ISCTM
THE INTERNATIONAL SOCIETY FOR CNS CLINICAL TRIALS AND METHODOLOGY

# Methodological Issues Associated with the New FDA Alzheimer's Draft Guidance

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# Disclosures – Adam Butler

- Stockholder in CRF Bracket

Regulatory Evolution on Alzheimer's Disease Trials

# Early Alzheimer's Disease: Developing Drugs for Treatment

## Guidance for Industry

***DRAFT GUIDANCE***

**This guidance document is being distributed for comment purposes only.**

# The Field is Changing, Quickly

- Draft FDA Guidance Presents Several New Concepts
  - Outcome Measures
  - Diagnostic Criteria
  - Time-to-Event Analysis?
  - Randomized Start or Randomized Withdrawal Designs?

# Co-Primary Endpoints?

*"This historical dichotomy of functional and cognitive assessments has led to common use of the terms cognition and function with respect to outcome assessment in AD clinical trials, with the implication that an effect on cognition is non meaningful unless accompanied by a benefit on an independent endpoint assessing function in a meaningful manner."*

# Co-Primary Endpoints?

*"**FDA rejects this dichotomy** and finds such usage inappropriate, because it implies that an effect on cognition itself, regardless of the nature of the observed effect and the manner in which it is assessed, cannot be clinically meaningful."*

# Agenda

- ADCOMS Demonstrates Sensitivity to Disease Progression and Treatment Effects
  - Veronika Logovinsky, MD, PhD
- Bayesian Adaptive Design Employing ADCOMS for Dose Selection
  - Chad Swanson, PhD
- A Data Driven Approach to Developing Composite Endpoints
  - Clinton Hagen, MS
- Is There A Cognitive Test that can Detect Cognitive Impairment Associated with AB+ in the Absence of Dementia?
  - Jason Hassenstab, PhD
- Informant Report to Detect Amyloid Related Cognitive Decline in the Absence of Dementia
  - Anna-Karin Berger, MSC, PhD
- Discussion