I AM ALS ● 2019

Agenda
September 26, 2019

- Review prior expectations from February 11th, 2019 meeting
  Sandy Morris

- Overview of Finalized ALS FDA Guidance Document
  Dr. Peter Marks or Dr. Billy Dunn

- Dialogue about any gaps from I AM ALS Recommendation Document submitted August 28th, 2019
  Group Discussion

- Encourage patient representation at future IND Meetings
  Deb Bellina

- Review future deliverables
  Sandy Morris

February 11, 2019 Expectations

- Point person for ALS community
  - Accomplished

- Supportive stance from the FDA leaders for Expanded Access
  - Accomplished

- Requested follow up meetings quarterly
  - This was not accomplished
  - We are re-requesting quarterly Follow Up meetings with FDA Leaders until we are ‘on track’

- Finalized ALS FDA Guidance Document incorporating ALS Patient Recommendations
  - Accomplished

ALS FDA Finalized Guidance Document Gaps - what was missed? From I AM ALS Recommendation

- Interim Analysis
- Addressing Disease Heterogeneity
- Use of PRO-ACT Database

Interim Analysis

- Every trial should include an Independent Review Board (IRB) to examine safety as well as success on an interim basis.

- The IRB can also supervise any re-randomization as part of the trial

Addressing Disease Heterogeneity

- Encouragement of a crossover design so that the same patient participants are included in both trial arms. The control can still include a second control of a shared placebo group, thus creating two alternative control arms. Appropriate where drug/biologic half life does not create the need for an abnormally long wash out period

- Re-randomization of outlier progressors - 300% or more of mean ALS monthly progression rates

Use of PRO-ACT Database

- Consists of progression data of over 10,000 patients who participated in the control arms of prior ALS trials receiving placebos

- Can be used in two ways:
  - Run historical control alongside actual control so that FDA and Sponsor can learn/study
  - Any shared placebo controlled group can be compared to the PRO-ACT data in order to ensure it reflects the disease population

September 26, 2019 Requests

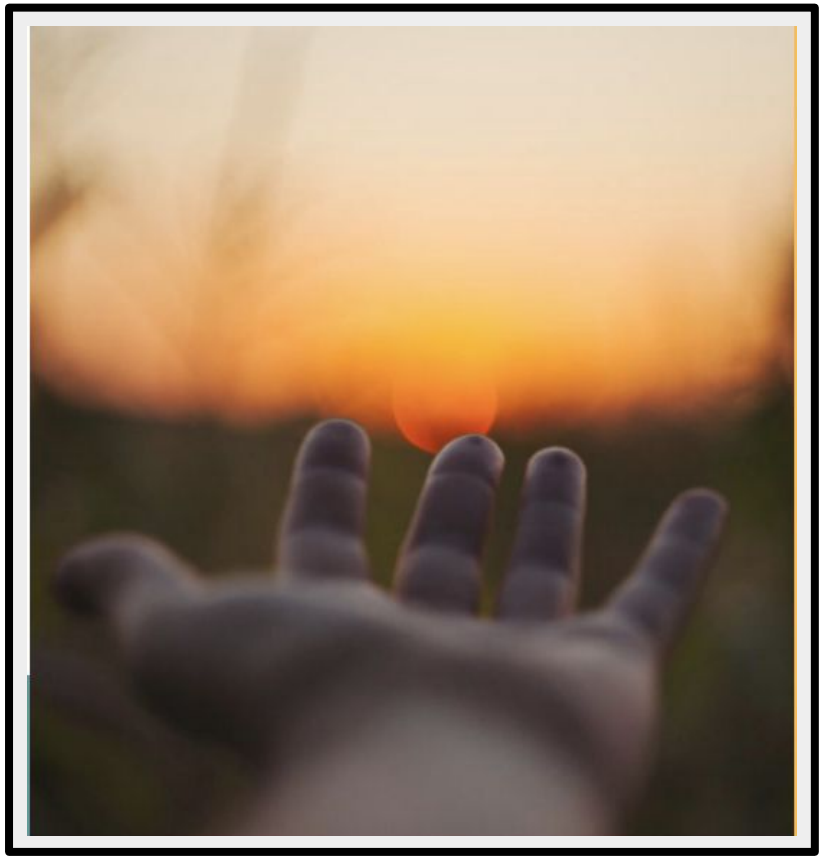
- Quarterly follow up meetings until ALS clinical trial design is on track

- De facto mandate the Patient Voice at IND meetings or any other meeting for clinical trial design with Drug Sponsors
  - “Which one of you is the patient?”

- Continue publicly and privately to encourage Drug Sponsors to include Expanded Access

- Do not lose sight of “Moonshot” - creating a Neurodegenerative Disease Department to combine forces rather than divide and ‘parcel’ in the current model

Thank you



Backup Slides

- *I AM ALS Recommendation Document*
  August 28, 2019

- *Clinical Trial Survey from Ipsos*