Overview
The Tuberous Sclerosis Alliance (TS Alliance) established the Tuberous Sclerosis Complex (TSC) Preclinical Consortium to:

- grow opportunities for clinical trials in TSC tumors, epilepsy and neuropsychiatric disorders (TAND)
- provide a forum for collaboration with academia and industry
- standardize models, tests and assays for preclinical drug development
- repurpose drugs
- evaluate analogs with improved safety
- investigate novel compounds and mechanisms of action
- ensure transparency, robustness, replication and rigor of research

Accelerating Drug Development
The Consortium complements our other research programs by providing preclinical proof of concept for potential new treatments.

Both preclinical and clinical biosamples are available to evaluate mechanism of action and test hypotheses between mice and humans.

Data Sharing and Exclusivity
Consortium is open to any investigator or company.

Public Screening
Bucket A
Reference compounds with results released to consortium
Consortium covers cost of experiment

Private Screening
Bucket B
Company’s compound with results released to consortium
Escrow period to protect IP

Bucket C
Company’s compound – results not released to consortium
No strings attached

TSC Tumor Mouse Models
105K (Tsc2-null) cell graft

TSC Epilepsy Mouse Models
TSC1-GFAP Conditional KO

Phenotype
- Tsc1flox/flox;GFAP-Cre+ from crossing Tsc1flox/flox with Tsc1flox/-;GFAP-Cre-
- Develop spontaneous and robust epilepsy beginning at age 3-5 weeks

Validation with rapamycin
- Rapamycin completely prevented seizures when administered beginning at P21
- Strong reduction of seizures when administered beginning at P35

MEK1 Inhibitor PD-0325901
- MEK1 inhibitor shrunk tumors comparably to rapamycin when administered beginning at day 16 (~100mm³)

RhebCA – in utero electroporation in CD1 mice

Phenotype
- Greater number of seizures per day compared to TSC1-GFAP CKO

Validation with rapamycin
- Rapamycin inhibited seizures when dosed at P15-132

Nominations are Welcomed!
Thirty compounds or combinations of mechanisms of action tested to-date, e.g., mTOR, PI3K, MEK1, checkpoint kinase, PD-1, CTLA4, and more.

For more information, contact Dean Aguiar at daguiar@tsalliance.org.