**Overview**

- **Part A: PK** Chemistry II. Volume 4, [3]
  - Targeted therapy benefit is expected for about 80% of patient population.
  - Full genomic analysis of ANAVEX®2-73 Phase 2a Alzheimer’s Disease Study Identifies KEM®-Focused Analysis on Subsets of Rules.

**Material and Methods: DNA and RNA Sequencing**

- DNA and RNA sample extraction
- Library preparation
- DNA and RNA sample enrichment
- DNA and RNA sample sequencing
- Analysis

**Data Analysis**

- Using data platform KEM® version 3.6.2
- Association rules provide unique, unbiased results and generate new hypotheses
- KEM® (Knowledge Extraction Management) helps overcome the challenges of analyzing biomarker data in small clinical studies (d) Rule example

**Results: COMT Gene Variant Associated with Differentiated Response**

- Patients with a wild-type COMT gene were found to have an improved benefit from ANAVEX®2-73.
- Gene Variant Markers Improve Effect Size (Cohen’s d) with ANAVEX®2-73

**Summary**

- Systematic analysis using KEM® identifies actionable parameters enabling a precision medicine approach to include best responders in follow-up Phase 2b/3 study
- Patients with a wild-type SIGMAR1 gene were found to have an improved benefit from ANAVEX®2-73.
- Gene Variant Markers Improve Effect Size (Cohen’s d) with ANAVEX®2-73