### Background

- The Coalition Against Major Diseases (CAMD), a public-private partnership, previously developed a regulatory-endorsed FDA (1 & EMA) clinical trial simulation tool (CTS) for Alzheimer’s disease (AD), using integrated standardized data from control arms of legacy trials in mild to moderate AD.
- Contemporary datasets acquired within CAMD after the initial regulatory endorsement warrant an update of the CTS.

### Objectives

- Acquire, standardize, and integrate contemporary patient-level datasets into the CAMD database according to the Clinical Data Interchange Standards Consortium (CDISC) standards.
- Utilize expanded database to update the existing CTS for mild-to-moderate AD using a Bayesian mixed effects modeling framework.

### Methods

**Data Sharing Initiative (Figure 1):**

- Consortia, such as CAMD, are initiated by collaborating with stakeholders to address an unmet medical need.
- Research questions are framed and data sources are identified.
- Acquisition of relevant data sets from data contributors is initiated with a legally binding data contribution agreement.
- An encrypted transfer is used to send data to a secure storage server.
- A comprehensive data remapping effort to CDISC standards is performed in conjunction with a thorough data curation.
- Standardized data sets are integrated into the consortium database.

**Figure 1. Schematic of an expanded data sharing initiative such as CAMD**

**Source:** Dj Corrigan, AO Karlsson, K Romero, C Sarris, J Wilkins. Open Innovation: towards sharing of data, models and workflows. Eur J Pharm Sci. 2017 (pub ahead of print)

### Results

**Expanded database overview:**

- The contemporary CAMD database contains 15 studies of control data from legacy trials, an increase of 6 studies since the development of the original CTS (Table 1).

**Table 1. Summary level statistics comparing original and contemporary CAMD database**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Original database</th>
<th>Expanded database</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of studies</td>
<td>9</td>
<td>15</td>
</tr>
<tr>
<td>Individuals</td>
<td>3255</td>
<td>4575</td>
</tr>
<tr>
<td>Mean age</td>
<td>73.9</td>
<td>74.1</td>
</tr>
<tr>
<td>% female</td>
<td>55.1%</td>
<td>55.4%</td>
</tr>
<tr>
<td>Mean years since dx</td>
<td>2.07</td>
<td>2.46</td>
</tr>
<tr>
<td>Mean baseline ADAScog</td>
<td>23.4</td>
<td>24.0</td>
</tr>
<tr>
<td>Info on number of APOE4 alleles</td>
<td>1486</td>
<td>1895</td>
</tr>
<tr>
<td>Concomitant medication info</td>
<td>2483</td>
<td>3271</td>
</tr>
</tbody>
</table>

### Envisioned outcome

- A completed update of the CTS will involve the following milestones:
  - Separation of natural progression and placebo effect component by incorporating observational longitudinal data from the Alzheimer’s Disease Neuroimaging Initiative (ADNI) database.
  - Confirm the additive allele effect of APOE4 and background medication use related finding with the ADNI data.
  - Develop a user-friendly interface to provide accessibility of the tool to all members of a clinical development team.

- Regulatory endorsement for the updated CTS will be pursued in order to provide the most up to date tool for clinical trial design and simulation for mild to moderate AD.

### References