months. Patients with Alzheimer’s disease had a transient improvement in cognitive function with conventional therapy (CT), but declined to a level similar to no treatment after 18 months. CT supplemented with herbal medicine provided additional benefit. The effect from herbal medicines became more pronounced over time. Expected decline of MMSE were calculated by formula produced from previous data. CT+H denotes conventional therapy with herbal medicine; CT denotes conventional therapy alone; MMSE, mini-mental state examination. * P<0.05.

**P1-056**

**POPULATION PHARMACOKINETIC-PHARMACODYNAMIC (PK/PD) MODELING OF E2027, A SELECTIVE PHOSPHODIESTERASE-9 (PDE9) INHIBITOR, FOLLOWING SINGLE ASCENDING ORAL DOSES IN HEALTHY VOLUNTEERS**

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**Background:** To develop a population pharmacokinetic/pharmacodynamic (PPK/PD) model for E2027, a selective PDE9 inhibitor, following single ascending oral doses in healthy volunteers (HV), which will be used to drive dose selection in subsequent studies. **Methods:** Plasma concentration-time data of E2027, from a 4-part randomized, double blind, placebo-controlled, single ascending dose, Phase 1 study in HV, were subjected to population PK analysis by nonlinear mixed effect modeling. The effects of various baseline, demographic characteristics and dose on PK were evaluated. Post-hoc estimates of final PPK parameters were used in subsequent development of a population PK/PD (PPK/PD) model to describe the changes in cerebrospinal fluid (CSF) cGMP concentrations over time. The final PK and PPK/PD models were used to predict E2027 steady-state exposures and percent increase in CSF cGMP from baseline following multiple oral doses. **Results:** The PK of E2027 was best described by a 2 compartment model with two input functions with five transit compartments, and first-order elimination. All parameters were estimated with good precision (CV% <10%). Weight, gender, and dose (>200 mg) significantly affected the PK of E2027. Percent CSF cGMP changes from baseline were best described by a sigmoidal inhibitory E max model on k out, with IC50 of 118 ng/mL, and I max of 0.813. Although, the PPK and PPK/PD models are being updated with PK and PD data from multiple ascending dose studies, simulations using the currently developed PPK/PD model suggest that once-daily E2027 dosed at, or above 100 mg should maintain cGMP at a 3-fold increase from baseline. **Conclusions:** A PPK/PD model for E2027 was successfully developed. This model supports selection of once daily doses for proof of concept studies, demonstrating target engagement that provides adequate CSF cGMP level elevations.

**P1-057**

**DEVELOPMENT, APPLICATION, AND RESULTS FROM A CLINICAL INFORMATICS PLATFORM THAT ENABLES A MULTI-MODAL TREATMENT PROTOCOL FOR ALZHEIMER’S DISEASE (AD)**

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**Background:** Clinical informatics platforms are improving the treatment of individuals with chronic, complex diseases. The pathologic drivers of Alzheimer’s disease are numerous and active simultaneously, with different etiologies for every individual. Muses Labs has deployed an informatics platform that integrates large datasets measuring different parameters of individuals to generate personalized, multi-modal treatment protocols for those at risk or in early stages of AD. **Methods:** The AD1 Protocol implemented by Muses Labs uses a data-analytics engine to optimize research-supported treatment recommendations to slow or reverse multiple factors associated with AD simultaneously. Data inputs comprise genomics, bio-synopsis measurements, imaging results, medical histories, medications, allergies, immunizations, comorbidities, and results of cognitive evaluations. Algorithms compare the status of multiple physiological and lifestyle states known to be contributors to cognitive decline against desired normative states. We observe that AD disease drivers are interlocked, comprising modifiable feedback loops. Software algorithms implement the protocol, and generated recommendations are delivered to physicians. Health coaches motivate individuals’ adherence and ongoing data collection. **Results:** One to five iterations of protocols were generated for self-selected individuals (n=183, 52% pre-MCI, 58.5% female, mean age 66.7 years, mean 17.6 years of education, mean BMI 24.6). Genome data files were obtained with patient consent (65.4% ApoE4 carriers). 100+ serum blood tests were collected in each iteration. Approximately 60% of individuals on the protocol for 6 months have improved memory function, as measured on standardized cognitive evaluations. **Conclusions:** An informatics-based platform enables an actionable combination therapy for AD. This allows the testing of the hypothesis that recommended intervention protocols for physician usage can consistently modulate a large number of factors. From an IT perspective,