

# TRanslational Initiative to DE-risk NeuroTherapeutics

## Who We Are

### The TRanslational Initiative to DE-risk NeuroTherapeutics (TRIDENT)

is a first-of-its-kind revolutionary preclinical testing platform for neurodegenerative diseases that redefines how therapies are evaluated before clinical trials.

### One Platform. Multiple Models. Faithfully Modeling Human Disease.

TRIDENT unifies iPSCs, organoids, and humanized mice and marmosets for cross-species modeling, facilitating translatable, high-confidence therapeutic testing.

### Clinically Aligned. Translational By Design.

TRIDENT mirrors clinical standards across touchscreen cognition, imaging, and molecular biomarkers to deliver preclinical data you can trust to translate.

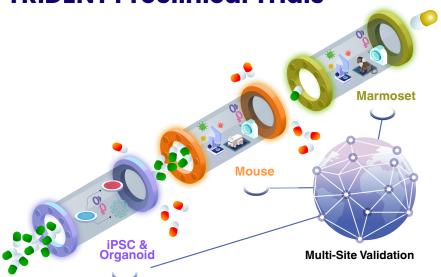
### De-risk Early. Invest Strategically. Succeed Faster.

TRIDENT will enable early, informed choices — helping biopharma advance the most promising therapies while minimizing delays, costs, and failure.

#### Transforming Preclinical Trials. Advancing Real-World Impact.

TRIDENT is reshaping preclinical trials to raise the standard for efficacy, paving the way for effective therapies to reach patients sooner.

## **TRIDENT Preclinical Trials**



Funded By





## What We Do Differently

### **De-Risking Therapeutics With TRIDENT Trials**

TRIDENT integrates human-derived iPSCs and organoids, and newly developed humanized mouse and marmoset models to enable matched, cross-species modeling of brain diseases.

We standardize:

- Cognition as a preclinical endpoint, using human-relevant touchscreen tasks similar to those used to assess patients in clinics, ensuring translatable and meaningful readouts.
- Brain imaging, aligned with clinical trial protocols, to evaluate therapeutic efficacy and detect adverse effects.
- Whole-brain pathology, to track molecular biomarkers and uncover disease and treatment mechanisms.
- Sex-Based Analysis Plus (SBA+), integrated across all models to identify sex-specific efficacy and safety profiles.
- Open science and multi-site validation, which enhances transparency, reproducibility, and generalizability across diverse research environments.

TRIDENT's unique, robust, and standardized approach maximizes predictive validity, **transforming preclinical trials** from a bottleneck into a launchpad for clinical translation.

### Alliance of Renowned Neuroscience Leaders



camh | womenmind

















## **Development & Validation Roadmap**

### **Establish TRIDENT** Workflow

#### **Biomarkers**

- Cognition
- **Imaging**
- Molecular

### **Develop Humanized Models**

- alphasynucleinopathies
- Alzheimer's Disease

### Validate TRIDENT Concept

- Known therapies
  - Failed
  - Passed
- New therapies

TRIDENT **Preclinical Trials Platform** 

### **TRIDENT Workflow Is Being Established In All Models**

Patient

iPSCs/

**Organoids** 

#### Modeling PFF Seeding & Uptake

**iPSCs** 

Organoids

**3iomarkers** 





Neurons & Glia

#### **Testing Therapeutics**

Uptake

High



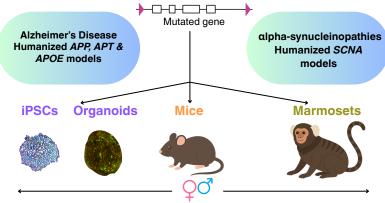
**iPSCs** 



**Organoids** 

### **Humanized Models Are Being Developed**

Same genetic mutations are modelled across models and species



Integrated Sex-Based Analysis Plus

### **Touchscreen** Cognition



### **Preclinical** MRI

herapy



Anatomy & Functional

Molecular



Clearing & Lightsheet

### TRIDENT Concept Is Being Validated



Failed in clinical trials Does it fail in TRIDENT trials faster?



Clinically promising therapies Do they clear TRIDENT trials as well?



**New therapies** 

**TRIDENT facilitates translational data-driven** go/no-go decisions.









15.2T MRI

Aggregates Labelled







Auto-fluorescence

### αlphasynucleinopathies

- Known
  - **Mouse Version of** Cinpanemab
  - PU-AD
- New
  - Vaccine

### Alzheimer's **Disease**

- Known
  - **Mouse Version of** Lecanemab
- New
  - Vaccine
  - o C-31















