

# Negative Symptoms Working Group

ISCTM

October 6, 2014

---

# Objectives

---

- Review recent clinical trials data and potential innovations that may impact future negative symptom clinical trial design.

# Data Presentations

---

- Dragana Bugarski-Kirola: Findings and Methodological Observations from the Bitoperin Negative Symptom Studies
- Eduardo Dunayevich: AMG 747 Phase II Studies: Study Designs and Baseline Patient Characteristics
- Jean-Pierre Lindenmeyer: Psychometric Testing of the New Integrated Negative Symptom Factor in the Catie Data Set
- Michael Green: Objective Measures of negative Symptoms
- Eva Velthorst: CONNECT: Social Engagement as a Primary Target for Cognitive Behavioral Treatment of Negative Symptoms in Schizophrenia

# Points of General Consensus

---

- Improvement in the placebo arm in negative symptom studies is likely to be sustained
- Potential strategies for reducing placebo arm improvement:
  - a. Minimize the number of evaluations per visit
  - b. Institute standardized paradigms for social engagement prior to and after randomization.
- The purported relationship between social engagement and placebo response should be formally tested

# Points of General Consensus

---

- Requirement of a informant may influence patient selection to sicker (eg, require caregiver) or more well (maintain relationships) population
- Potential benefits of more restrictive entry criteria must be balanced against enrollment challenges. Eg, One third or fewer of CATIE patients would qualify for prominent neg. sx
- PANSS Integrated Negative Symptom Factor (PINSF) (developed from principle component analysis and IRT of CATIE data set) is sensitive to change. Larger effect size than PANSS Neg. Subscale

# Points of General Consensus

---

- Objective measures of negative symptoms (eg, impaired motivation, emotional expression) might have less placebo response and measurement error than subjective measures
- Demoralization of patients should be addressed as a factor potential inhibiting improvement in clinical trials
- Social engagement is strongly predictive of hospitalization for schizophrenia

# Future Plans

---

- Meet yearly to review clinical trials data as it impacts recommendations for negative symptom trial design.