

Unleashing the Power of Tregs

COYA THERAPEUTICS, INC.

NASDAQ: COYA | Investor Presentation

January 2024

www.coyatherapeutics.com



Cautionary Note of Forward-Looking Statements and Disclaimers

This presentation and the accompanying oral presentation contain “forward-looking” statements that are based on our management’s beliefs and assumptions and on information currently available to management. Forward-looking statements include all statements other than statements of historical fact contained in this presentation, including information concerning our current and future financial performance, business plans and objectives, current and future clinical and preclinical development activities, timing and success of our ongoing and planned clinical trials and related data, the timing of announcements, updates and results of our clinical trials and related data, our ability to obtain and maintain regulatory approval, the potential therapeutic benefits and economic value of our product candidates, competitive position, industry environment and potential market opportunities. The words “believe,” “may,” “will,” “estimate,” “continue,” “anticipate,” “intend,” “expect,” and similar expressions are intended to identify forward-looking statements.

Forward-looking statements are subject to known and unknown risks, uncertainties, assumptions and other factors including, but not limited to, those related to the success, cost and timing of our product candidate development activities and ongoing and planned clinical trials; our plans to develop and commercialize targeted therapeutics; the progress of patient enrollment and dosing in our clinical trials; the ability of our product candidates to achieve applicable endpoints in the clinical trials; the safety profile of our product candidates; the potential for data from our clinical trials to support a marketing application, as well as the timing of these events; our ability to obtain funding for our operations; development and commercialization of our product candidates; the timing of and our ability to obtain and maintain regulatory approvals; the rate and degree of market acceptance and clinical utility of our product candidates; the size and growth potential of the markets for our product candidates, and our ability to serve those markets; our commercialization, marketing and manufacturing capabilities and strategy; future agreements with third parties in connection with the commercialization of our product candidates; our expectations regarding our ability to obtain and maintain intellectual property protection; our dependence on third party manufacturers; the success of competing therapies or products that are or may become available; our ability to attract and retain key scientific or management personnel; our ability to identify additional product candidates with significant commercial potential consistent with our commercial objectives; and our estimates regarding expenses, future revenue, capital requirements and needs for additional financing.

We have based these forward-looking statements largely on our current expectations and projections about future events and trends that we believe may affect our financial condition, results of operations, business strategy, short-term and long-term business operations and objectives, and financial needs. Moreover, we operate in a very competitive and rapidly changing environment, and new risks may emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. In light of these risks, uncertainties and assumptions, the forward-looking events and circumstances discussed herein may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements. Although our management believes that the expectations reflected in our forward-looking statements are reasonable, we cannot guarantee that the future results, levels of activity, performance or events and circumstances described in the forward-looking statements will be achieved or occur. We undertake no obligation to publicly update any forward-looking statements, whether written or oral, that may be made from time to time, whether as a result of new information, future developments or otherwise.

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We have filed a registration statement on Form S-1 (including a preliminary prospectus) with the SEC for the offering to which this presentation relates. The registration statement has not yet become effective. Before you invest, you should read the preliminary prospectus in the registration statement (including the risk factors described therein) and other documents we have filed with the SEC for more complete information about our company and the offering. You may get these documents for free by visiting EDGAR on the SEC web site at <http://www.sec.gov/>. The preliminary prospectus, as amended, is available on the SEC website at <http://www.sec.gov>.

Coya's Leadership Has Demonstrated Deep Expertise in Biotech

Management Team



Howard Berman, Ph.D.
Chief Executive Officer &
Chairman of the Board



Fred Grossman, D.O., FAPA
President & Chief Medical
Officer



David Snyder
Chief Financial Officer &
Chief Operating Officer

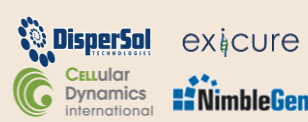


Arun Swaminathan, Ph.D.
Chief Business Development
Officer



Michelle Frazier
Senior Vice President
of Regulatory Affairs

Prior Experience*



Board of Directors



Ann Lee, Ph.D.
Chief Technical Officer
of Prime Medicine



Anabella Villalobos, Ph.D.
Head of Biotherapeutics and
Medicinal Sciences of Biogen



Dieter Weinand
Former Chairman of Board and
CEO, Bayer Pharma, AG

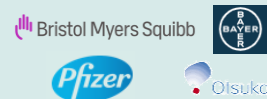


Dov Goldstein, M.D., MBA
Chief Financial Officer
of BioAge Labs



Hideki Garren, M.D., Ph.D.
Chief Medical Officer
of Prothena Biosciences

Prior Experience*



SAB Comprised of Seminal Leadership in Tregs



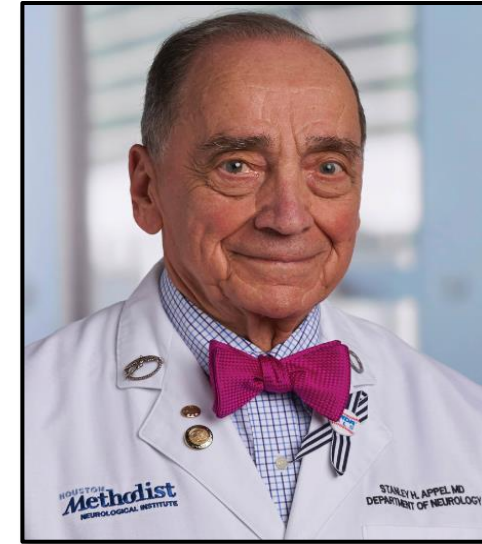
Following the discoveries of Dr. Sakaguchi and Dr. Appel, Coya is developing multiple product modalities to enhance the therapeutic potential of Tregs for the treatment of disorders of high unmet need



Shimon Sakaguchi, MD, PhD

Distinguished Professor at the World Premier International Research Initiative (WPI)-Immunology Frontier Research Center (IFReC) at Osaka University

Discovered Tregs in 1995 and their role in inflammation and autoimmune conditions



Stanley Appel, MD

*Former Chair of the Stanley H. Appel Department of Neurology
Director of the Ann Kimball & John W. Johnson Center for Cellular Therapeutics
Houston Methodist Hospital*

Pioneered research in neuro-inflammation and the development of Treg targeted therapies

Robust Treg-focused Pipeline

Product Type	Discovery	Preclinical	IND-Enabling	Phase 1	Phase 2	Phase 3	Partnerships / Collaborations	Milestones
Treg-Enhancing / T Effector & Macrophage Depleting Biologics	COYA 302 (Low Dose IL-2 + CTLA4 Ig)* <i>Amyotrophic Lateral Sclerosis (ALS)</i>							H1 2024: IND filing and Ph2 initiation H1 2024: PoC Peer-Reviewed publication H1 2024: Biomarker data publication
Treg-Enhancing Biologic	COYA 301 (Low Dose IL-2)** <i>Alzheimer's Disease (AD)</i>							Summer 2024: Academic double blind Ph2 top-line data
Allogeneic Treg-Derived Exosomes	COYA 201 <i>Undisclosed Indications</i>							2024: Additional animal model data
Antigen-Directed Allogeneic Treg-Derived Exosomes	COYA 206 <i>Undisclosed Indications</i>							2024: Target validation and cargo validation data

Focused on Advancing Clinical Programs in 2024

Coya Therapeutics' Highlights



Focused on Regulatory T Cells (Tregs)

- **Most clinically-advanced company focused on Treg-modulating therapies**
- Multi-modality approach:
 - Biologics (COYA 300 series)
 - Exosomes (COYA 200 series)

COYA 301= Proprietary Low Dose Interleukin-2 (IL-2)- (Licensed from ARScience Bio)

COYA 302 = COYA 301 + CTLA4 Ig (Licensed From Dr. Reddy's Laboratories)



Strong Early Clinical Data

- **COYA 301 completed PoC IIT study*** in Alzheimer's Disease (AD)
- **COYA 302 completed PoC IIT study*** in Amyotrophic Lateral Sclerosis (ALS)
- COYA 200 series for neurodegenerative diseases, autoimmune / inflammatory conditions, and metabolic diseases

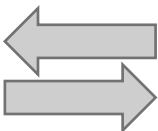


Multiple Near-Term Catalysts (12-18 months)

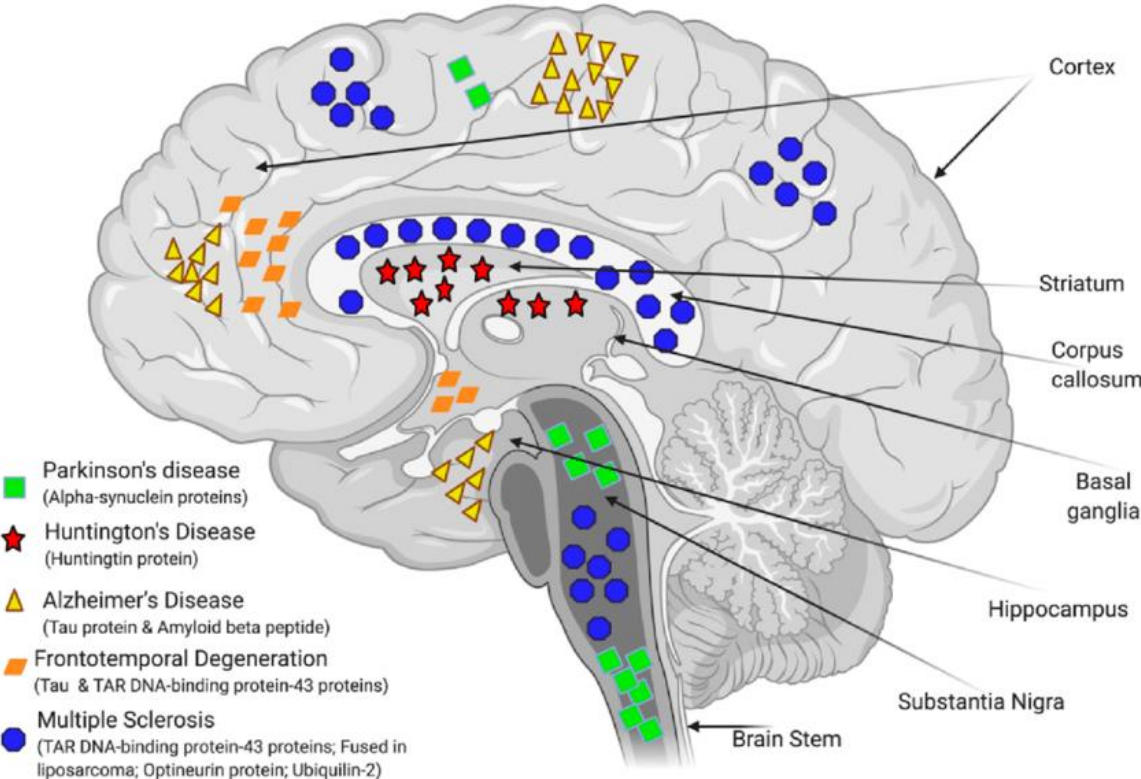
- **COYA 301** Peer-Reviewed publication (2H 2023), Academic double-blind Phase 2 POC top-line data (Summer 2024), AD/PD Conference Data Presentation (Q1 2024), 301 combination animal study in AD (2H 2024)
- **COYA 302** Biomarker data (ALS) release and publication (Q1 2024), IND filing and Phase 2 initiation in ALS (1H 2024), Peer-Reviewed POC trial in ALS publication (Q1 2024)
- **COYA 200** Platform Series animal model validation data (2024)/ out-license discussions
- **COYA 206** target validation & custom cargo validation (2024)/ out-license discussions

Inflammation Plays a Critical Role in Neurodegeneration: Regulatory T cells (Tregs) Dysfunctional

Neurodegeneration: Loss of Selective Population of Neurons



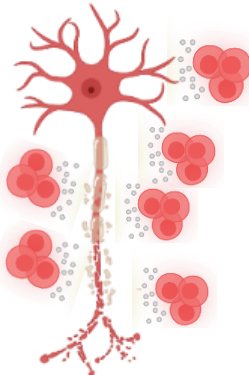
Inflammation in the Nervous System



Healthy Neuron



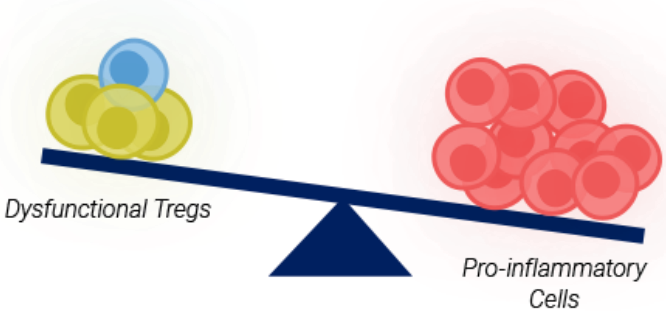
Sick Neuron



Dead Neuron



Tregs play central role in inflammation and progression of neurodegeneration

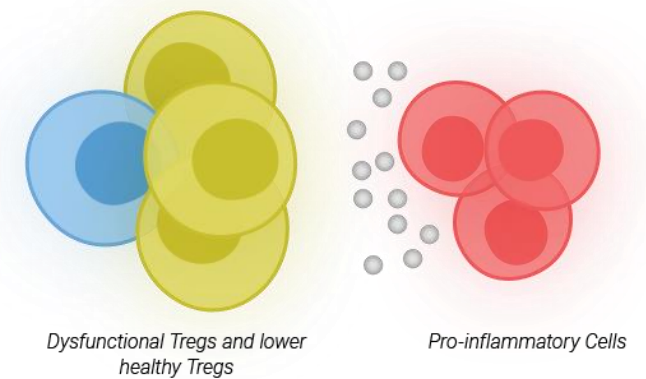
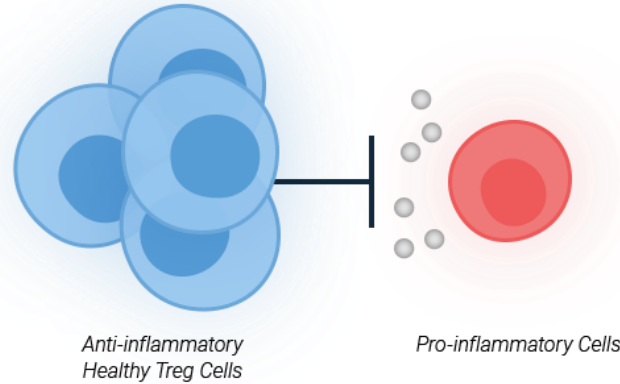


What Are Tregs and How They Are Dysfunctional

Tregs are a type of lymphocyte that modulate the body's immune response

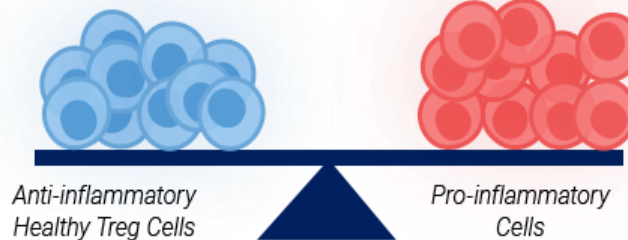
The main functions of Tregs are:

- *Ameliorate inflammatory mechanisms and reactions*
- *Inhibit the release of pro-inflammatory cytokines*
- *Maintain self-tolerance*



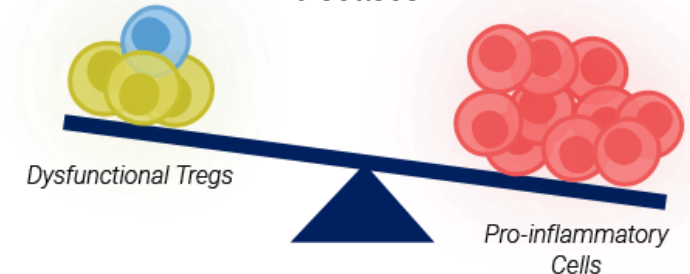
Healthy Tregs

Tregs are important anti-inflammatory immune cells involved in homeostasis. Tregs act on multiple immune cells to down-regulate the release of pro-inflammatory cytokines.

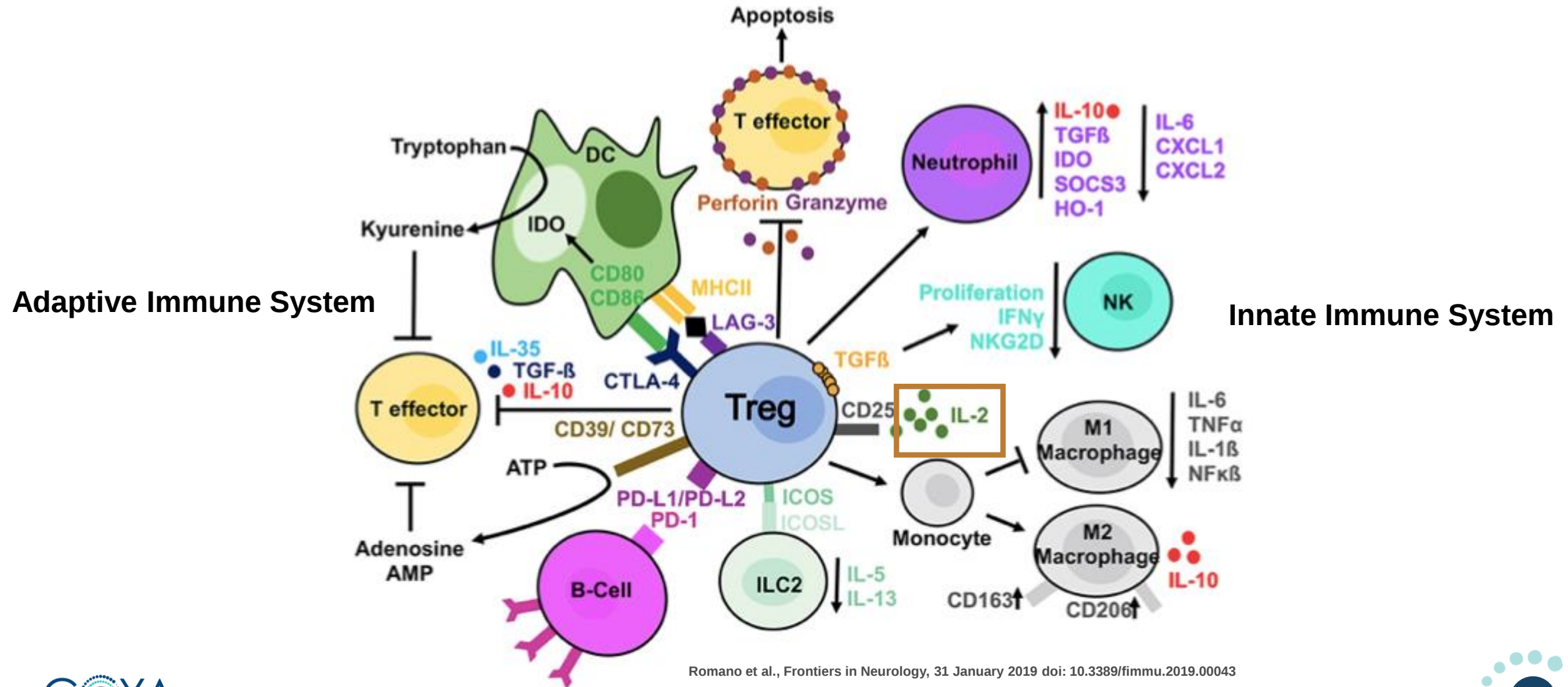


Dysfunctional Tregs

When Tregs become dysfunctional, a cytokine-mediated inflammatory state can arise leading to neurodegenerative, autoimmune, and metabolic diseases.



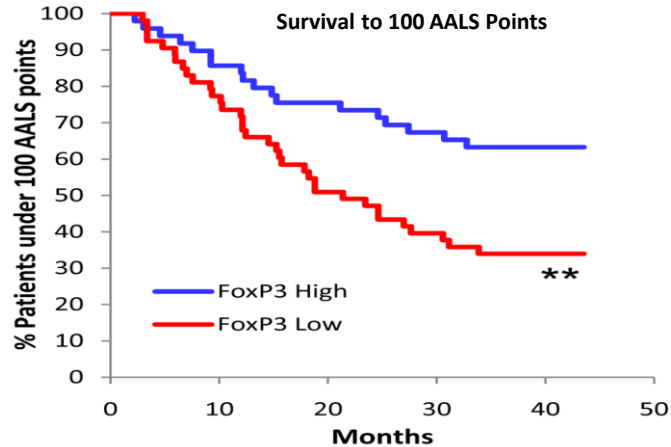
Treg regulate multiple downstream pathways to reduce inflammation



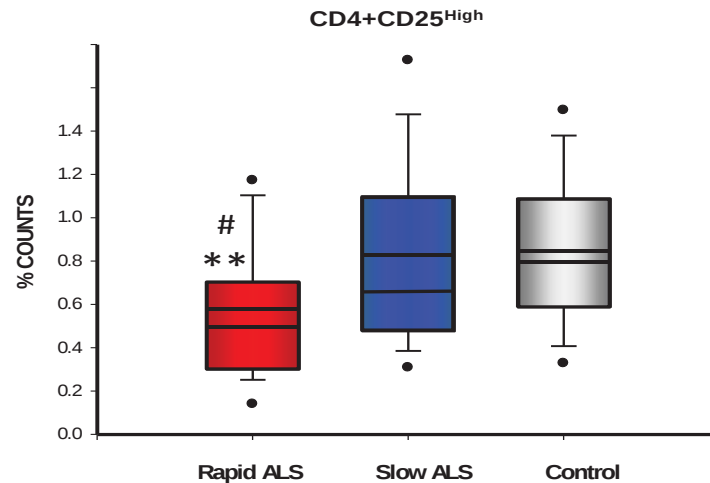
Adaptive Immune System Involvement in ALS: Treg Dysfunction Is a Core Driver of Neurodegeneration

Treg dysfunction is associated with ALS disease progression and burden of disease...

Treg Dysfunction is Associated with ALS Survival

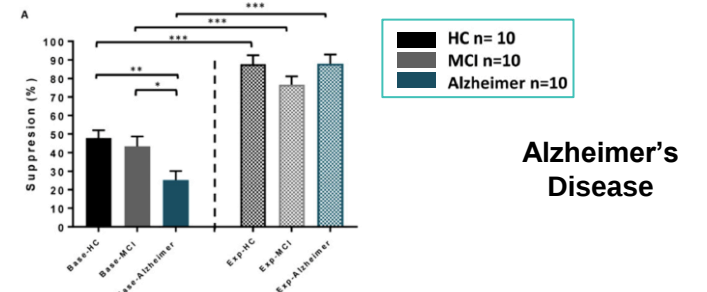
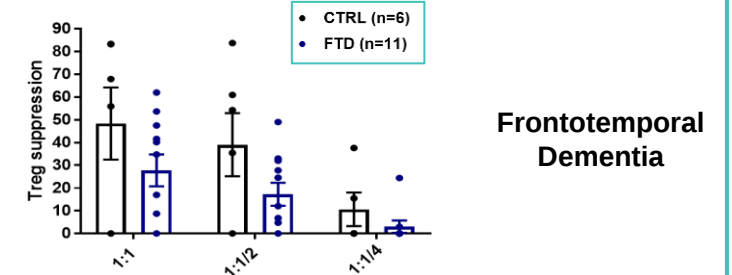


Treg Dysfunction Plays a Role in the Rate of Decline in ALS

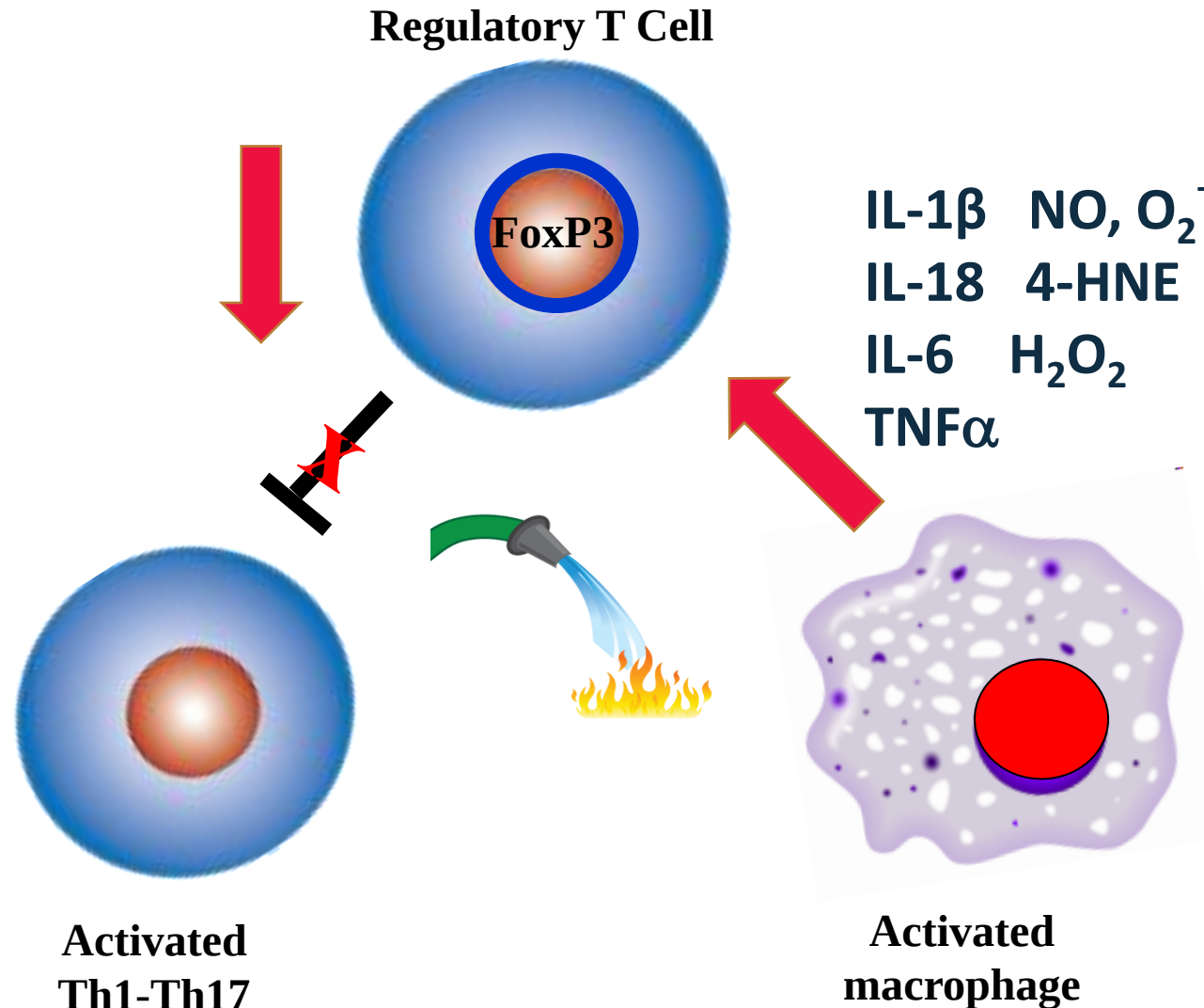


...and is similarly associated in other neurodegenerative diseases

Treg Dysfunction Is Implicated in FTD & AD



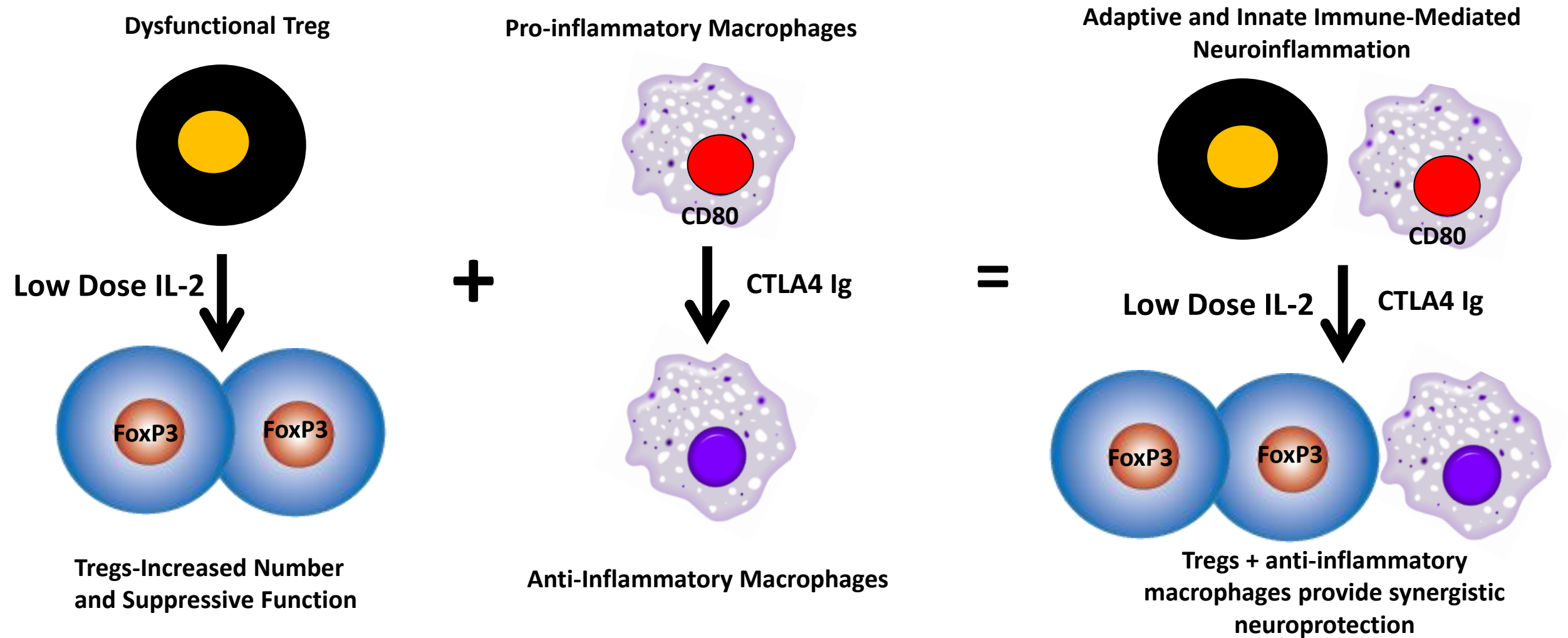
Innate Immune System Involvement in ALS : Macrophages Promote Dysfunction of Tregs Releasing Proinflammatory Cytokines and Oxidative Stress



Proinflammatory cytokines and oxidative stress/lipid peroxides contribute to the pathophysiology of neuronal injury and cell death in ALS



COYA 302: Combination Immunotherapy-Targeting the Adaptive and Innate Immune System that Drives ALS Pathophysiology



COYA 302: A Novel Approach to the Treatment of Neurodegenerative Diseases

Unique products compared to commercial IL-2 (High Dose Lyophilized Format) or CTLA4-Ig (Orencia)

**New Indications
including ALS,
Alzheimer's,
other ND
diseases**

**Unique low dose
strength and
dosing regimen**

**Ready-to-
administer stable
subcutaneous
formulation**

**Well-established
GMP
manufacturing**

Strong IP

COYA 302 is an investigational product, not yet approved by the US Food and Drug Administration

Strong Proof-of-Concept Clinical Data

COYA 302 for the Treatment of Amyotrophic Lateral Sclerosis*

Open-label academic study in 4 ALS patients, conducted at Houston Methodist

Results were presented at MDA Conference in March 2023

No disease progression at week 24 and minimal progression at week 48 (by mean ALSFRS-R score)

Consistent and significant Treg function enhancement and increased Treg numbers

Expression of blood biomarkers of inflammation were downregulated, correlating with disease severity and treatment response

Safe and well tolerated

Coya 301 for the Treatment of Alzheimer's disease*

Open-label academic study in 8 mild-to-moderate AD patients, conducted at Houston Methodist

Results were presented at Keystone Conference in May 2023 and at Alzheimer's Association International Conference in July 2023

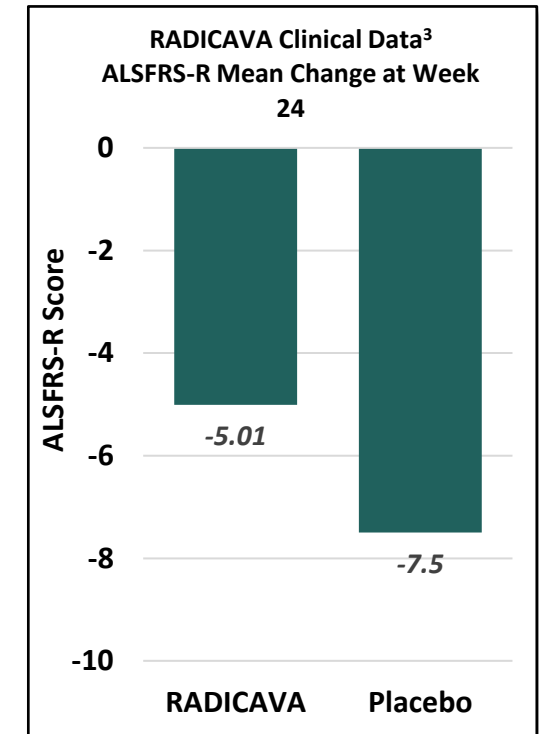
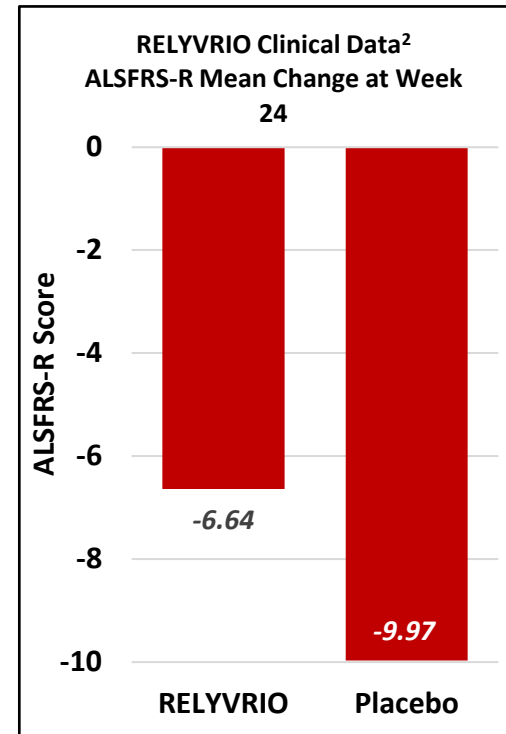
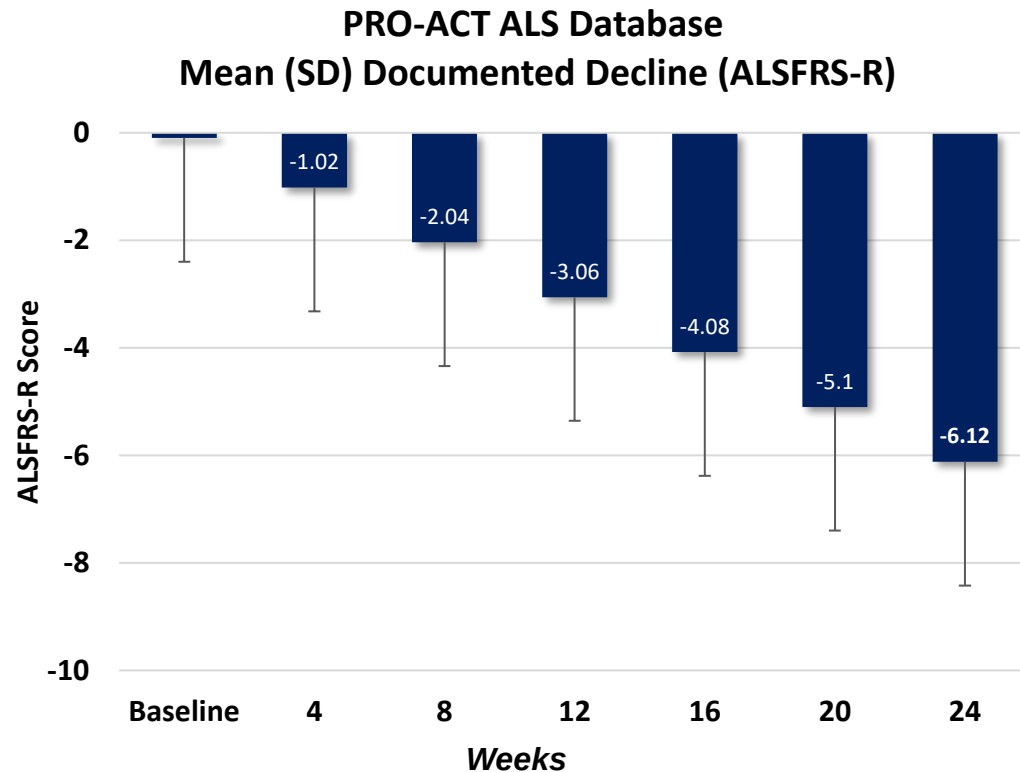
Statistically significant improvement in cognitive function, as measured by the Mini-Mental State Examination test (MMSE)

Restored peripheral Treg function and numbers, and lowered the levels of systemic pro-inflammatory chemokines and biomarkers

Safe and well tolerated

Current Therapies for ALS Aim to Slow Disease Progression

Many companies have garnered significant value by demonstrating a *limited* benefit of slowing the rate of ALS progression



Average rate of patient decline is 1.02 points/month in ALSFRS-R score¹

COYA 302: Open-Label, Single-Arm PoC Clinical Study in ALS Patients (N=4)

Screening

20 weeks

Screening Assessments

- ✓ Clinical Labs
- ✓ ALSFRS-R Score
- ✓ Electrocardiogram (ECG)
- ✓ Physical & Neurological Exam

Study patients had well-documented disease progression prior to treatment (-1.1 points/month prior to treatment with COYA 302)

Treatment Period

COYA 302 was administered via subcutaneous injection over 48 weeks

Treatment Period Assessments

- ✓ Safety and Tolerability
- ✓ Treg Function and Numbers
 - ✓ Serum Biomarkers
 - ✓ ALSFRS-R Score

Safety and tolerability assessments included reported adverse events, periodic physical and neurological exams, clinical labs, and ECGs

Follow-Up

8 weeks

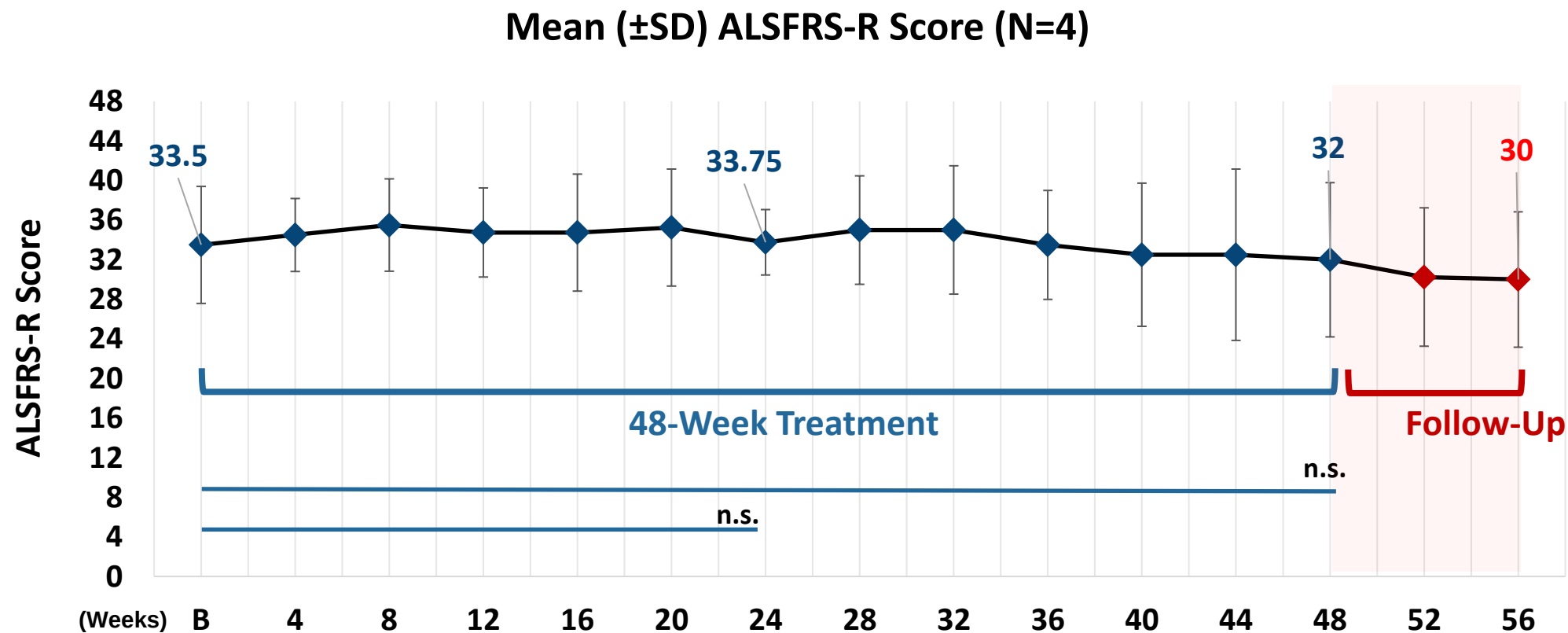
Post-Treatment Assessments

- ✓ Safety and Tolerability
- ✓ Treg Function & Numbers
 - ✓ Serum Biomarkers
 - ✓ ALSFRS-R Score

COYA 302: Patients' Demographics and Baseline Characteristics

	Age (years)	Sex	Type	Onset	ALS Progression Prior to Baseline (ALSF _{RS} -R score)	Respiratory Status	Respiratory Support
Patient 1	47	Female	Familial	Limb	-1.6 points / month	No Respiratory Insufficiency	None
Patient 2	54	Male	Sporadic	Limb	-1 points / month	Respiratory Insufficiency	Non-invasive Ventilation
Patient 3	57	Female	Sporadic	Bulbar	-1 point / month	Respiratory Insufficiency	Non-invasive Ventilation
Patient 4	84	Female	Sporadic	Bulbar	-0.7 points / month	Respiratory Insufficiency	None

COYA 302: Appears to Ameliorate ALS Progression Over 48-weeks

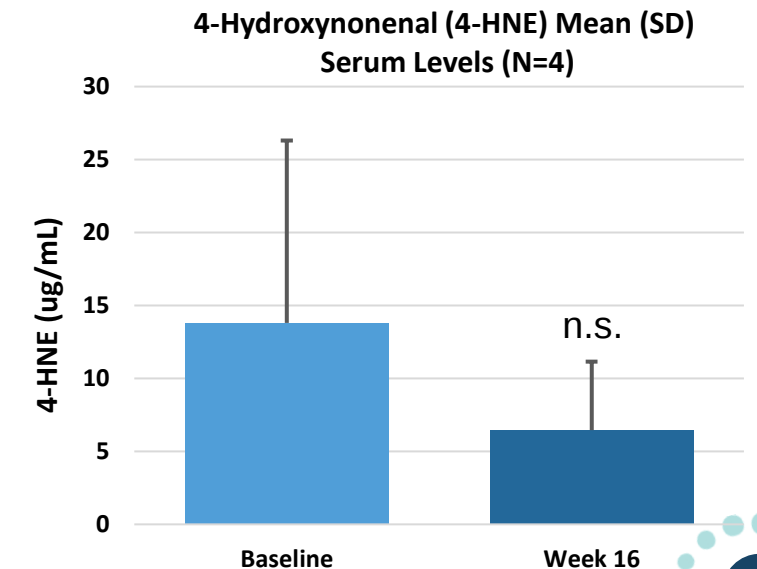
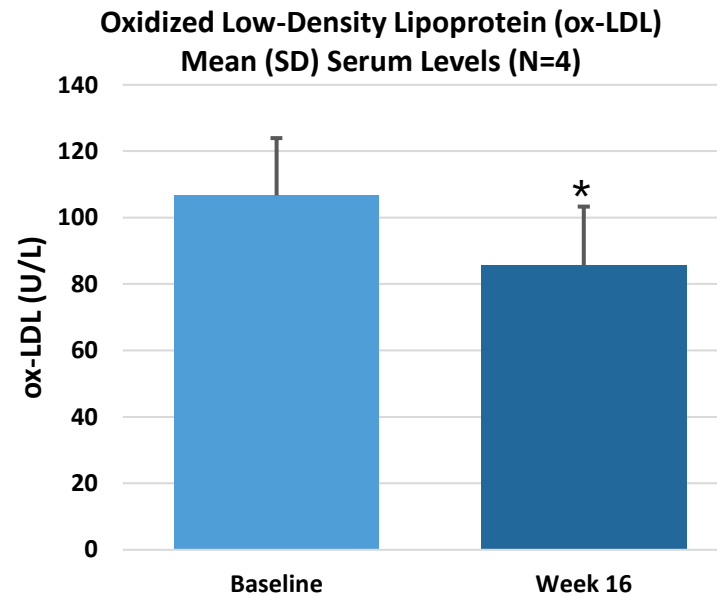
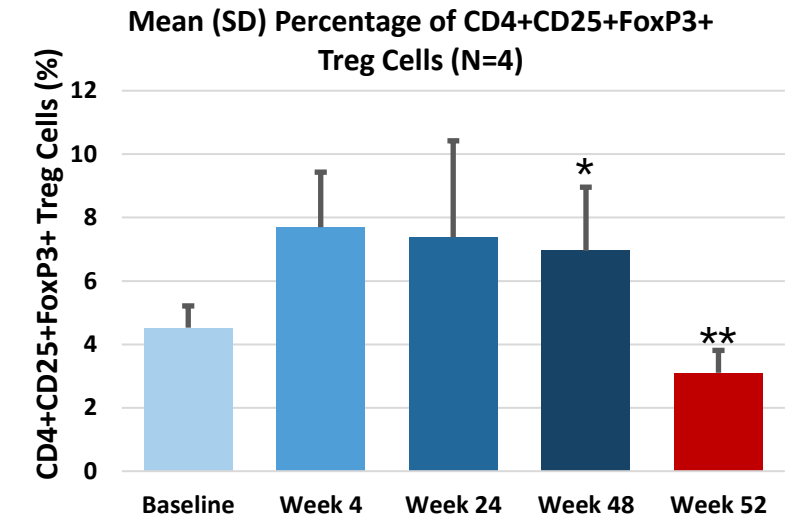
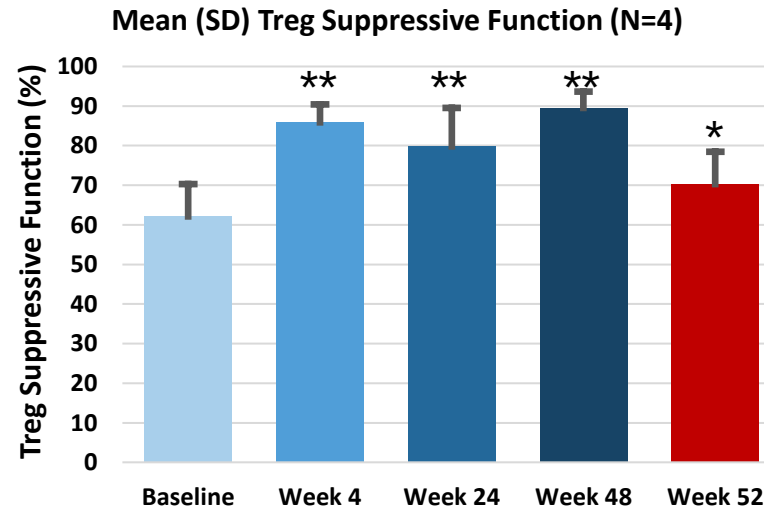


COYA 302 was well tolerated over 48 weeks; the most common AE was mild injection site reaction. All patients completed the study; no death or serious AEs (SAEs) occurred over the course of the study.

COYA 302: Enhanced Biologic Activity

Key Takeaways

- ✓ **COYA 302 significantly expands Treg suppressive function** as early as 4 weeks after initiation of treatment and maintained a significantly increased Treg function.
- ✓ **COYA 302 increased Treg numbers as early as 4 weeks** after initiation of treatment and maintained a higher number over the course of treatment.
- ✓ **COYA 302 enhanced suppression of macrophage-mediated oxidative stress and proinflammatory cytokine biomarkers over 48 weeks**

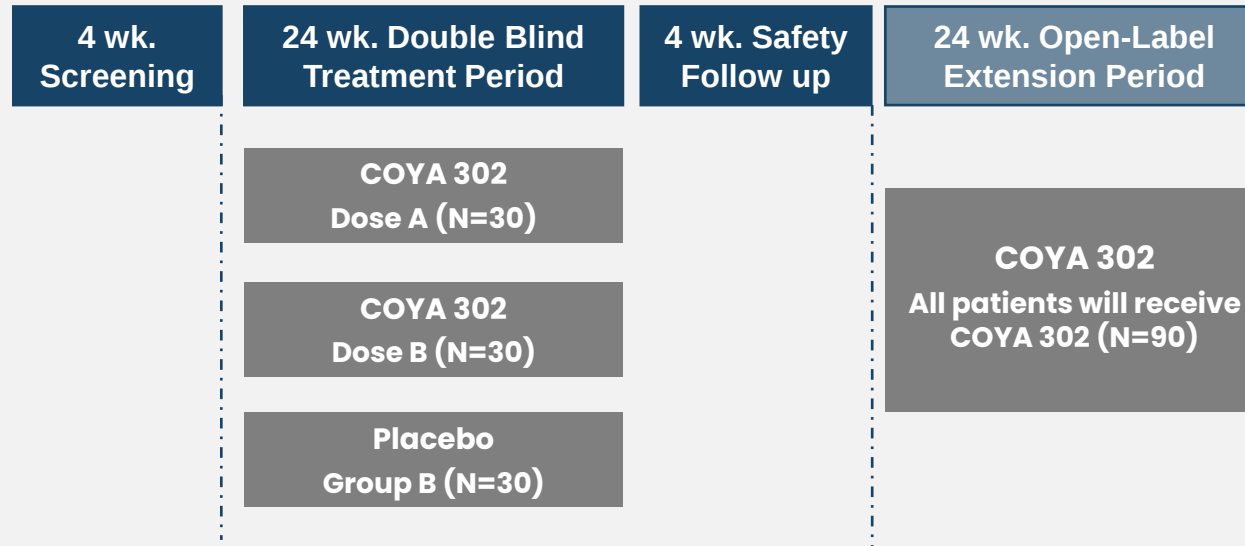


COYA 302: Overview of Phase 2 Study Design in ALS

Key Inclusion Criteria

- Diagnosis of sporadic or familial ALS
- Time since onset of ALS symptoms $\leq$ 24 months from Screening
- ALSFRS-R score $\geq$ 35 at Screening
- A score of at least 2 points in each ALSFRS-R item
- Forced vital capacity (FVC) $\geq$ 70% of predicted capacity for age, height, and gender at Screening
- Documented disease progression (by ALSFRS-R score) for at least 16 weeks prior to Screening

Randomized, Double-Blind, Placebo-Controlled Phase 2 with Open-Label Extension



Primary Endpoint

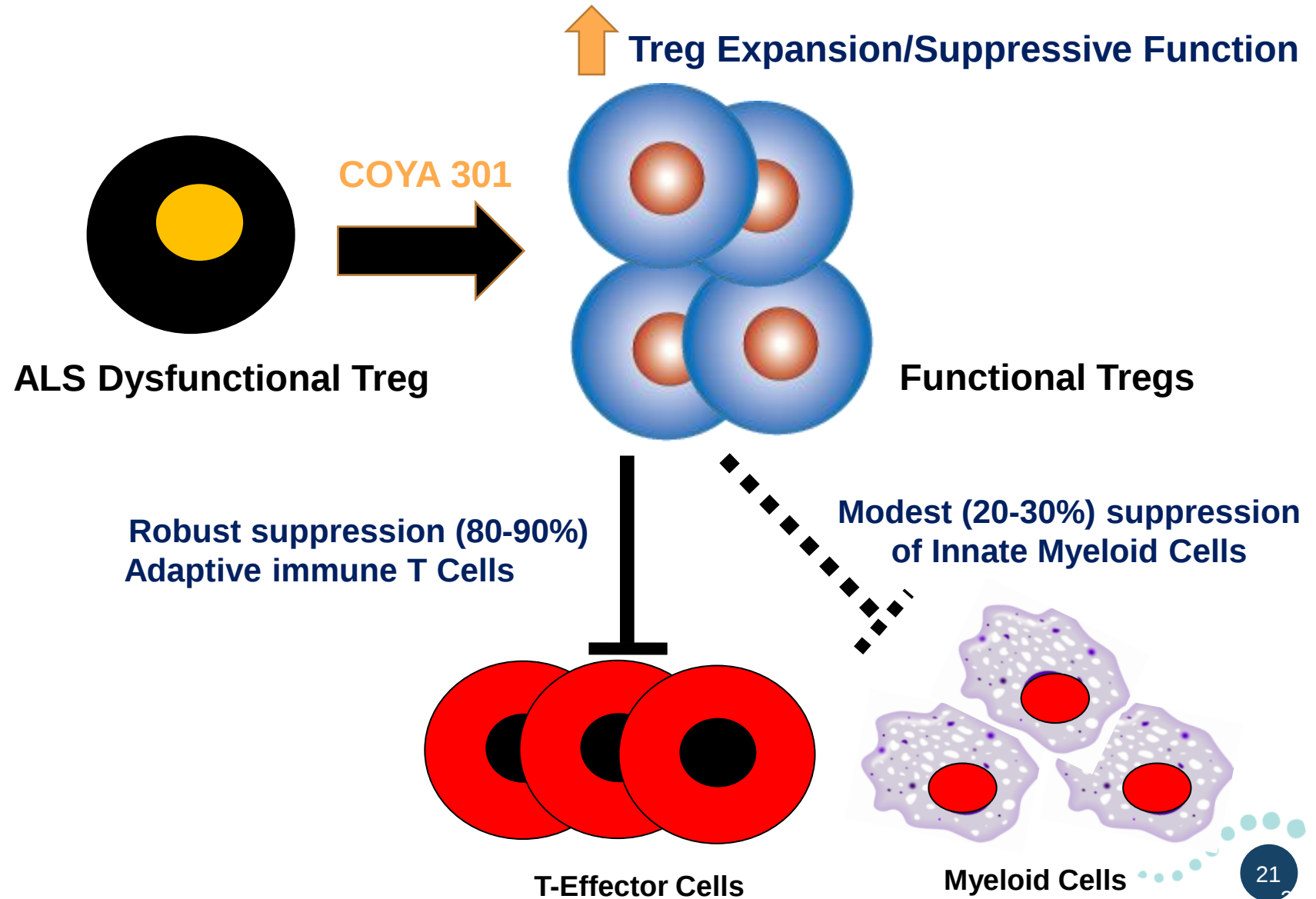
Combined Assessment of Function (ALSFRS-R) and Survival (CAFS)

Study Objectives

1. Efficacy
2. Safety and Tolerability
3. Biological Activity
4. Biomarker levels

COYA 301: Proprietary Treg Enhancing Low-Dose Il-2 Suppresses Adaptive Immunity - Robustly - and Innate Immunity - Modestly

Dysfunctional Tregs are associated with neuroinflammation promoted by activated T effector cells and activated innate myeloid cells



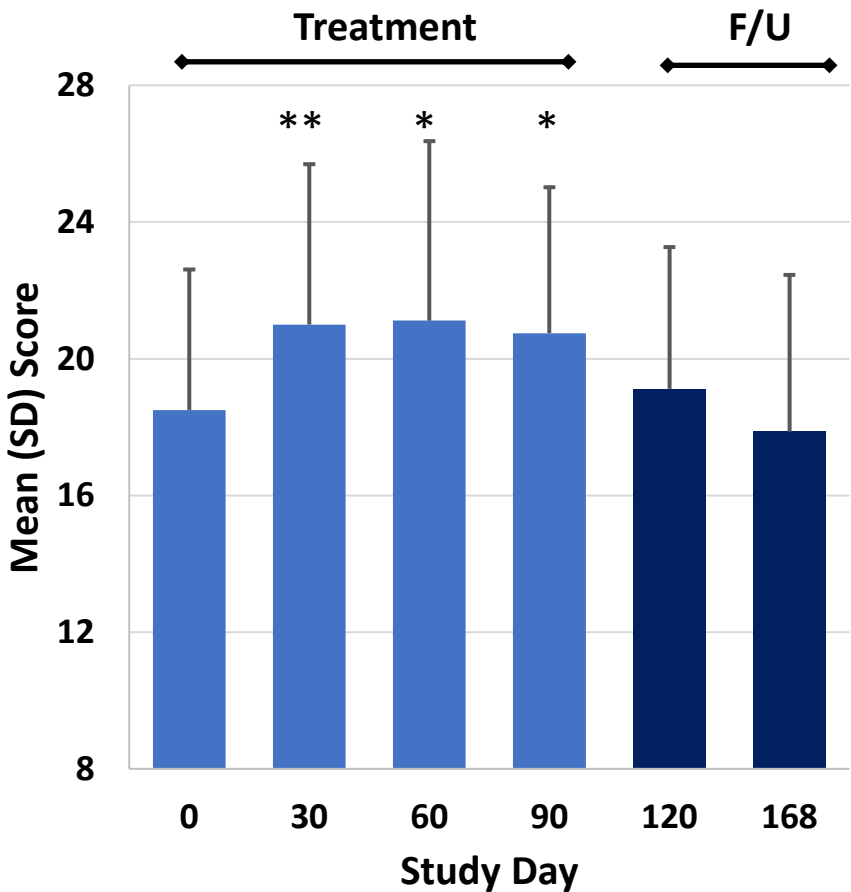
COYA 301: Investigator-Initiated Study in Alzheimer's Disease (AD)

Overall Study Design

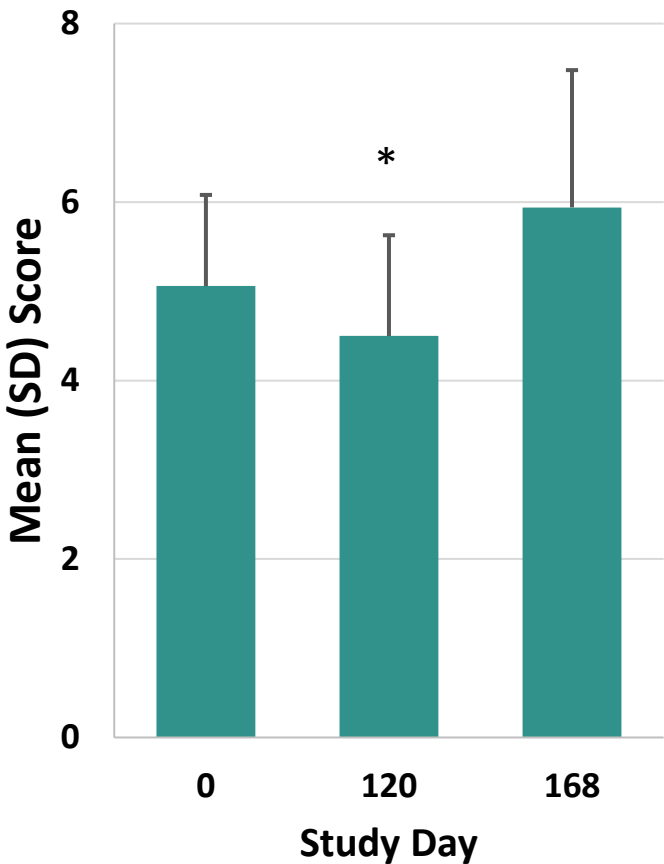
- Proof-of-Concept open-label study, conducted at Houston Methodist Hospital
- Population: 8 patients with mild-to-moderate AD
- Treatment: 4 monthly COYA 301 cycles administered subcutaneously, followed by 2-month post-treatment observation. The study was conducted with commercially available product.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

COYA 301 Improved or Halted Cognitive Decline in AD Patients

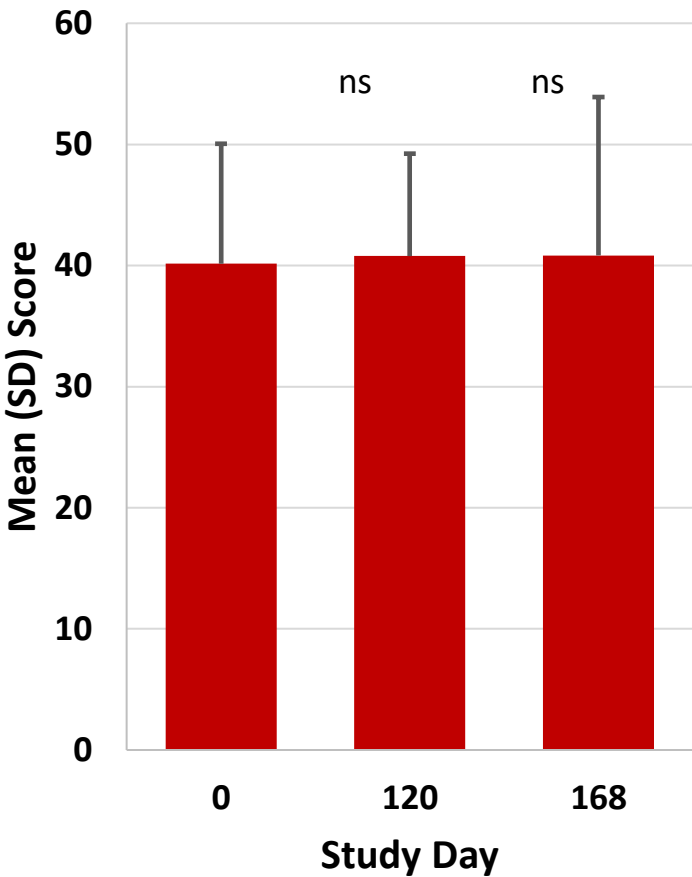
MMSE Score (N=8)



CDR-SB Score (N=8)



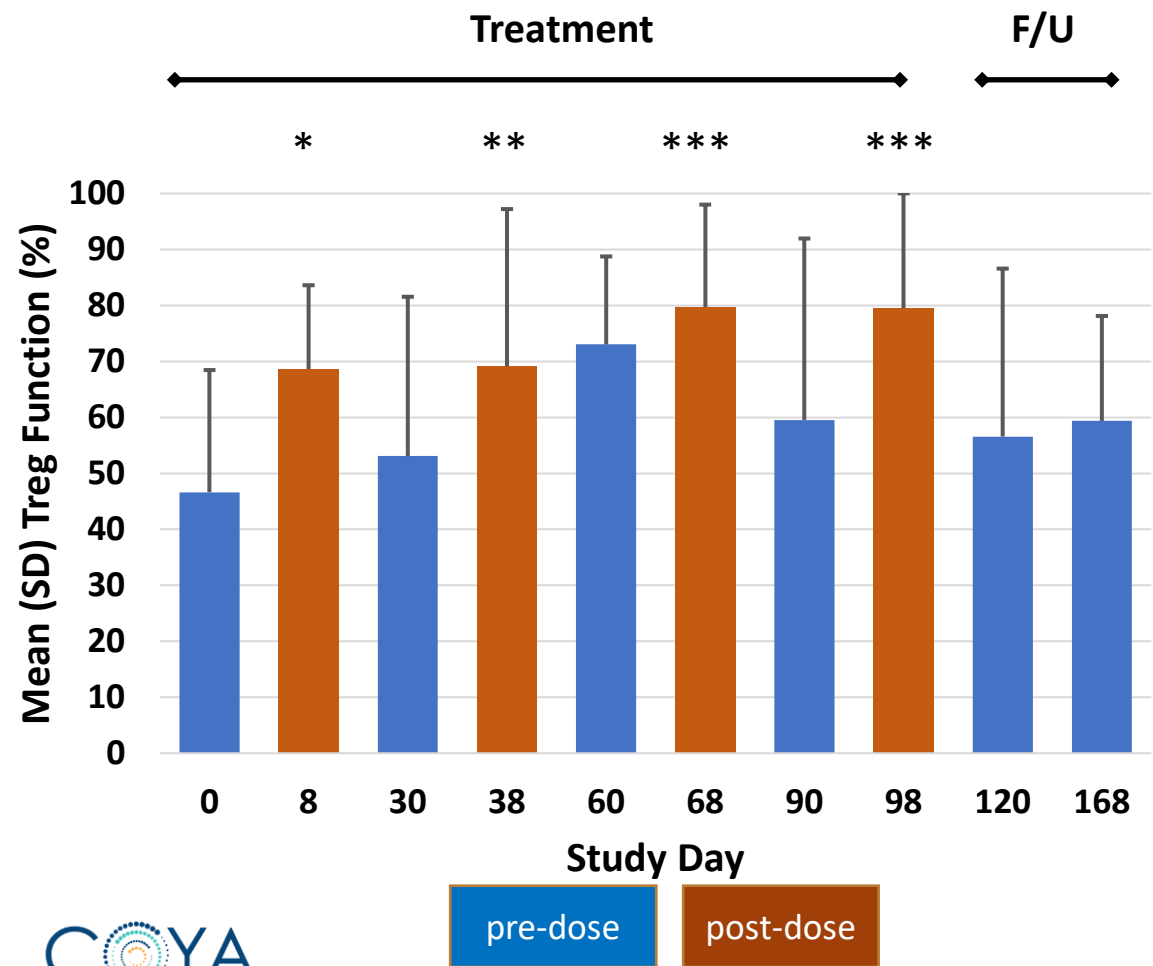
ADAS-Cog Score (N=8)



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

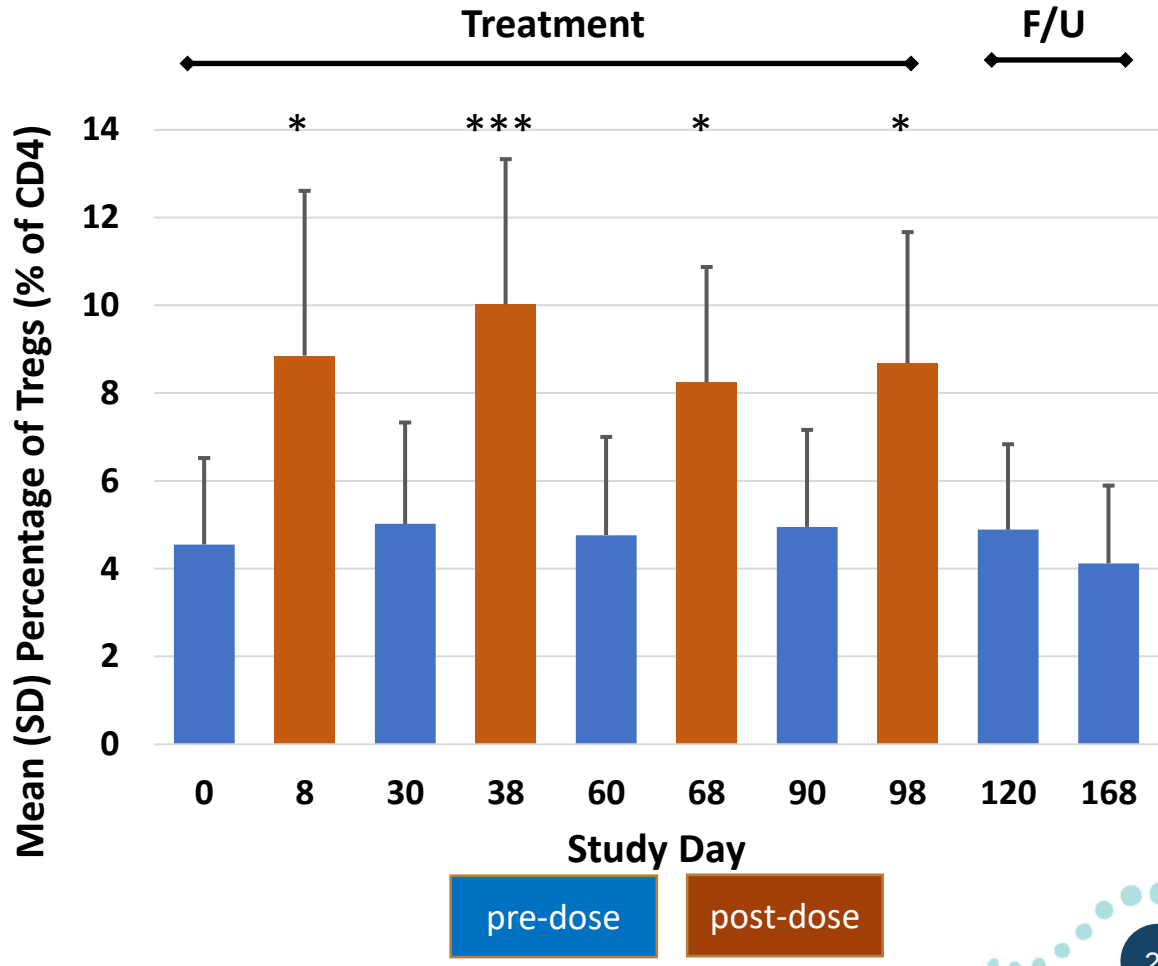
COYA 301 Enhances Treg Function and Numbers *in vivo* in AD Patients (N=8)

Statistically Significant Enhancement
of Treg Suppressive Function



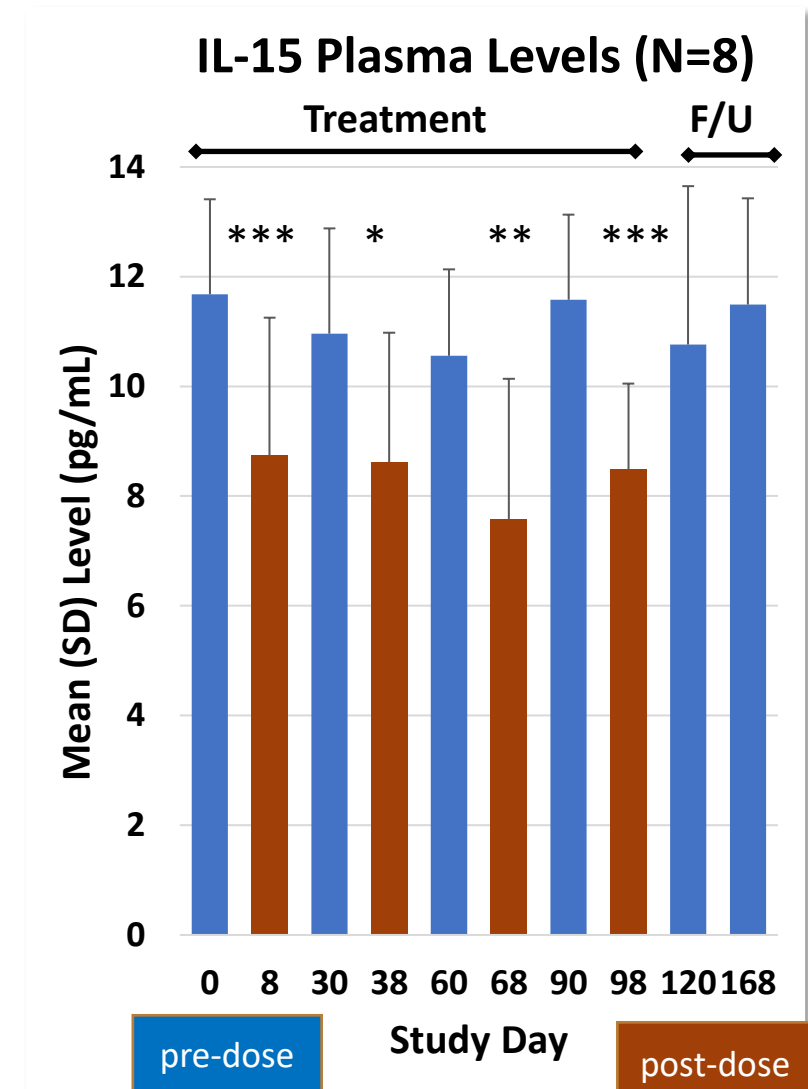
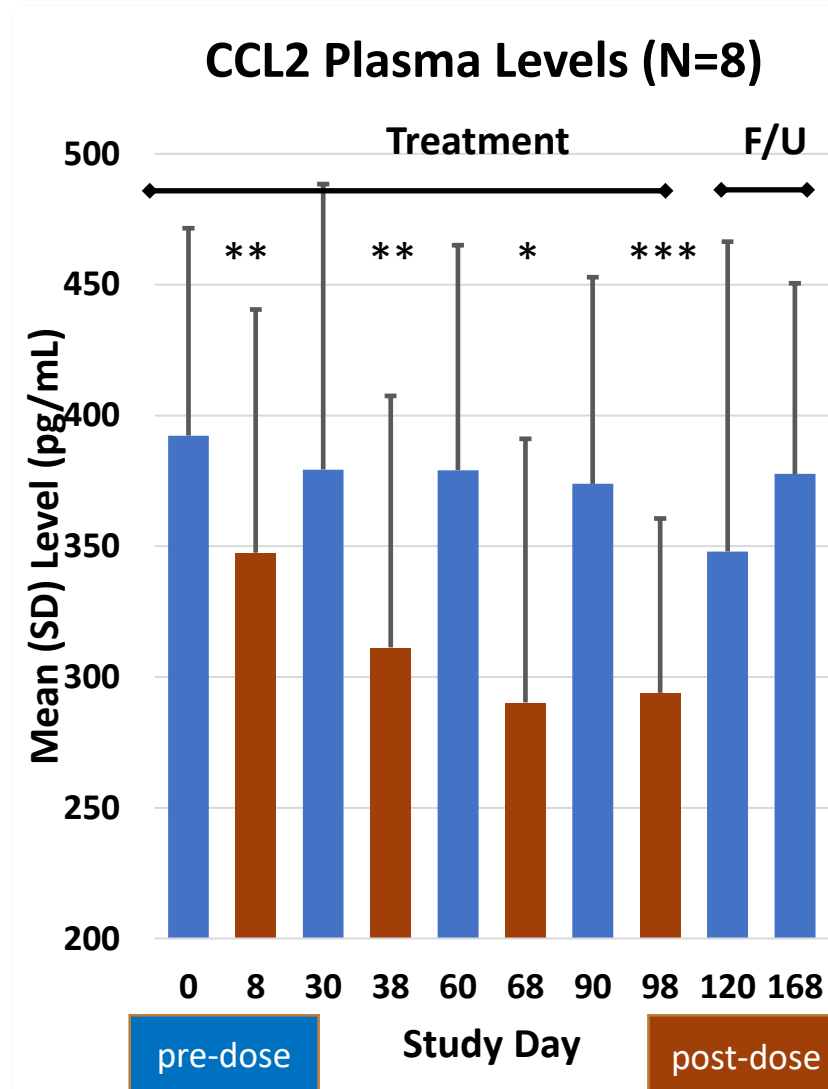
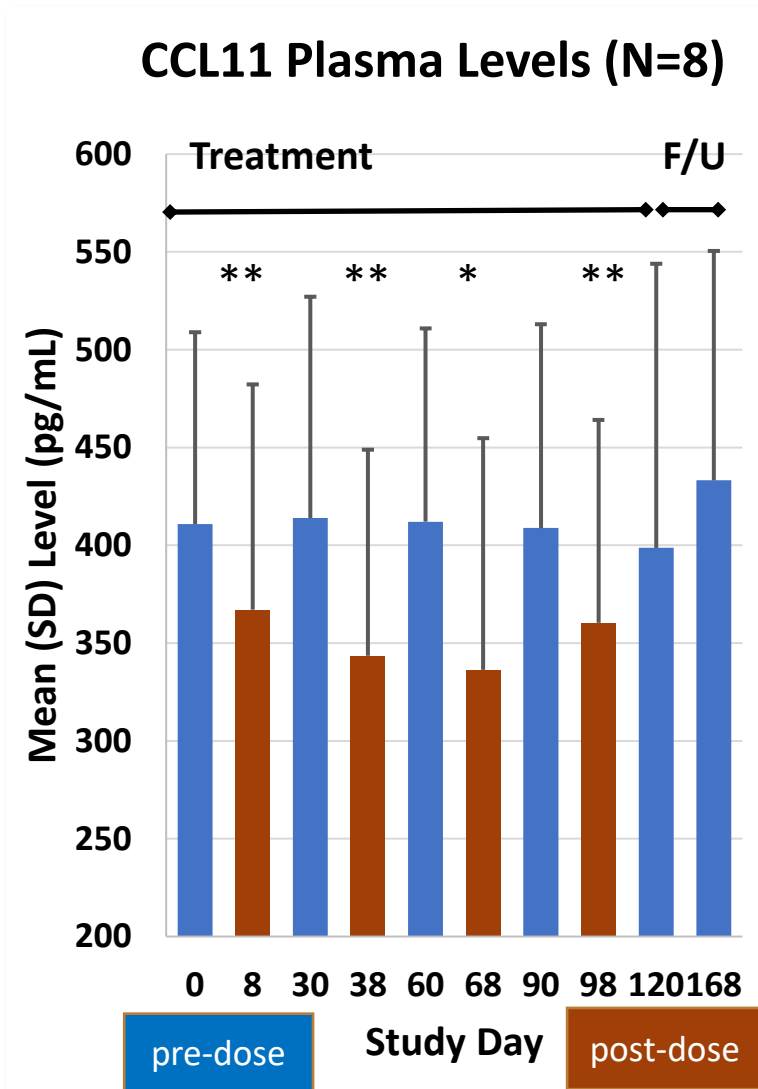
*p<0.05, **p<0.01, ***p<0.001

Statistically Significant Enhancement
of Treg Numbers

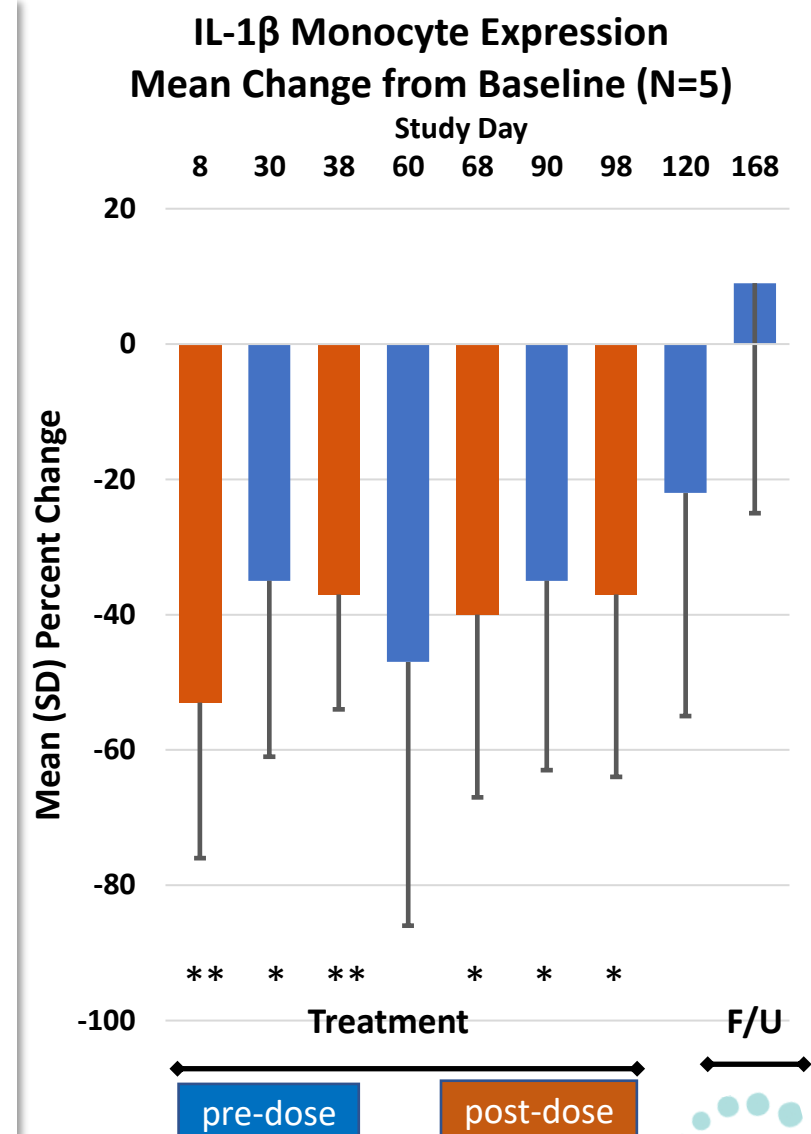
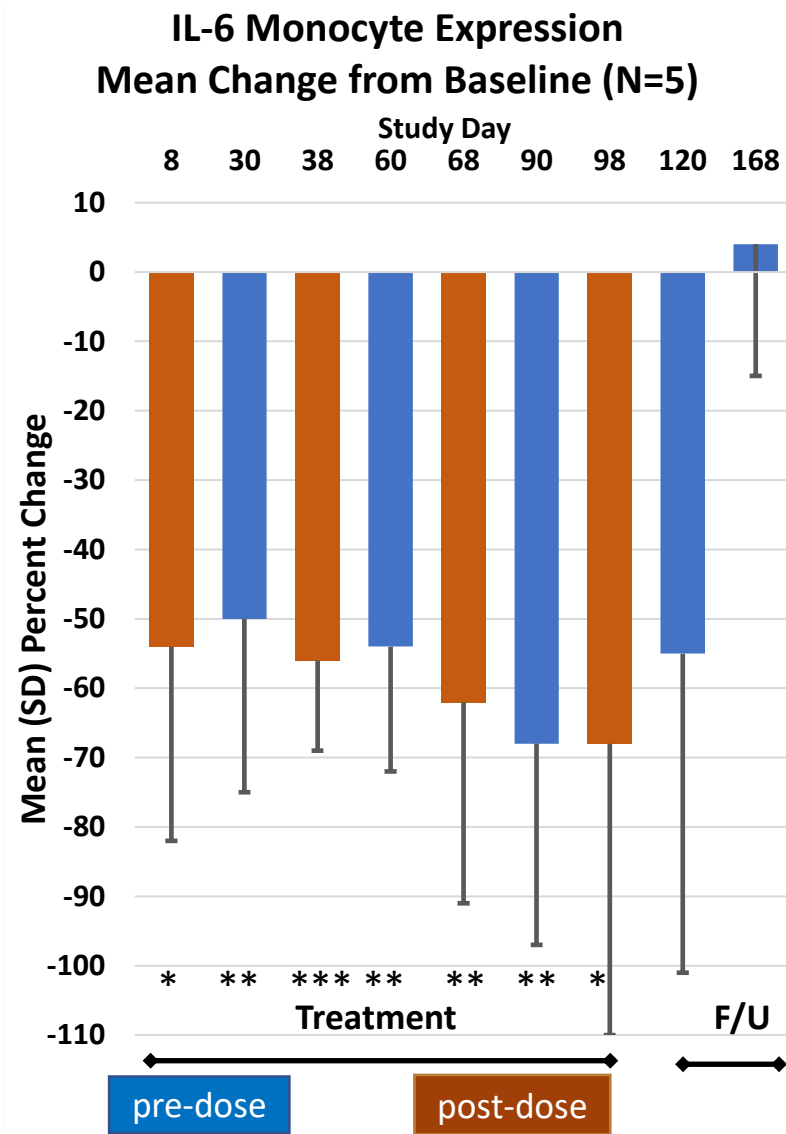
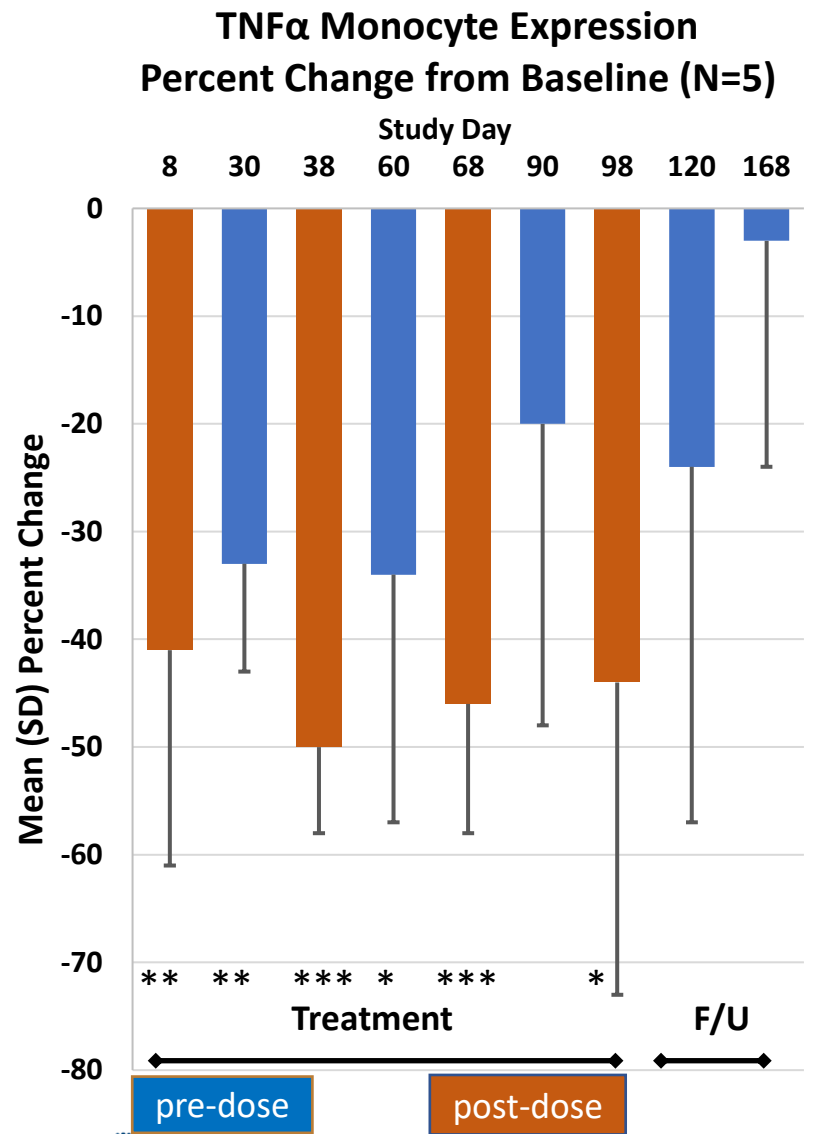


*p<0.05, ***p<0.001

COYA 301 Significantly Lowers Plasma Proinflammatory Chemokines and Cytokines in AD Patients

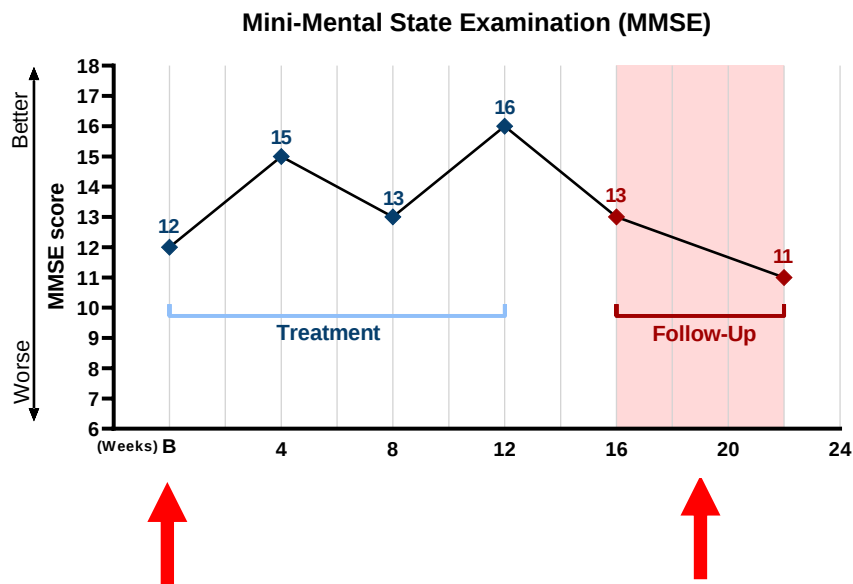


COYA 301 Significantly Lowers Expression of Proinflammatory Cytokines in AD Patients



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 MRI
Other Rx: Donepezil 10mg

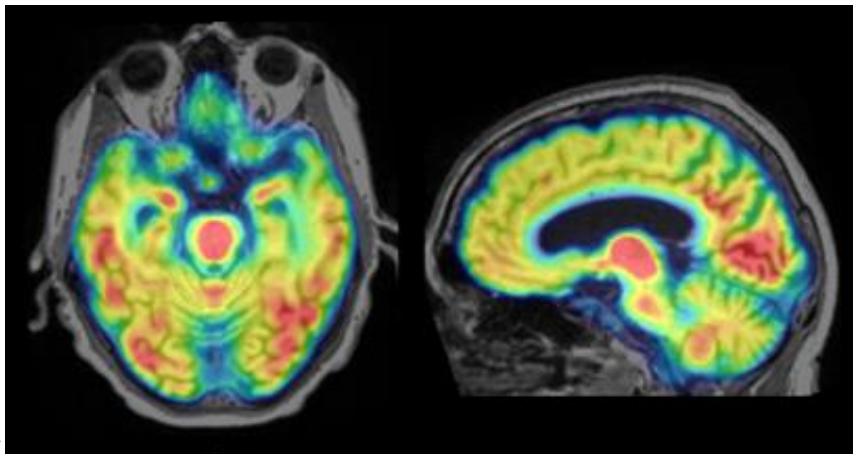


Neuroinflammation (TSPO)
(¹¹C) ER-176 PET Scan at
baseline and after 4-monthly
cycles of low dose IL-2.

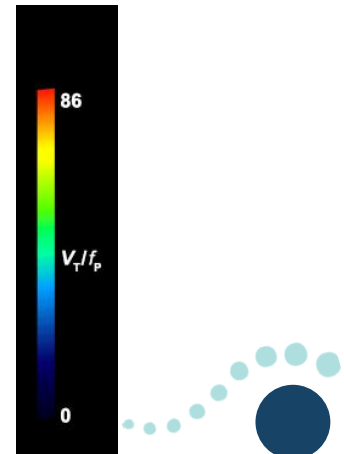
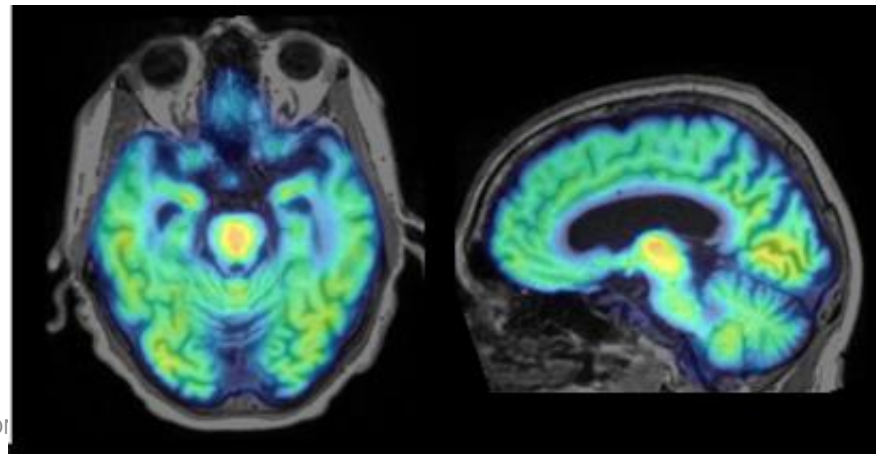
The second PET scan was
done 2 weeks after last dose.

PET: Positron Emission Tomography
TSPO: translocator protein

PET Scan (Baseline)



PET Scan (2 weeks after last dose)



COYA 301 Safety & Tolerability

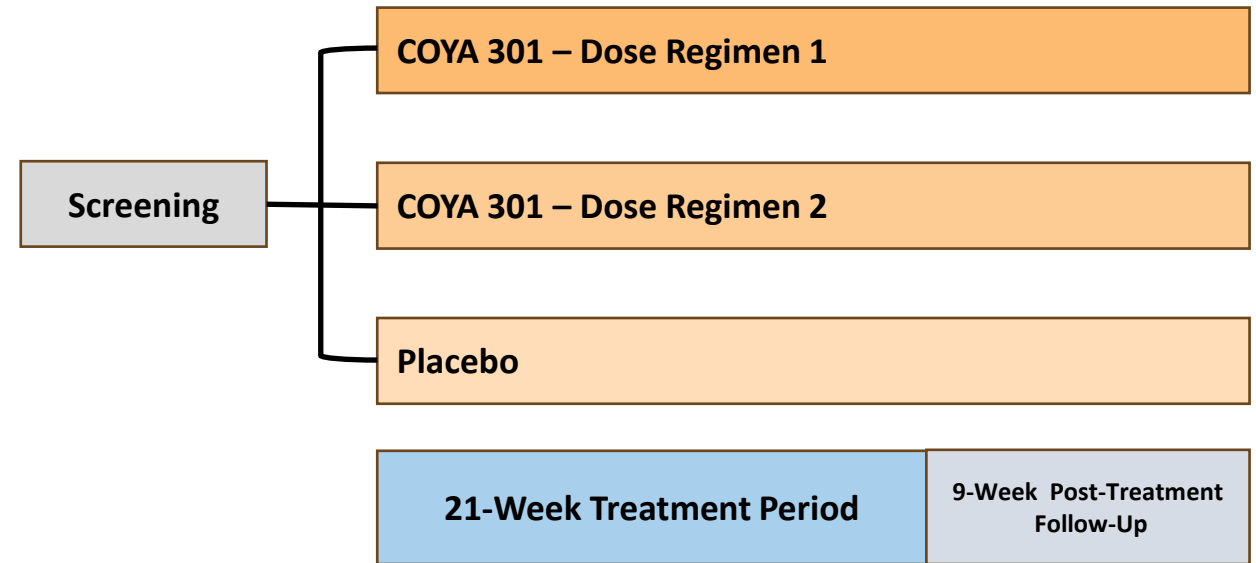
- Overall, COYA 301 was well tolerated in patients with AD.
- Most common adverse events (AEs) were mild injection site reactions and mild leukopenia.
- All patients completed the study.
- No death or other serious AE occurred over the course of the study.

COYA 301: Double-Blind, Placebo-Controlled Study in AD Patients is Ongoing

The encouraging results of the open-label, proof-of-concept study in AD (N=8) support conducting the ongoing randomized, double-blind, well-controlled phase 2 study in 38 patients with mild-to-moderate AD.

Study Objectives

- Safety & tolerability
- Biological activity (Treg function)
- Blood and CSF biomarkers
- Cognitive function



Enrollment completed in October 2023

Topline results are anticipated in Summer 2024

Dose Regimen 1: 1 million IU administered SC daily for 5 days, **every 4 weeks**

Dose Regimen 2: 1 million IU administered SC daily for 5 days, **every 2 weeks**

**Study funded by the Gates Foundation
and Alzheimer's Association**

COYA 301 as a Backbone for Combination Immunotherapy

↓ Activated T effector Cells ↓ Activated Macrophages/Microglia

↑ Treg Function
and numbers

COYA 301

Subcutaneous
Low-Dose
Interleukin-2

+

CTLA4 Ig

**COYA
302**

Shown therapeutic
benefit in ALS
patients

Beta
Amyloid
Inhibitors

**COYA
303***

Alzheimer's Disease

Ferroptosis
Inhibitor

**COYA
304***

Neurodegenerative
Autoimmune
Metabolic

**Backbone
Therapy**

**Multifactorial inflammatory pathways may require
synergistic combination therapies**

COYA – Critical Catalysts Over the Next 2-3 Years

2023	1H 2024	2H2024	2025/6
Publication of COYA 301 clinical data in AD (phase 1 IIT)	COYA 302 Initiate ALS Phase 2 Presentation of COYA 301 phase 1 clinical data in AD at 18 th annual AD + PD Conference Publication of COYA 302 clinical data in ALS (Phase 1 IIT) Publication of Biomarker data on COYA 302 and blood registry	COYA 301 Proof of Concept combination data with Drug X in mice model COYA 301 Phase 2 Investigator Initiated Trial Topline AD data (Summer)	COYA 302 Phase 2 ALS data