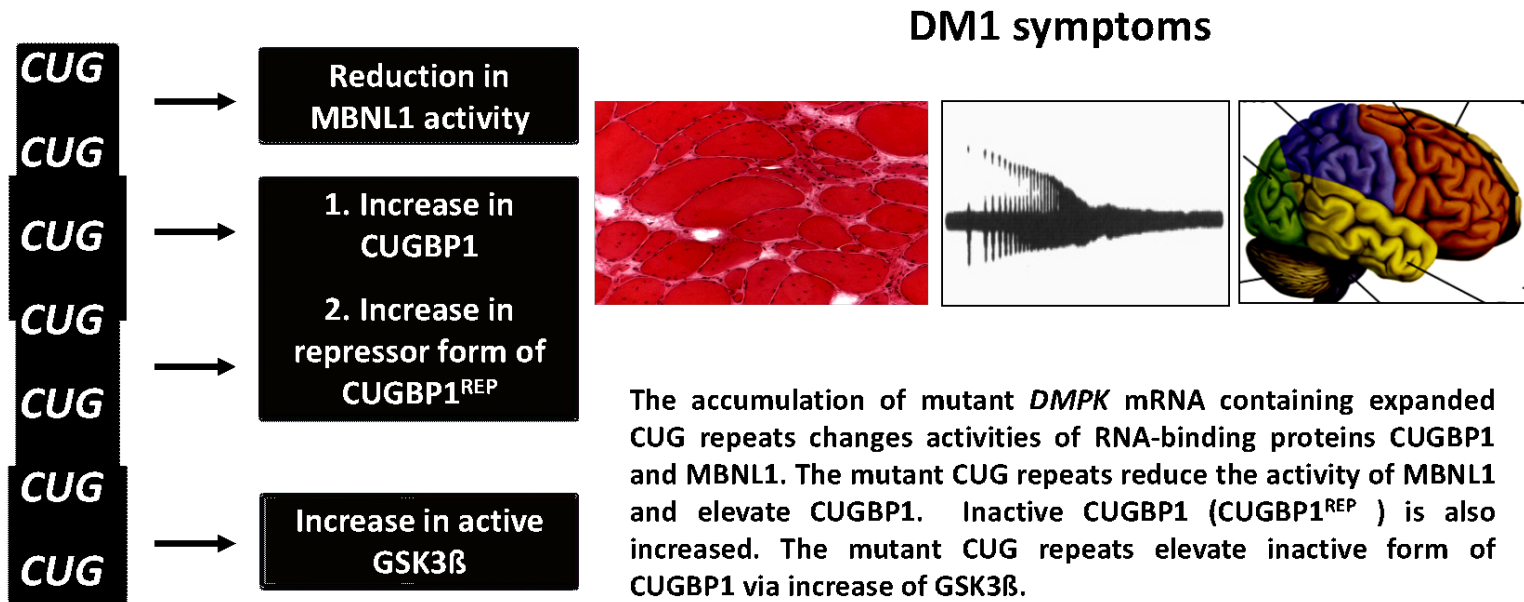
- AMO Pharma Ltd founded in 2015
- UK/US Company
  - Private funding
  - Experienced UK / US management team with significant experience in clinical development including in orphan diseases, neuromuscular and neurodevelopmental disorders
  - Focused on debilitating diseases with limited or no treatment options
  - Particular interest in the clinical presentation and treatment of these disorders in all age groups, ranging from early childhood to adulthood
  - Experienced in therapeutic areas that lack gold standard precedents study designs, outcome measures, etc.



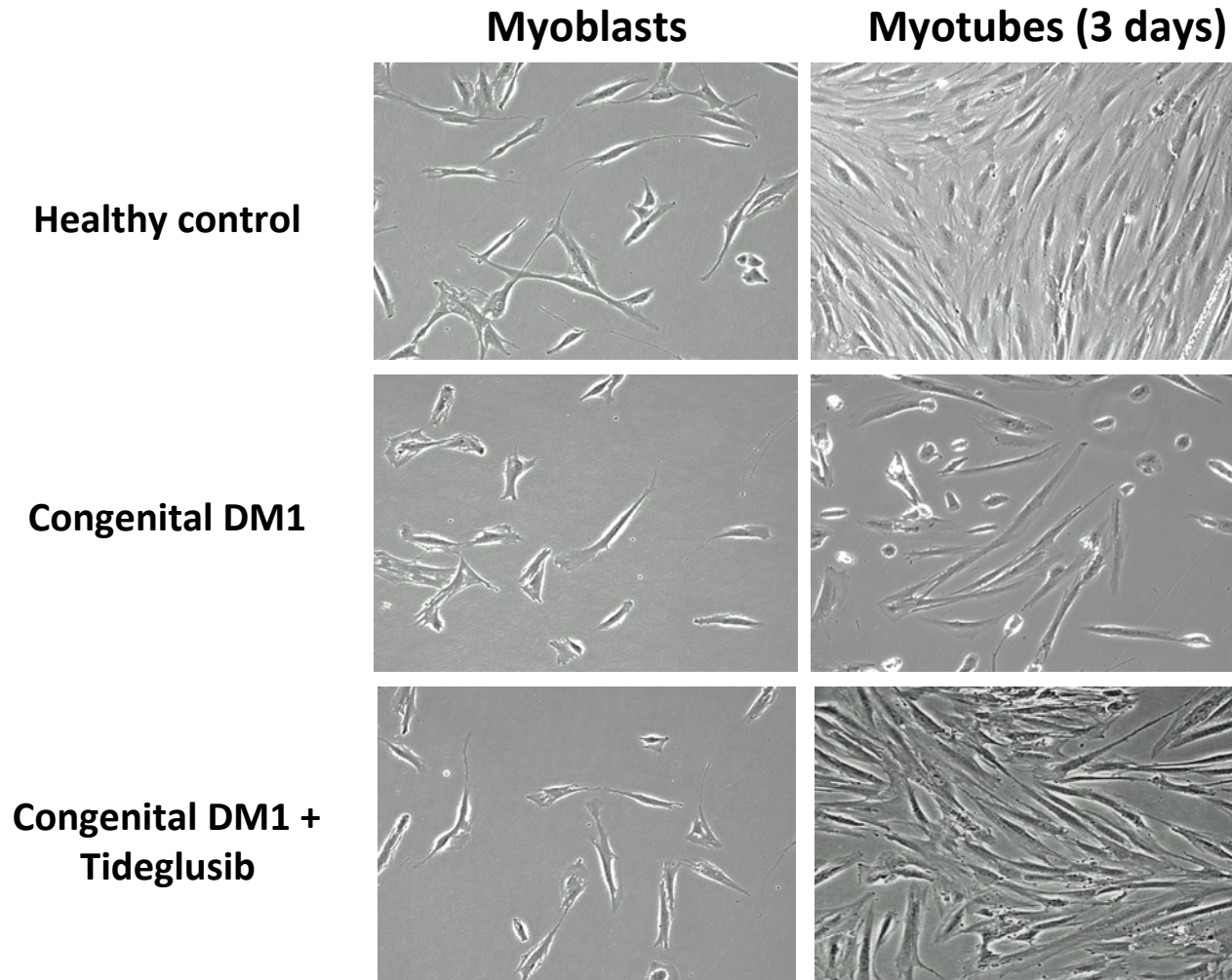
- Tideglusib (also referred to as AMO-02) is a GSK3 $\beta$  enzyme inhibitor
  - This enzyme plays an important role in muscle cells and in other cells in the body, including in the brain
- Several experiments (with “*in vitro*”, “*ex vivo*” and “*in vivo*” study designs) indicate that tideglusib has the potential to improve muscle structure and function in myotonic dystrophy, as well as to improve some of the cognitive problems that may be associated with this condition
- AMO-02-MD-2-001 is the first study in patients to test this potential

## GLYCOGEN SYNTHASE KINASE

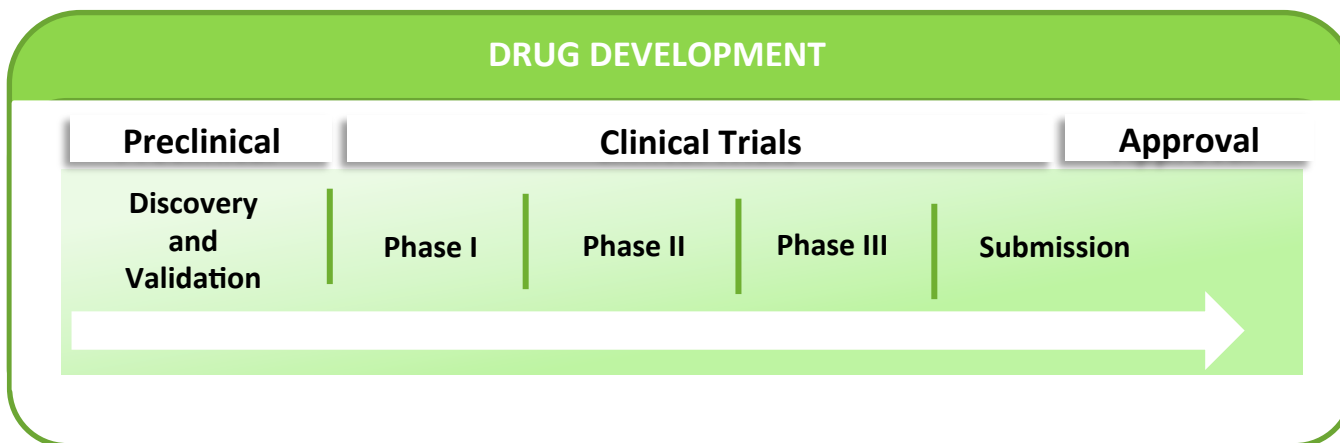
- Glycogen Synthase Kinase 3 beta (GSK3 $\beta$ ) is an intracellular enzyme important in the formation of new tissues
- GSK3 $\beta$  plays a role in formation of muscle fibers and in the connections between nerve cells
- GSK3 $\beta$  shows abnormally high activity in the presence of the myotonic dystrophy DM1 gene expansion
- We are testing the idea that reversing this increased GSK3 $\beta$  will have therapeutic benefit



# THE EFFECT OF TIDEGLUSIB ON MYOGENESIS OF PRIMARY MYOBLASTS FROM PATIENTS WITH CONGENITAL MYOTONIC DYSTROPHY



**Effect of tideglusib on the differentiation of congenital DM1 myoblasts.** The fusion of un-treated Congenital DM1 myoblasts is reduced relative to myoblasts from healthy controls. Congenital DM1 myoblasts treated with Tideglusib (4.7  $\mu$ M) show improved differentiation in 3 days in fusion medium (C). Magnification is 10 x.



- **Phase 2 study**
- **Adolescents and adults with congenital and juvenile-onset myotonic dystrophy**
  - Genetic diagnosis of type 1 myotonic dystrophy since birth or since before the age of 12 years old
- **Primary goal is to investigate the safety and tolerability of tideglusib in this clinical population**
- **Secondary goals are to investigate whether tideglusib alleviates the symptoms of myotonic dystrophy, and to understand how blood levels of tideglusib change across time in myotonic dystrophy patients**

## AMO-02-MD-2-001 STUDY DESIGN (CONT)

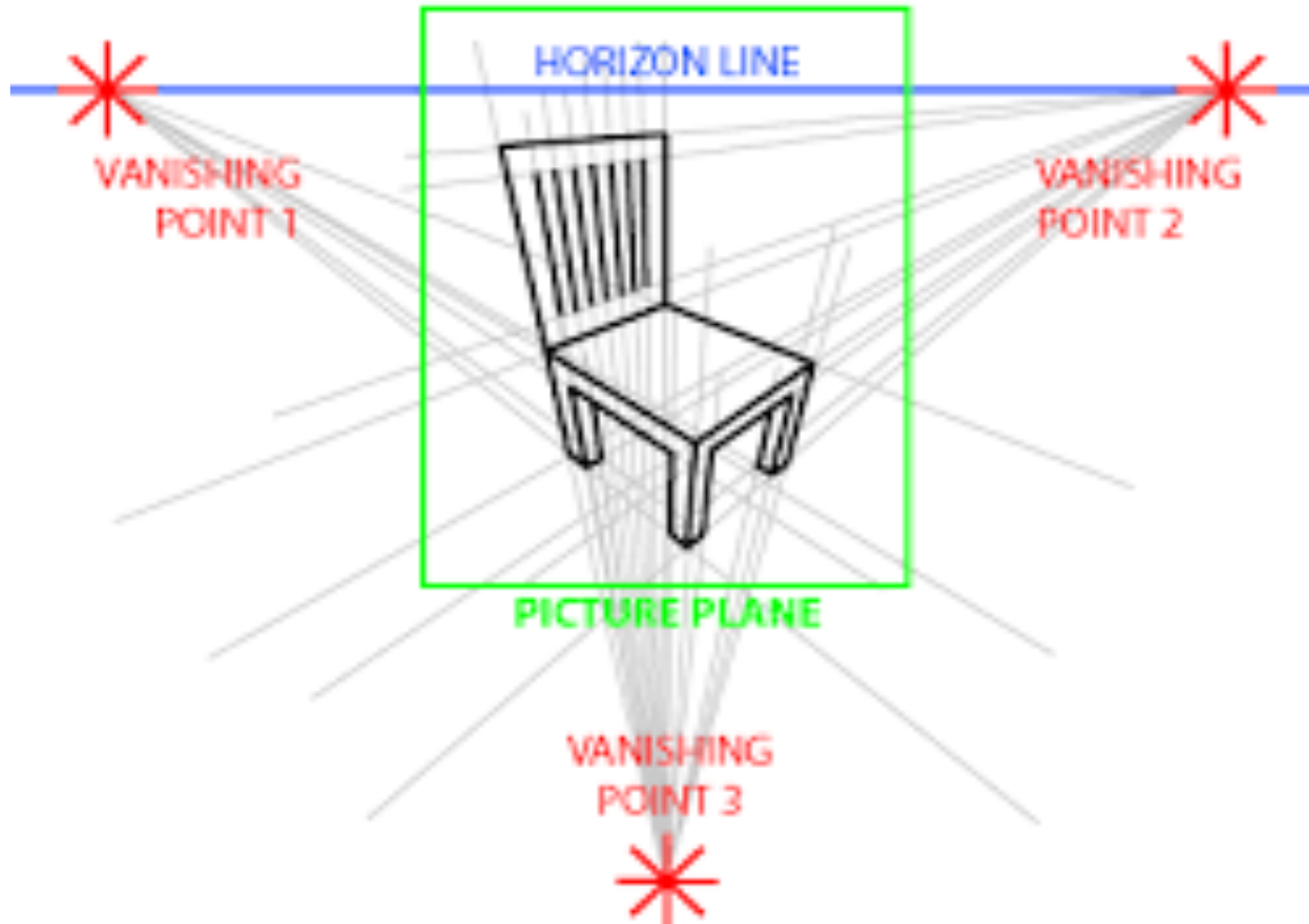
- **The study commenced in June of this year in the UK at the Newcastle University Institute for Genetic Medicine**
  - Principal investigator: Professor Hanns Lochmuller
- **Will assess two dose levels of tideglusib across a 14 week period**
  - Total study duration for each participant is up to 20 weeks, including screening and follow-up periods
  - All participants will receive both active and placebo but, the participant and their caregiver will be unaware when they are receiving study drug and placebo during this 14 week period
- **N = 16**
- **The study will involve a number of cognitive and muscle function tests, lung function tests, patient/caregiver reported outcome questionnaires, as well as clinician rating scales**
- **Independent Data Safety Monitoring Committee**

## AMO-02-MD-2-001 STUDY DESIGN (CONT)

- **Assessments of muscle functioning and muscle mass**
  - Examples: 10 meter walk/run test, computerized handgrip measure of grip strength and relaxation time
- **Clinician and caregiver rating scales**
  - Examples: Clinical Global Impressions Scale (CGI-S and CGI-I), and Top 3 Concerns (caregiver and where possible, patient; related to the patient's myotonic dystrophy)
- **Assessments of cognitive functioning and neurodevelopmental symptoms**
  - Example: Peabody Picture Vocabulary Test
- **Blood-based biomarkers**
  - Example: GSK3 $\beta$  levels and activity



## THREE-POINT PERSPECTIVE



## PHASE 2 STUDIES - GOALS

- **Generate initial safety and tolerability profile in this patient population**
- **“Proof of concept”**
  - Desirable to avoid a Type II error (‘false negative’)
    - Especially when there are options concerning the ideal dose, the ideal dosing regimen, the ideal treatment period, the ideal measures/assessments, etc.
  - Pattern recognition – clinical benefit
- **Dose selection for Phase 3 studies**
- **Development and selection of outcome measures**
  - Rating scales
    - Clinician-completed vs patient/caregiver-completed
  - Syndrome-specific
  - Informed by natural history study
  - Role of biomarkers

## NEXT STEPS



- Earlier this year AMO Pharma completed discussions with the U.S. Food and Drug Administration (FDA) for a planned investigational new drug (IND) application for tideglusib
- AMO Pharma is planning additional global studies of tideglusib in both congenital and adult onset myotonic dystrophy
- Based on FDA feedback, AMO Pharma is currently working to finalize plans to advance its clinical development program