INTERNATIONAL ALLIANCE OF ALS/MND ASSOCIATIONS

# Cytokinetics – Reldasemtiv
# Spring 2020

## Background

Cytokinetics is a company that was founded in 1997 to develop treatments targeting impairments in muscle function.

Cytokinetics has recently tested reldasemtiv after previously working on their initial ALS drug tirasemtiv. Tirasemtiv showed promising results in a Phase 2 clinical trial (BENEFIT-ALS) in 2014, and was followed by a phase 3 clinical trial (VITALITY-ALS) that failed to show any significant positive effects on the disease. One of the key problems with tirasemtiv was tolerability. Despite targeting muscle, it also entered the brain and caused nausea, dizziness and other symptoms that were considered safe, but not particularly tolerable, as it caused participants to drop out of trials, thereby reducing the statistical power needed to determine any benefit.

Prior to the completion of the phase 3 trial, Cytokinetics also began a phase 2 trial of reldasemtiv, which had all the muscle benefits of tirasemtiv, but without the ability to cross the blood-brain barrier into the central nervous system and cause the unwanted side effects of dizziness and nausea. This was a large phase 2 clinical trial (over 400 participants) that had vastly improved tolerance, but did not meet it's goals of showing statistically significant slowing of breathing capacity, disease progression rate or muscle strength. However, as the dosing was only for 12 weeks and the trends were in the direction of a positive result, the interpretation is not necessarily that of a failed trial, but rather one that would need further testing to determine if reldasemtiv has value for treating ALS.

Cytokinetics is currently planning a phase 3 clinical trial with recruitment aiming to start in 2020.

## Recommendation

**Currently there is no knowledge as to whether reldasemtiv works to improve muscle function or slow disease progression in ALS. Results from the reldasemtiv phase 2 clinical trial show increased tolerance and safety compared to tirasemtiv. The potentially promising results on disease progression, breathing function and muscle strength will require the forthcoming phase 3 clinical trial to examine any significance.**