Unleashing the Power of Tregs
Dysfunctional Tregs are associated with neuroinflammation promoted by activated T effector cells and activated innate myeloid cells.

**COYA 301: Proprietary Treg Enhancing Low-Dose IL-2 Suppresses Adaptive Immunity and Innate Immunity**

- Robust suppression (up to 90%) of adaptive immune T cells
- Limited (up to 30%) suppression of innate myeloid cells

**Treg Expansion/Suppressive Function**

- ALS Dysfunctional Treg
- Functional Tregs
- T-Effecto Cells
- Myeloid Cells

COYA 301: Proprietary Treg Enhancing Low-Dose IL-2 Suppresses Adaptive Immunity and Innate Immunity
Overall Study Design

- Proof-of-Concept open-label study, conducted at Houston Methodist Hospital
- Population: 8 patients with mild-to-moderate AD
- Treatment: 4 monthly COYA 301 cycles administered subcutaneously, followed by 2-month post-treatment observation. The study was conducted with commercially available product.
- Assessments:
  - Treg suppressive function and Treg numbers
  - Peripheral proinflammatory biomarkers
  - Cognitive status
  - Safety and tolerability
COYA 301 Enhances Treg Function and Numbers \textit{in vivo} in AD Patients (N=8)

**Statistically Significant Enhancement of Treg Suppressive Function**

- Treatment
- F/U

**Statistically Significant Enhancement of Treg Numbers**

- Treatment
- F/U

*\( \text{p}<0.05 \), **\( \text{p}<0.01 \), ***\( \text{p}<0.001 \)
COYA 301 Significantly Lowers Plasma Proinflammatory Chemokines and Cytokines in AD Patients

CCL11: chemokine C-C motif ligand 11 (eotaxin-1); CCL2: chemokine monocyte chemoattractant protein 1
IL-15: interleukin 15

**p<0.05, **p<0.01, ***p<0.001
COYA 301 Significantly Lowers Expression of Proinflammatory Cytokines in AD Patients

**TNFα Monocyte Expression**

- Pre-dose: 30, 60, 90, 120, 168
- Post-dose: 30, 60, 90, 120, 168
- Mean (SD) Percent Change

**IL-6 Monocyte Expression**

- Pre-dose: 30, 60, 90, 120, 168
- Post-dose: 30, 60, 90, 120, 168
- Mean (SD) Percent Change

**IL-1β Monocyte Expression**

- Pre-dose: 30, 60, 90, 120, 168
- Post-dose: 30, 60, 90, 120, 168
- Mean (SD) Percent Change

**Notes:**
- TNFα: tumor necrosis factor alpha; IL-6: interleukin 6; IL-1β: interleukin 1 beta
- Mean Change from Baseline (N=5)
- *p<0.05, **p<0.01, ***p<0.001
COYA 301 Improved or Halted Cognitive Decline in AD Patients

**MMSE Score (N=8)**

- **Treatment**
- **F/U**

**CDR-SB Score (N=8)**

* **p<0.05, ** **p<0.01**  
ns: not significant

**ADAS-Cog Score (N=8)**

MMSE: Mini-Mental State Examination, ADAS-Cog: Alzheimer's Disease Assessment Scale-Cognitive Subscale  
CDR-SB: Clinical Dementia Rating scale – Sum of Boxes
Case Study of Brain Imaging of AD Patient before and after COYA 301 treatment

70-Year-Old Male
Baseline MMSE: 12
Positive PIB PET Scan
Positive Neurodegeneration MR
Other Rx: Donepezil 10mg

The second PET scan was done 2 weeks after last dose.

PET: Positron Emission Tomography
TSPO: translocator protein

Neuroinflammation (TSPO)

(11)C ER-176 PET Scan at baseline and after 4-monthly cycles of low dose IL-2.
COYA 301 Safety & Tolerability

• Overall, COYA 301 was well tolerated.
• Most common adverse events (AEs) were mild injection site reactions and mild leukopenia.
• All patients completed the study.
• No death or other serious AE occurred over the course of the study.