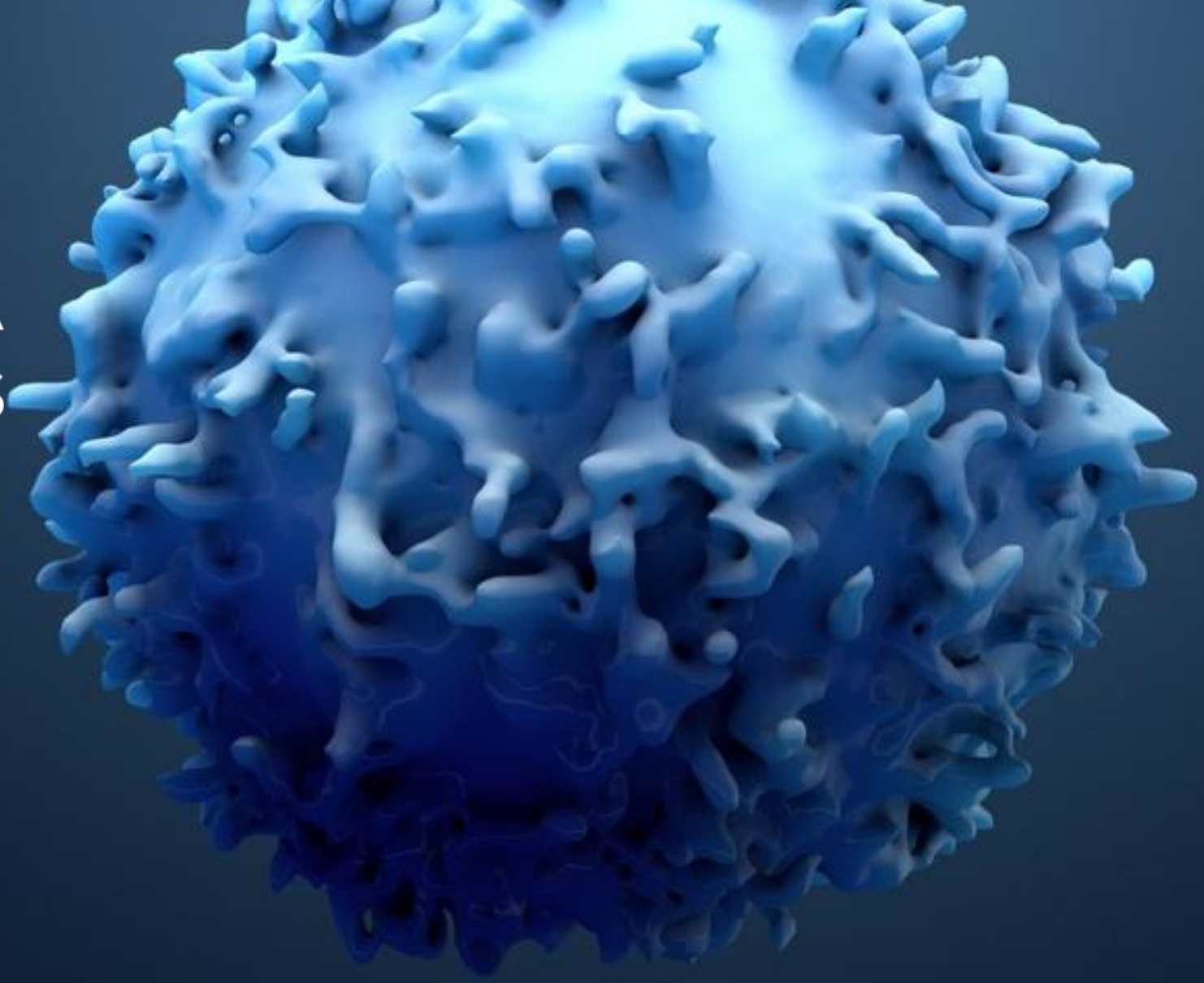
COYA THERAPEUTICS



Unleashing the Power of Regulatory T cells (Tregs)

Investor Presentation

September 2024

NASDAQ: COYA

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 risks associated with the impact of COVID-19; 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 preclinical or 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 will 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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Coya Therapeutics: A Clinical Stage Biotechnology Company

Our Mission	Clinical stage company developing innovative and proprietary therapies to address the significant unmet medical needs **of patients with serious neurodegenerative and autoimmune diseases.**
Targeting Regulatory T Cell (Treg) Biology	Developing treatments focused on the biology of **Tregs** to target **systemic inflammation and neuroinflammation.**
Combination Targeting Strategy	Targeting multiple immune pathways to restore the anti-inflammatory functions of Tregs while inhibiting harmful pro-inflammatory pathways
Lead Asset	**COYA 302 is a biologic combination for subcutaneous and/or intravenous administration intended to enhance Treg function while depleting T effector function** and activated macrophages: Mechanisms may be synergistic in suppressing inflammation
COYA 302: Pipeline within a Product	Advancing COYA 302 in **multiple neurodegenerative disorders**
Recent Business Development	**Executed a potential $700M+ transaction for COYA 302 in Amyotrophic Lateral Sclerosis (ALS) with Dr. Reddy's** Laboratories and a strategic $5M investment by Alzheimer's Drug Discovery Foundation (ADDF)

Coya Therapeutics: Combination Therapies Are Integral for Complex Neurodegenerative Diseases

"Inflammation has emerged as a promising novel pathway for chronic neurological diseases like FTD. A combination drug, like COYA 302, is an innovative approach being developed to suppress neuroinflammation by targeting multiple inflammatory pathways. Combination therapy will be integral to slowing – and eventually halting – cognitive decline for a disease as complex as FTD, and exploring combined therapeutic modalities is an important advancement in the development of future care regimens."

Howard Fillit, MD, Co-Founder and Chief Science Officer of the Alzheimer's Drug Discovery Foundation
Press Release: May 20th, 2024 following announcement of a $5M strategic investment in Coya

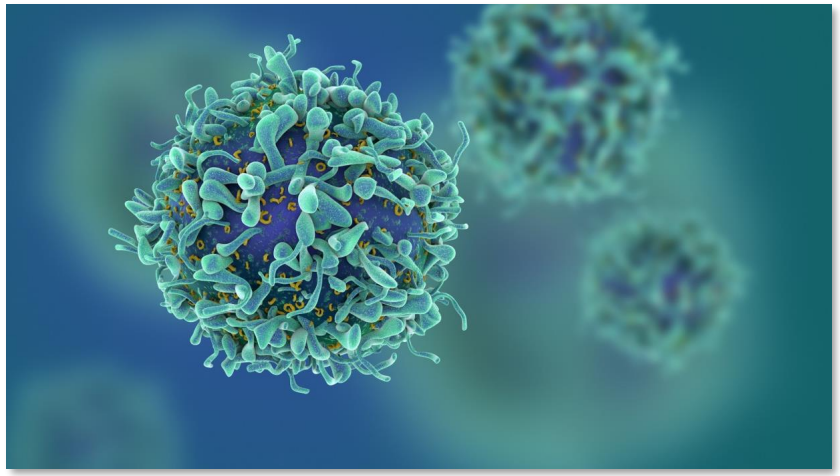
Coya Therapeutics: Investment Highlights

- Clinically stage company focused on Treg therapies with strong early clinical data
  - COYA 302 – filed IND in 2Q24 in ALS (aka “Lou Gehrig’s disease”). FDA has requested additional non-clinical toxicology/pharmacology data must be submitted prior to initiation of our planned Phase 2 trial. COYA intends to discuss the recommendations with the FDA to align on the revised pre-clinical plan (4Q24)
  - COYA 302 also being explored in Alzheimer’s, Parkinson’s, and Frontotemporal Dementia
  - COYA 301 – Ph. 2 IIT topline data in Alzheimer’s will be presented at CTAD24 on October 29th, 2024 and will serve as proof-of-concept for advancing COYA 302 into Alzheimer’s
  - IIT PoC clinical data for both COYA 302 in ALS and COYA 301 in Alzheimer’s showed both efficacy and safety[1]
- Established exclusive licensing partnership with Dr. Reddy’s Lab for COYA 302 in ALS patients in December 2023
  - $7.5M upfront payment + $8.4M in additional milestone payments expected in 2024
  - Up to $40M in additional regulatory milestone payments
  - Up to $677M in cumulative sales-based milestone payments
  - Sales royalty from low to mid-teens
- Strong balance sheet ($36.6 M in cash[2]) with runway into 2026
- Active calendar in 2024 and 2025 encompassing regulatory, clinical, and publication milestones for COYA 302 and COYA 301
- Management with significant equity stake and personal stake in corporate mission
- Notable investors include David Einhorn/Greenlight Capital as lead investor (~9% equity stake) and Wilbur Ross, former U.S. Secretary of Commerce, who joined Board

Market Capitalization Table

Symbol	NASDAQ: COYA
Recent Price (as of 8/9/24)	$6.06
Market Cap	$92M
Cash*	$36.6M
Shares Outstanding*	15.2M
Options + Warrants*	4.5M @ $6.23 WAEP

* As of 6/30/24

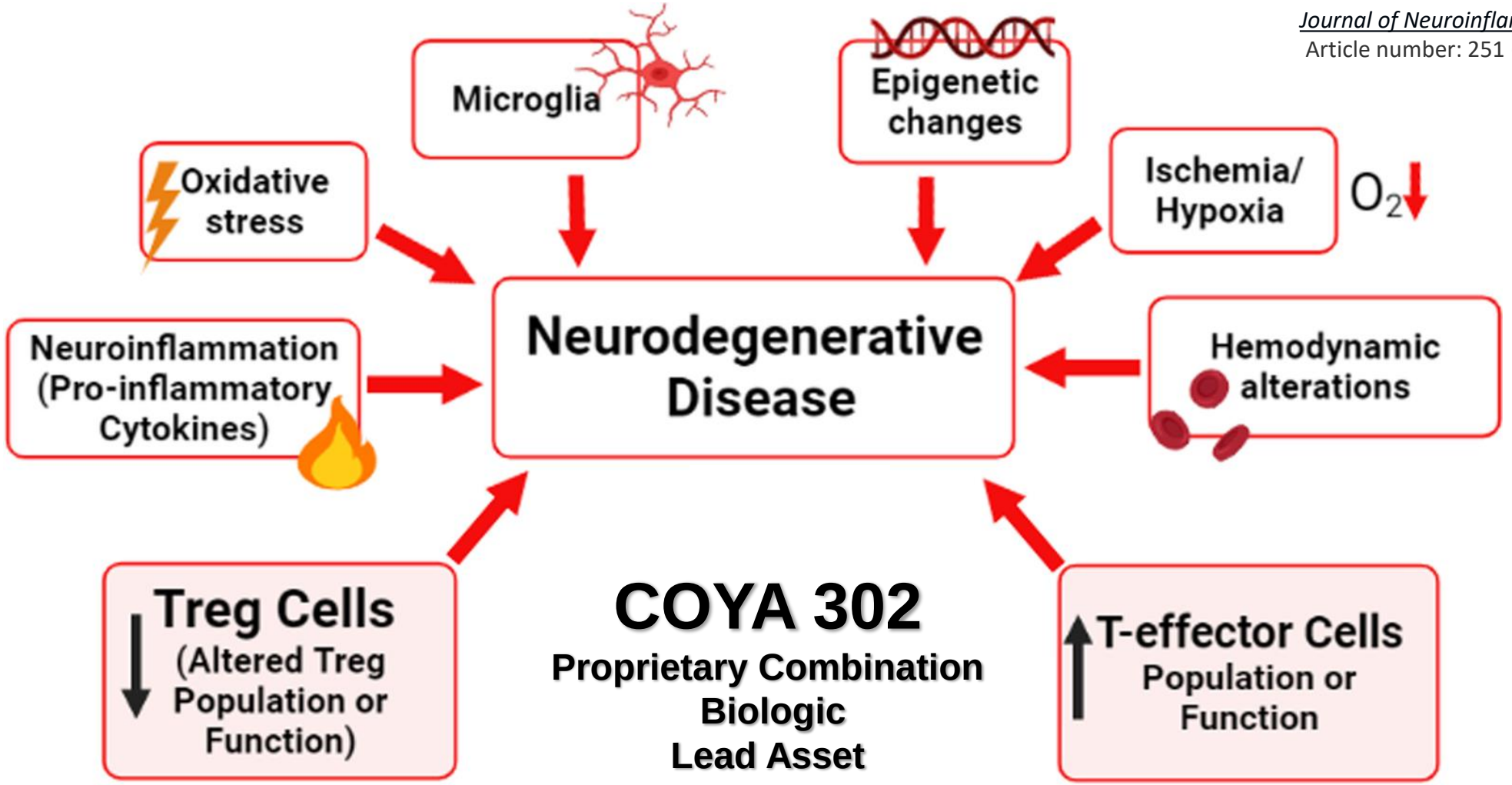


1 Studies were conducted with commercially available product
2 As of 6/30/24

IIT: Investigator Initiated Trial
PoC: Proof of Concept

Neurodegenerative Diseases Involve Complex Pathophysiology
Multi-modal Combination Therapies May be Transformative

Journal of Neuroinflammation **volume 19**, Article number: 251 (2022)



Like Oncology and Viral Disease, Combination Therapies May Be Transformative in the Treatment of Neurodegeneration

COYA THERAPEUTICS

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) in patients who were progressing prior to therapy

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

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 proinflammatory chemokines and biomarkers

Well tolerated

COYA THERAPEUTICS

* Studies were conducted with commercially available product.

Coya's Leadership Has Demonstrated Deep Expertise in Biotech

Management Team



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

Prior Experience*
abbvie · Lilly · NOVARTIS · The University of Texas MD Anderson Cancer Center · imaware



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

Prior Experience*
Johnson & Johnson · sunovion · Bristol Myers Squibb · GlenMark · mesoblast · Lilly



David Snyder
Chief Financial Officer & Chief Operating Officer

Prior Experience*
DisperSol Technologies · exicure · Cellular Dynamics International · NimbleGen



Arun Swaminathan, Ph.D.
Chief Business Development Officer

Prior Experience*
Bristol Myers Squibb · Actinium Pharmaceuticals, Inc. · ALTEOGEN Inc.



Michelle Frazier
Senior Vice President of Regulatory Affairs

Prior Experience*
RVNC · CytomX · FDA · Coherus BioSciences

Board of Directors



Wilbur Ross
Former U.S. Secretary of Commerce

Prior Experience*
ROSS Acquisition Corp. I · ISG · U.S. Department of Commerce



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

Prior Experience*
Bristol Myers Squibb · Genentech · MERCK · JUNO Therapeutics



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

Prior Experience*
Pfizer



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

Prior Experience*
Bristol Myers Squibb · Bayer · Pfizer · Otsuka



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

Prior Experience*
Vicuron Pharmaceuticals · INDAPTA THERAPEUTICS · SCHRÖDINGER · AISLING CAPITAL



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

Prior Experience*
BAYHILL THERAPEUTICS · NOVARTIS · Roche · Genentech

COYA THERAPEUTICS

*Logos illustrated represent past experience

SAB Comprised of Seminal Leadership in Tregs

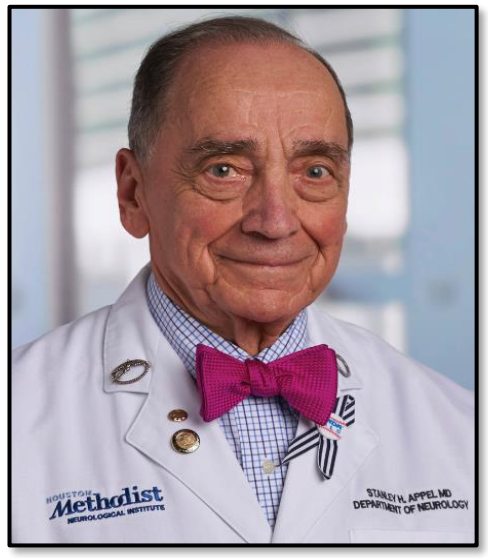
Following the discoveries of Dr. Sakaguchi and Dr. Appel, Coya is developing multiple product modalities to enhance the therapeutic potential of Tregs for the treatment of disorders of high unmet need



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



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 Role of Tregs in Neurodegeneration

COYA THERAPEUTICS

SAB: Scientific Advisory Board

COYA 302 Program

Product Type	Discovery	Preclinical	IND-Enabling	Phase 1	Phase 2	Phase 3	Partnerships / Collaborations	2024 Milestones
COYA 302 Treg-Enhancing / T Effector & Macrophage Depleting Biologics	**COYA 302 (Low Dose IL-2 + CTLA4-Ig)** → ***Amyotrophic Lateral Sclerosis (ALS)*** Completed POC IIT open label study in patients with ALS*						**Licensing Transaction on 12/6/23:** **Dr. Reddy's Laboratories**	**1H 2024:** IND filing **2H 2024:** Planned FDA meeting in 4Q 2024 **1H 2024:** PoC Peer-Reviewed publication **1H 2024:** Biomarker data publication
COYA 302 Treg-Enhancing / T Effector & Macrophage Depleting Biologics	**COYA 302 (Low Dose IL-2 + CTLA4-Ig)** → ***Frontotemporal Dementia (FTD)***						**Retained Worldwide Rights**	**4Q 2024:** Update IND filing timing post FDA meeting 4Q2024
COYA 302 Treg-Enhancing / T Effector & Macrophage Depleting Biologics	**COYA 302 (Low Dose IL-2 + CTLA4-Ig)** → ***Alzheimer's Disease (AD)***						**Retained Worldwide Rights**	**4Q 2024 (CTAD Conference)**: Academic IIT double-blind Ph2 data of Low dose IL-2 alone in AD
COYA 302 Treg-Enhancing / T Effector & Macrophage Depleting Biologics	**COYA 302 (Low Dose IL-2 + CTLA4-Ig)** → ***Parkinson's Disease (PD)***						**Retained Worldwide Rights**	**1H/2H 2024:** Animal data **2025:** IND filing and Ph1/2 initiation upon IND acceptance

COYA THERAPEUTICS

POC- Proof of Concept; IIT- Investigator Initiated Trial
* Conducted using commercially available products

COYA-302: A Pipeline Within a Product With > $10B Potential

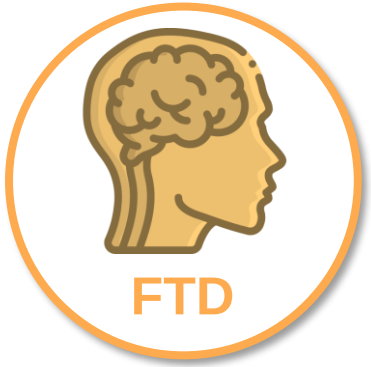
Coya is prioritizing ALS, FTD, AD and PD as key initial neurodegenerative diseases



- High Unmet Need
- Regulatory Flexibility
- >$1B Sales Potential
- Fast Path to Approval if Effective

ALS = Amyotrophic Lateral Sclerosis

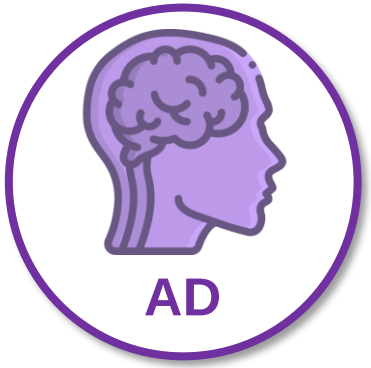
Orphan Indication



- No Approved Therapies
- Regulatory Flexibility
- >$1B Sales Potential
- Fast Path to Approval if Effective

FTD = Frontotemporal Dementia

Orphan Indication



- High Unmet Need
- Most common Neurodegenerative Disease
- >$5 B Sales Potential

AD = Alzheimer's Disease



- High Unmet Need
- Second most common Neurodegenerative Disease
- >$5 B Sales Potential

PD = Parkinson’s Disease

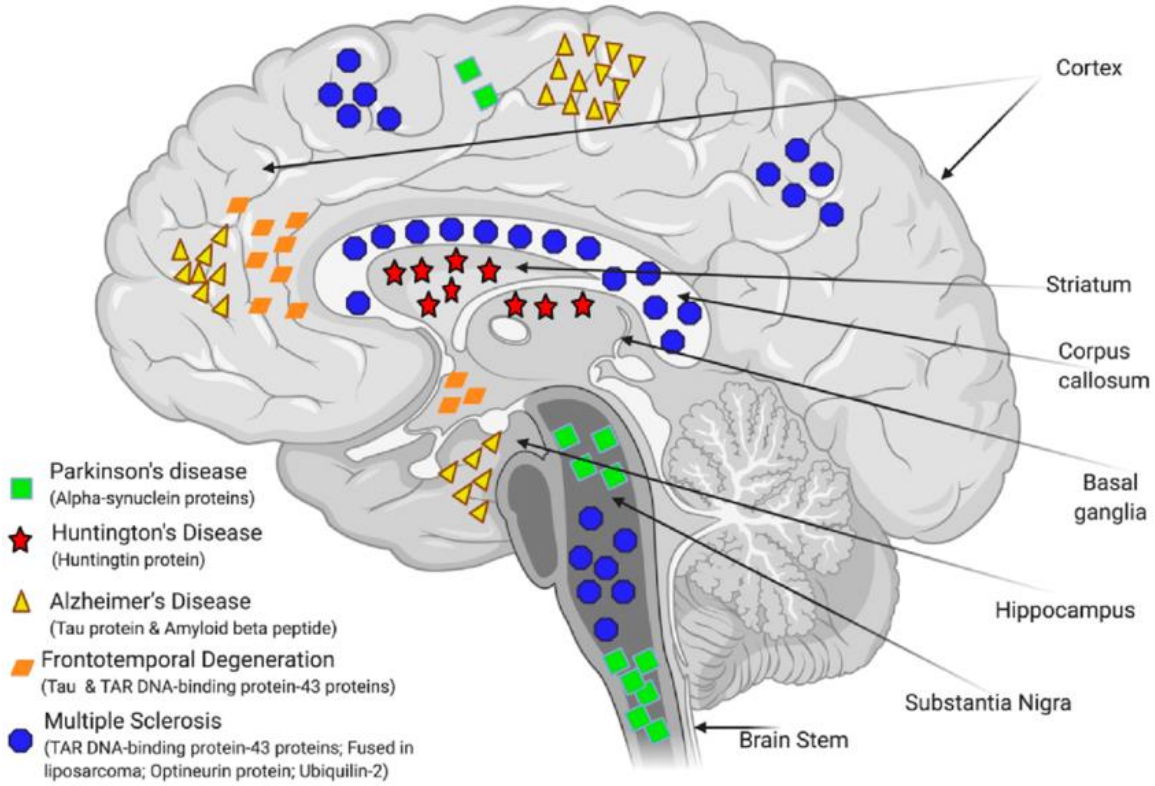
Additional Pipeline Assets

Product Type	Discovery	Preclinical	IND-Enabling	Phase 1	Phase 2	Phase 3	Partnerships / Collaborations	2024 Milestones
COYA 301 **Treg-Enhancing Biologic**	**COYA 301 (Low Dose IL-2)** ***Alzheimer's Disease (AD)*** **Completed POC IIT open label study in patients with AD***						**Retained Worldwide Rights**	**4Q 2024 (CTAD Conference):** Academic IIT double-blind Ph2 data ****Note: Data from 301 trial will guide the design for COYA-302 in AD****
COYA 303 **Low Dose IL-2 (COYA 301) + GLP-1 Agonist**	**COYA 303** ***Undisclosed***						**Retained Worldwide Rights**	**2H 2024 :** File IP on the combination Initiate pre-clinical characterization
COYA 201 **Allogeneic Treg Derived Exosomes**	**COYA 201** ***Undisclosed***						**Retained Worldwide Rights**	**2024:** Additional animal model data
COYA 206 **Antigen-Directed Allogeneic Treg-Derived Exosomes**	**COYA 206** ***Undisclosed***						**Retained Worldwide Rights**	**2024:** Target validation and cargo validation data

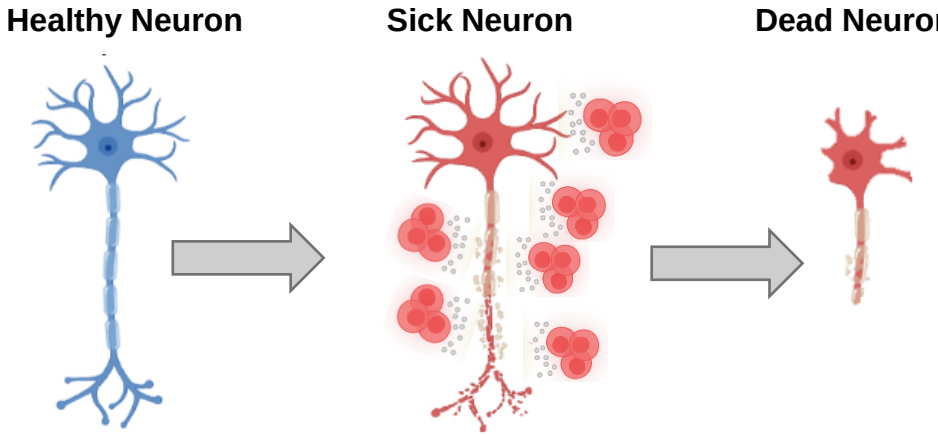
POC- Proof of Concept; IIT- Investigator Initiated Trial
* Conducted using commercially available products

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

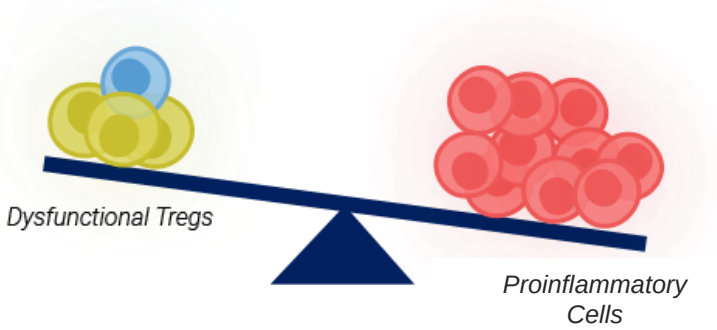
Neurodegeneration: Loss of Selective Population of Neurons



Inflammation in the Nervous System



Tregs play central role in inflammation and progression of neurodegeneration



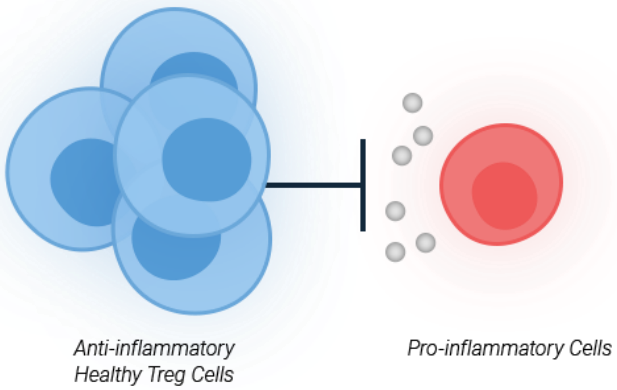
Bioengineering 8(2):30
DOI:10.3390/bioengineering8020030

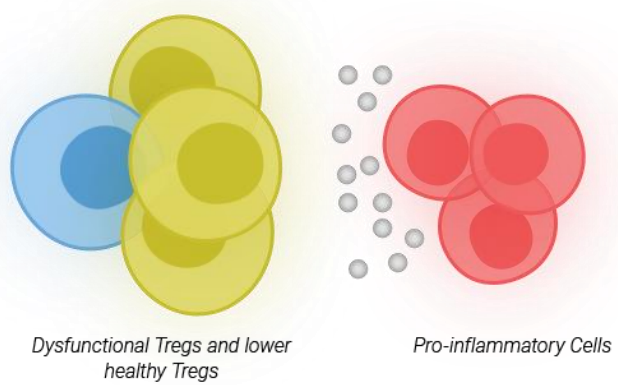
What Are Tregs and How They Are Dysfunctional

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

The main functions of Tregs are:

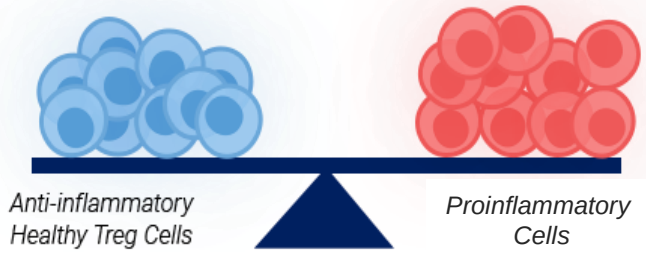
- *Ameliorate inflammatory mechanisms and reactions*
- *Inhibit the release of proinflammatory cytokines*
- *Maintain self-tolerance*





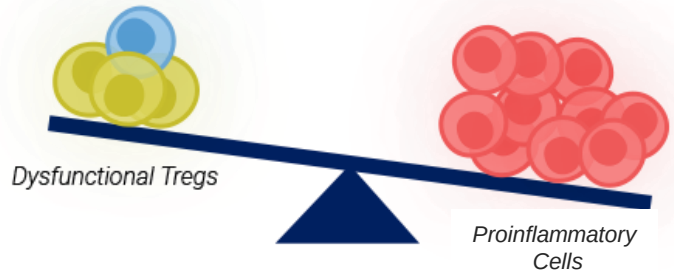
Healthy Tregs

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



Dysfunctional Tregs

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



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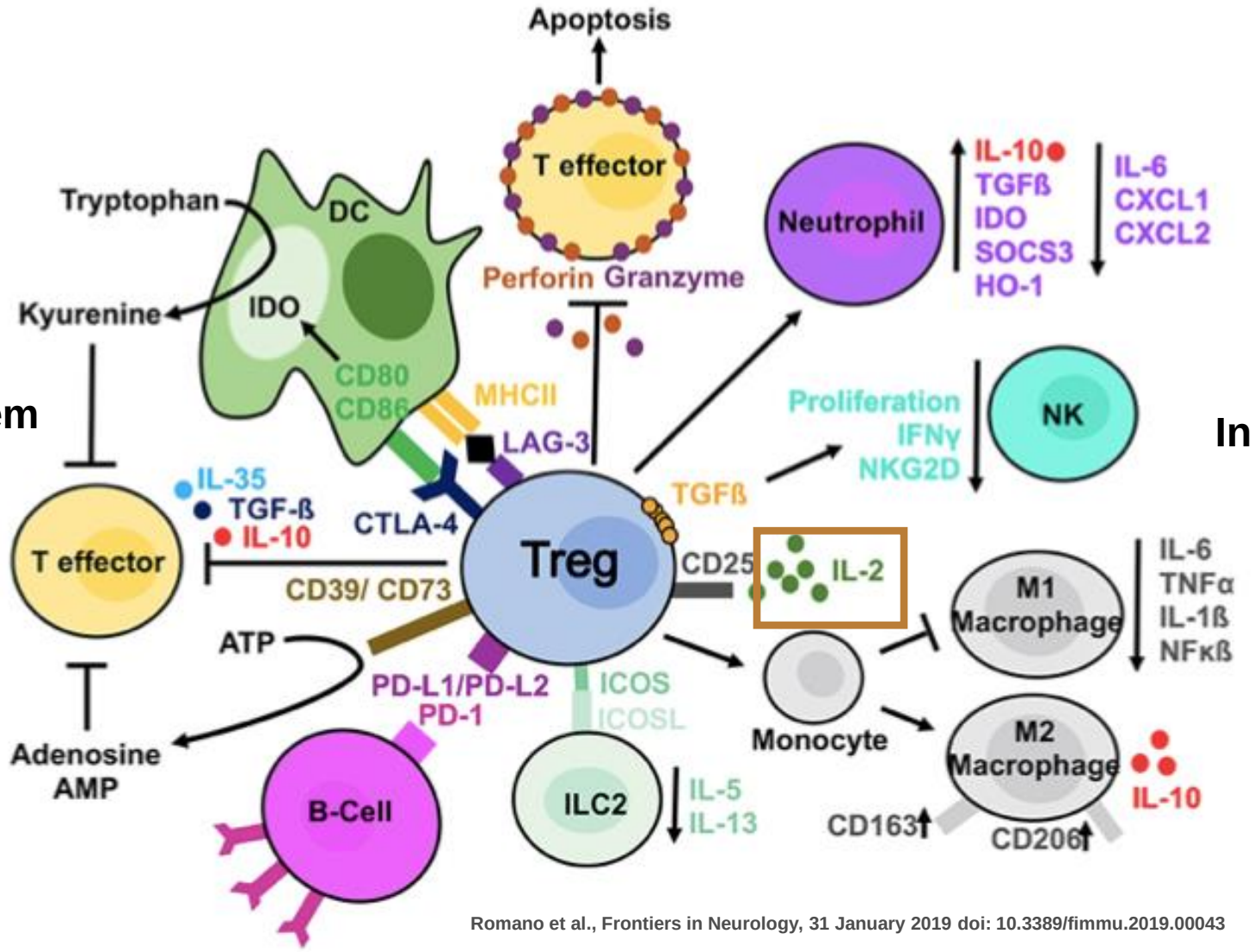
Tregs Regulate Multiple Downstream Pathways to Reduce Inflammation

Adaptive Immune System



Innate Immune System

Romano et al., Frontiers in Neurology, 31 January 2019 doi: 10.3389/fimmu.2019.00043

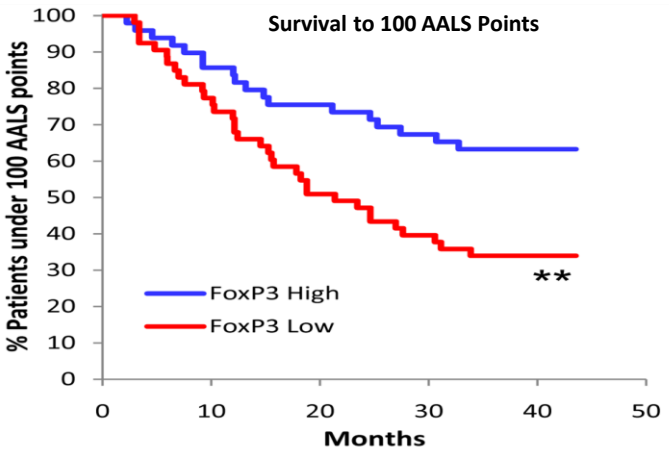
COYA THERAPEUTICS

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

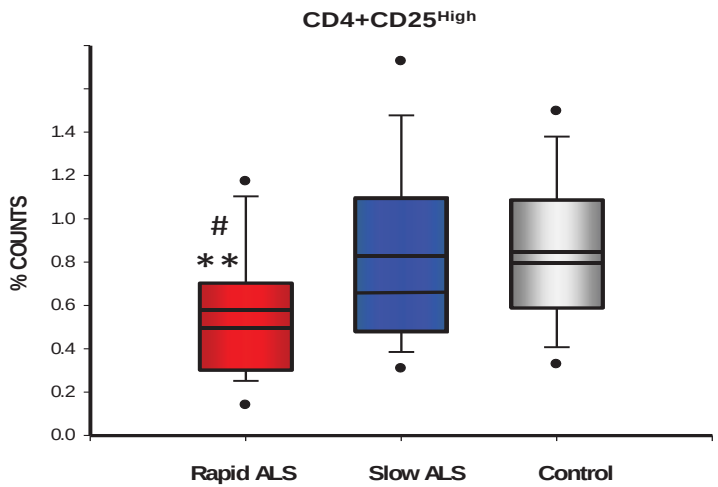
Treg dysfunction is associated with ALS disease progression and burden of disease…

…and is similarly associated in other neurodegenerative diseases

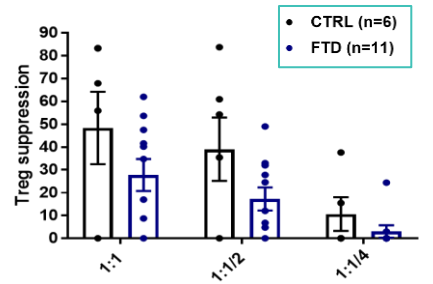
Treg Dysfunction is Associated with Reduced Survival in ALS



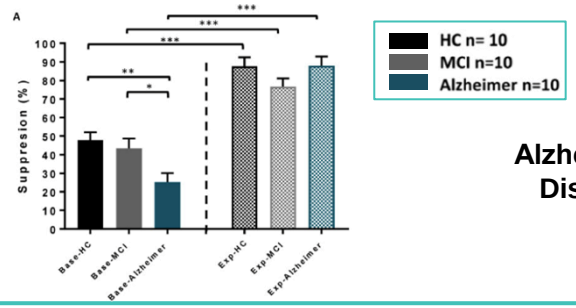
Treg Dysfunction Plays a Role in the Rate of Decline in ALS



Treg Dysfunction Is Implicated in FTD & AD



Frontotemporal Dementia

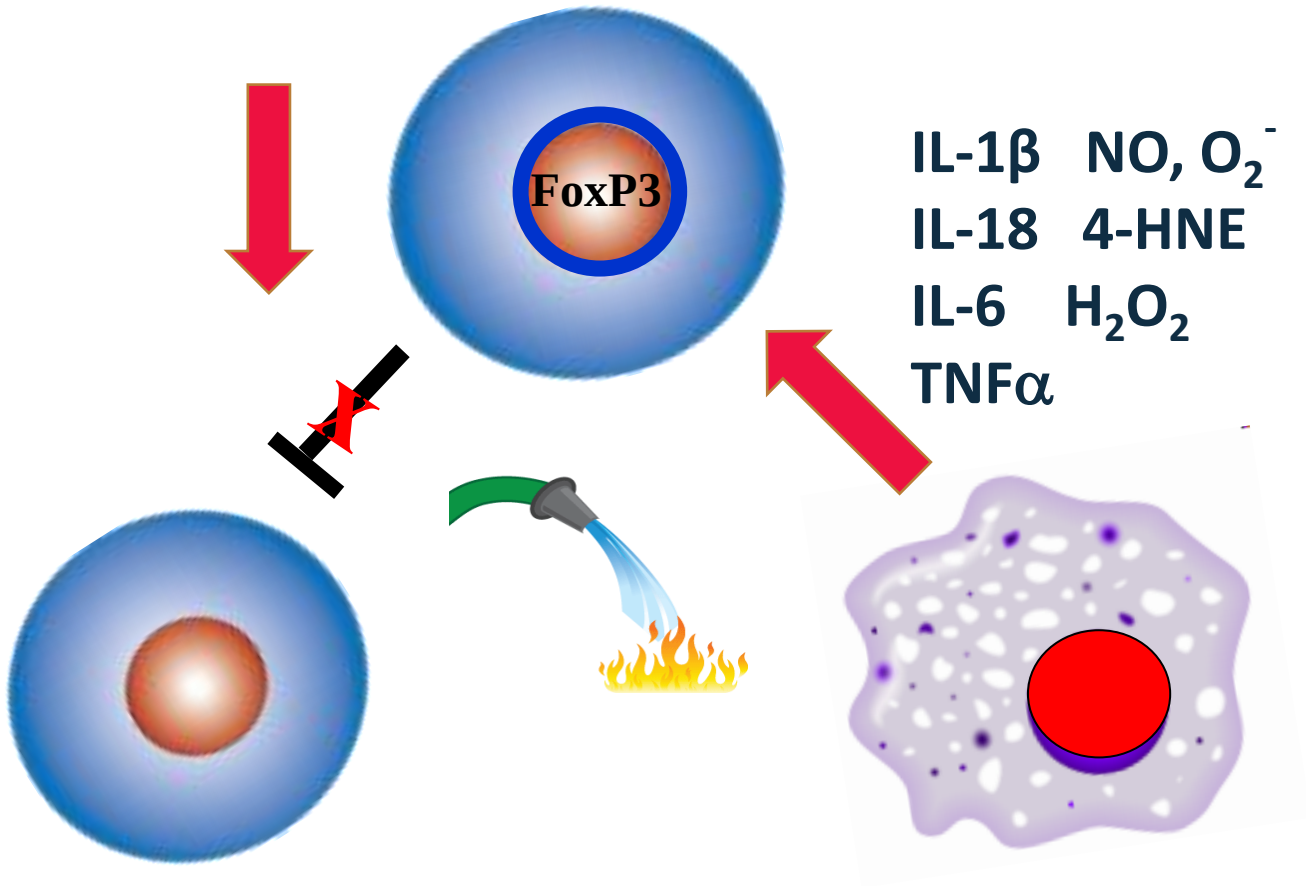


Alzheimer's Disease

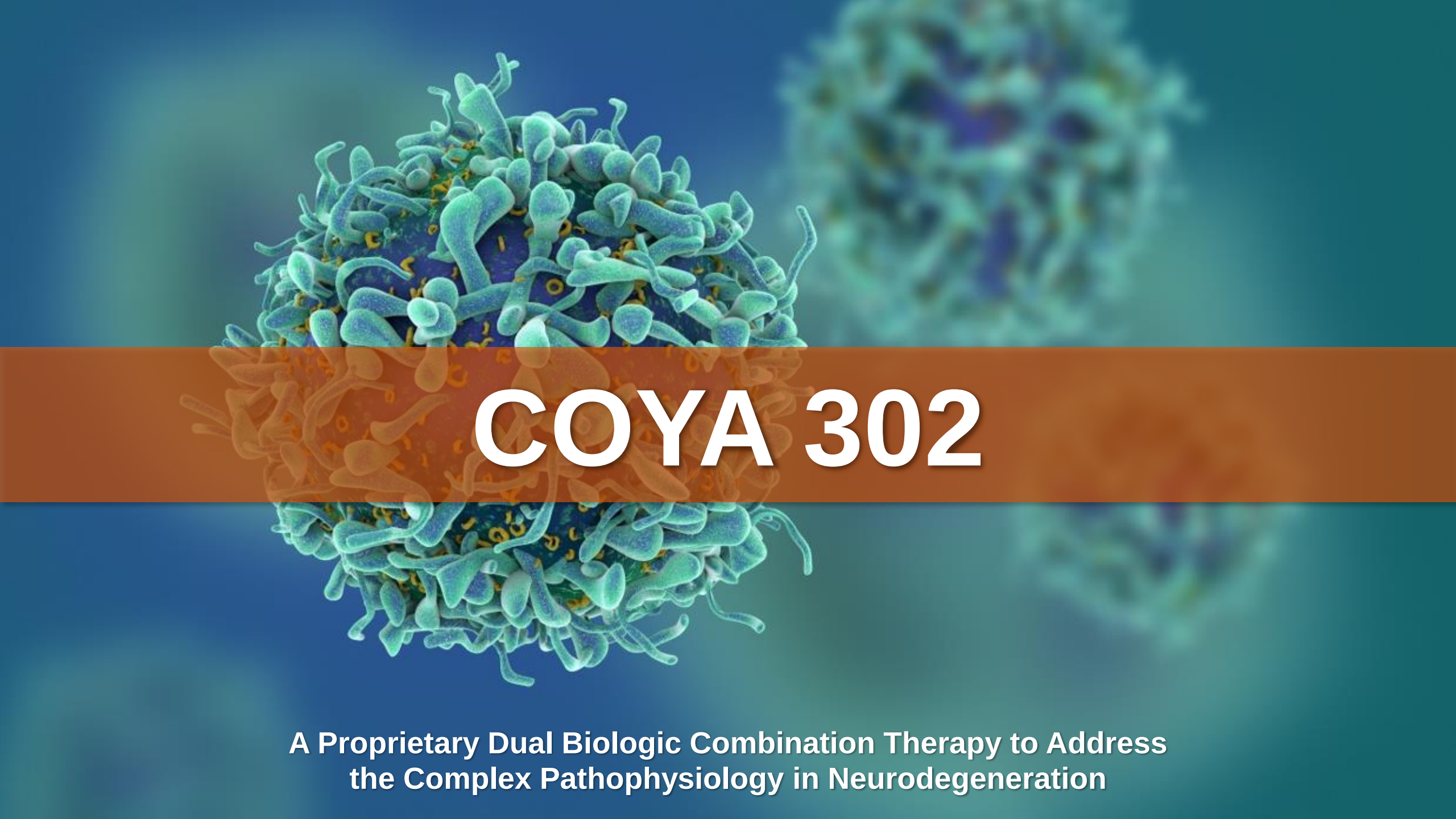
Henkel et al, EMBO Mol Med. 2012 Nov 9
Faridar et al, Brain Communications, Volume 2, Issue 2, 2020, fcaa112

Multiple Immune Pathways Involved in Complex Neurodegenerative Diseases

Macrophages Promote Dysfunction of Tregs Releasing Proinflammatory Cytokines and Oxidative Stress



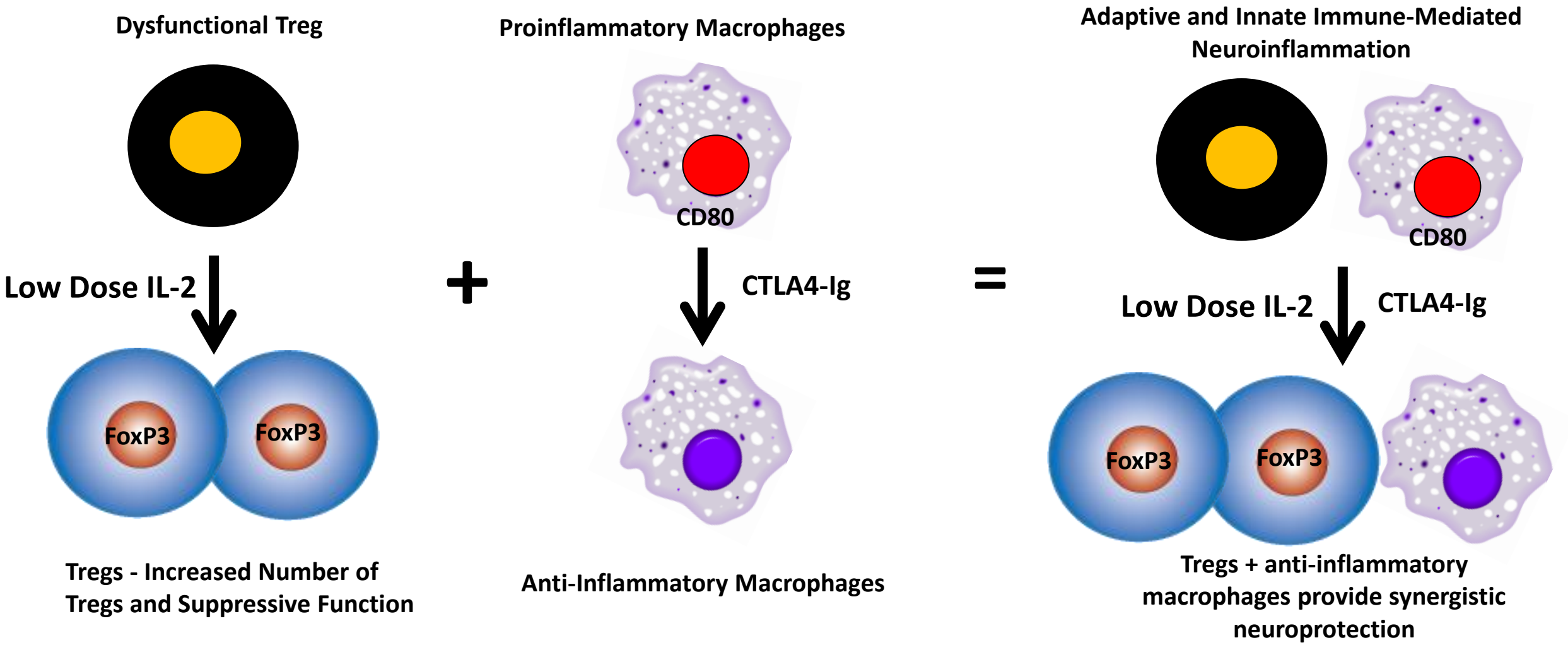
Oxidative Stress/Cytokines contribute to pathophysiology of neuronal injury and cell death in ALS



COYA 302

A Proprietary Dual Biologic Combination Therapy to Address the Complex Pathophysiology in Neurodegeneration

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

COYA 302 is a proprietary combination of drugs versus:

Commercial High Dose IL-2 (22 million IU Lyophilized IV for Cancer) or CTLA4-Ig (Orencia for Rheumatoid Arthritis)

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

Strong IP

Well-established GMP manufacturing

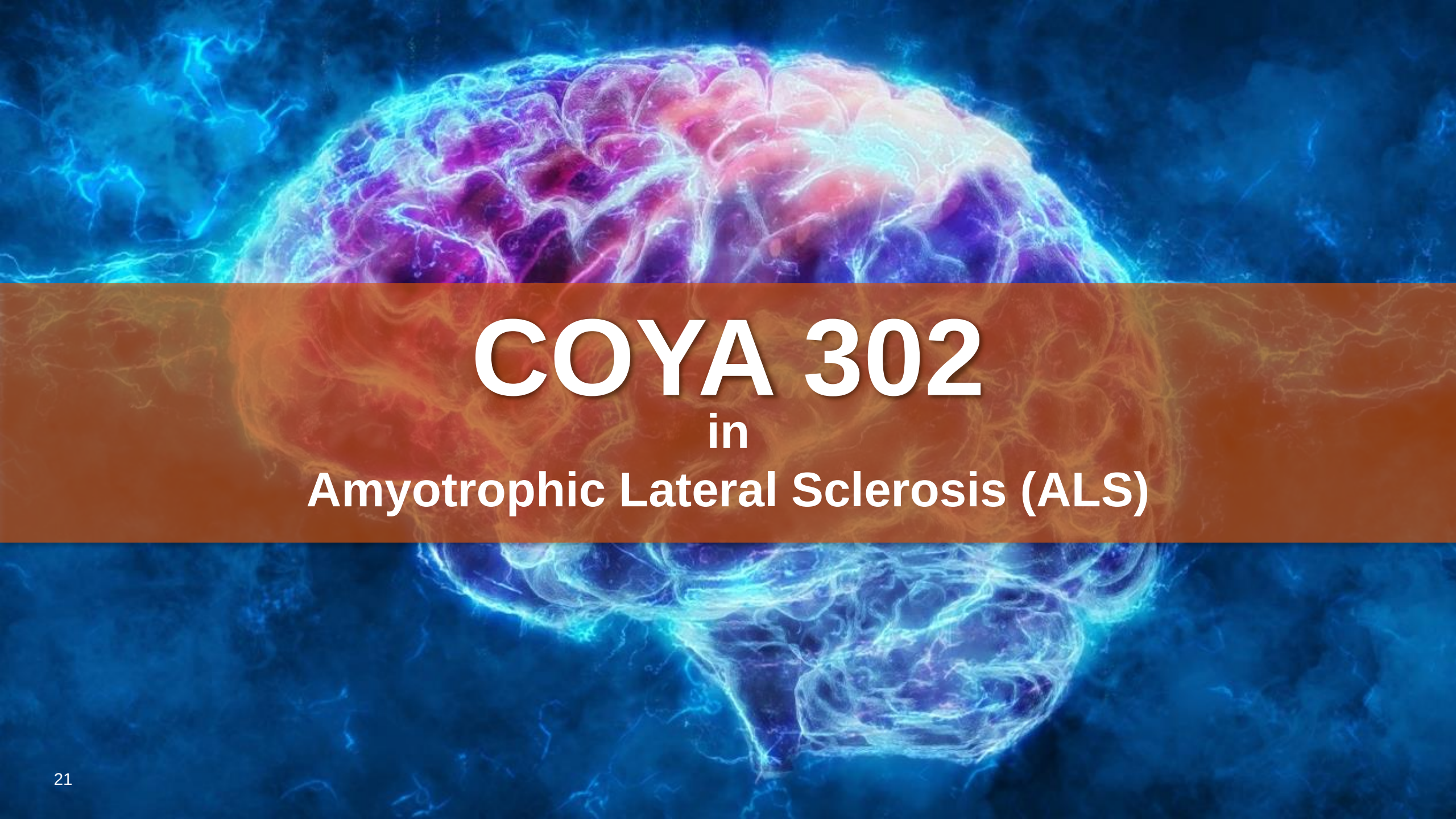


Unique low dose strength (1 million IU per injection) and dosing regimen

Ready-to-administer stable subcutaneous formulation

COYA THERAPEUTICS

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



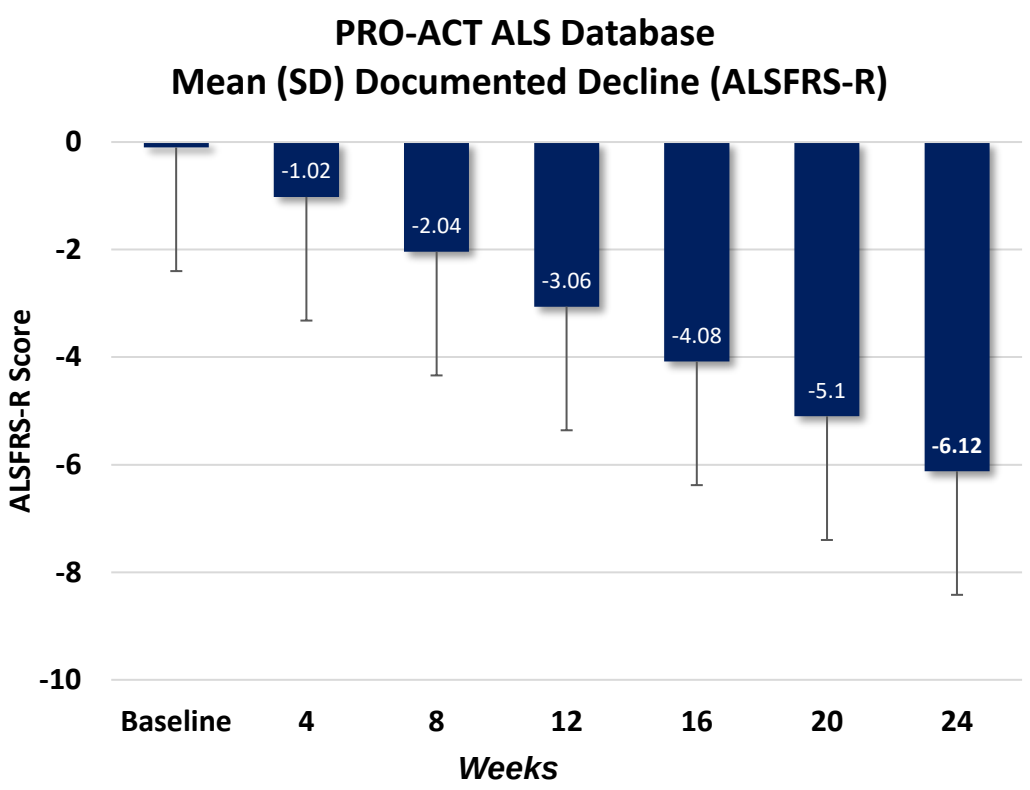
COYA 302

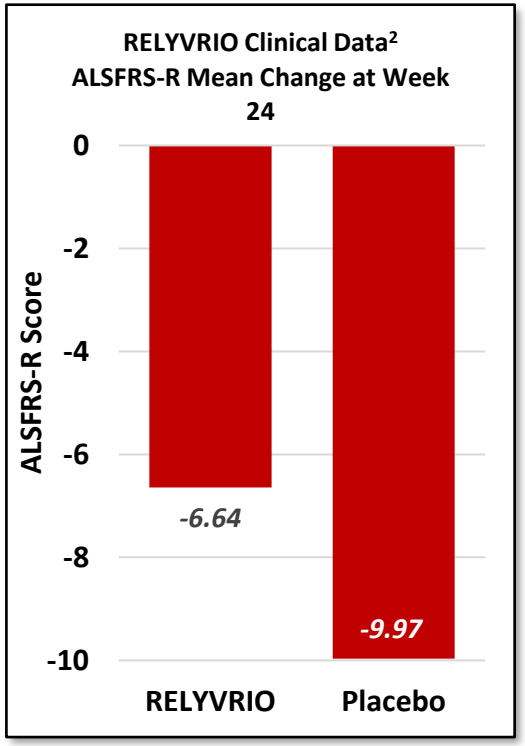
in

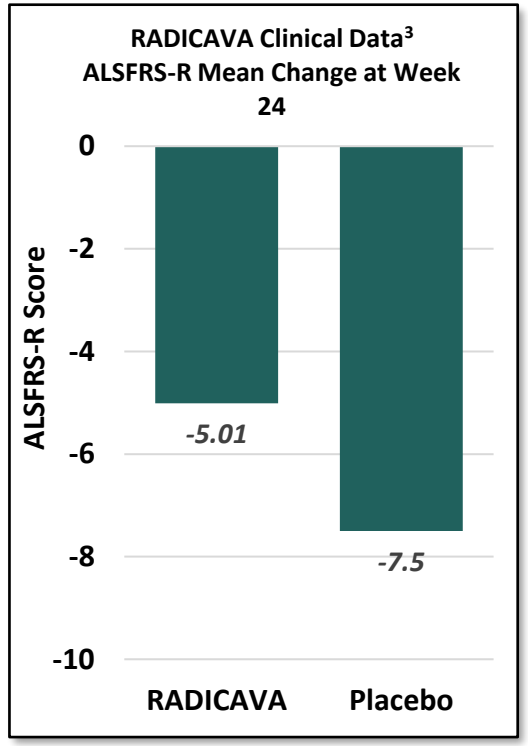
Amyotrophic Lateral Sclerosis (ALS)

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 score[1]

1. The PRO-ACT database is the largest ALS data repository (Atassi et al, 2014)
2. Relyvrio US Prescribing Information (9/2022)
3. Radicava US Prescribing Information (5/2022)

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

Screening

20 weeks

Treatment Period

***LD IL-2 + CTLA4-Ig** was administered via subcutaneous injection over 48 weeks*

Follow-Up

8 weeks

Screening Assessments

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

Treatment Period Assessments

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

Post-Treatment Assessments

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

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

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

COYA THERAPEUTICS

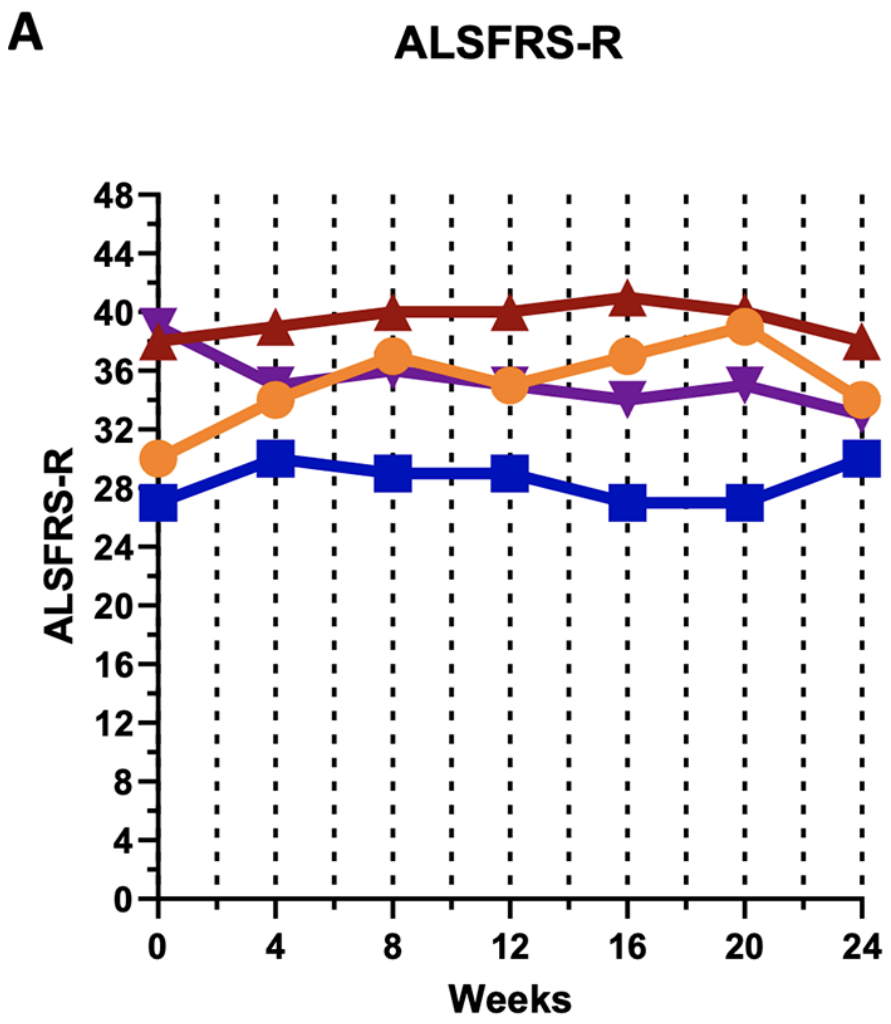
Conducted using commercially available products

COYA 302:
PoC Trial Patient Demographics and Baseline Characteristics

	Age (years)	Sex	Type	Onset	ALS Progression Prior to Baseline (ALSFRS-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 THERAPEUTICS

ALSFRS-R Individual Scores



Participant 1: +4 points
Participant 2: +3 points
Participant 3: Stable
Participant 4: -6 points*

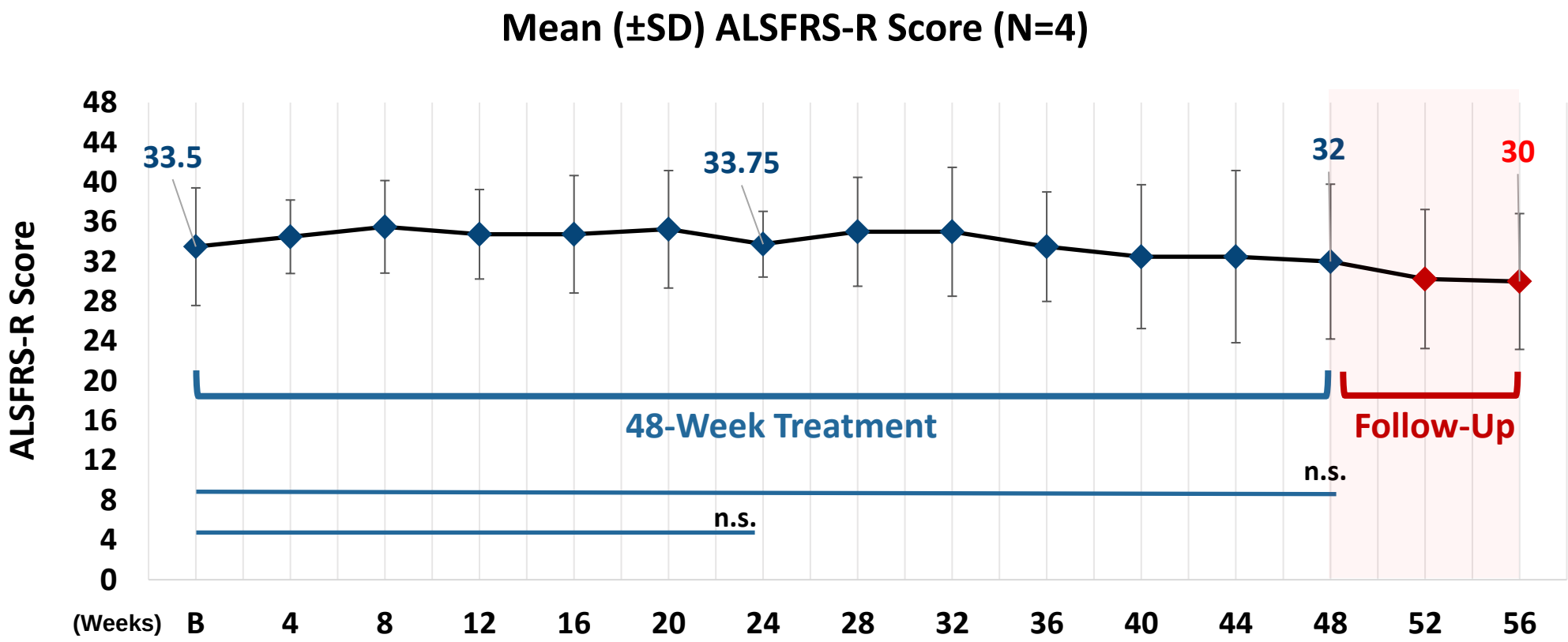
Participant #1
Participant #2
Participant #3
Participant #4

*Declined at month 1 and remained stable thereafter

Thonhoff JR, Beers DR, Zhao W, et al. A Phase 1 Proof-of-Concept Study Evaluating Safety, Tolerability, and Biological Marker Responses with combination therapy of CTLA4-Ig and Interleukin-2 in Amyotrophic Lateral Sclerosis. Frontiers in Neurology, 2024. In press.

COYA THERAPEUTICS

COYA 302:
Appears to Ameliorate ALS Progression Over 48 Weeks



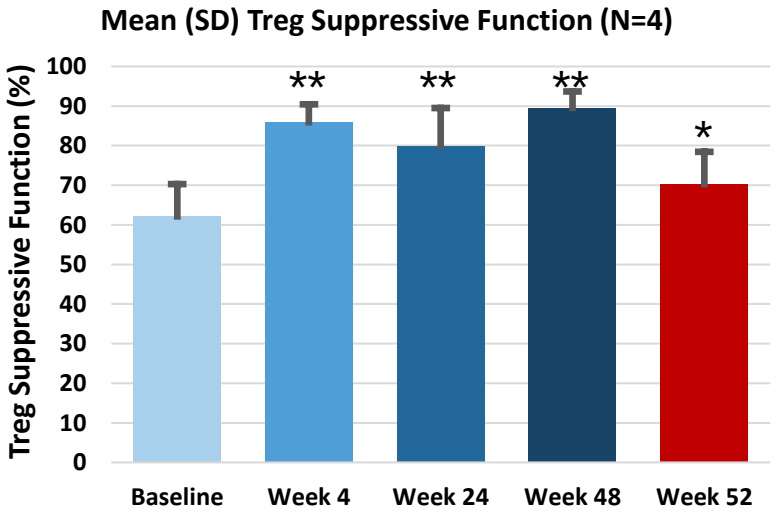
LD IL-2 + CTLA4-Ig was well tolerated over 48 weeks; the most common AE was mild injection site reaction. All patients completed the study; no deaths or serious AEs (SAEs) occurred over the course of the study.

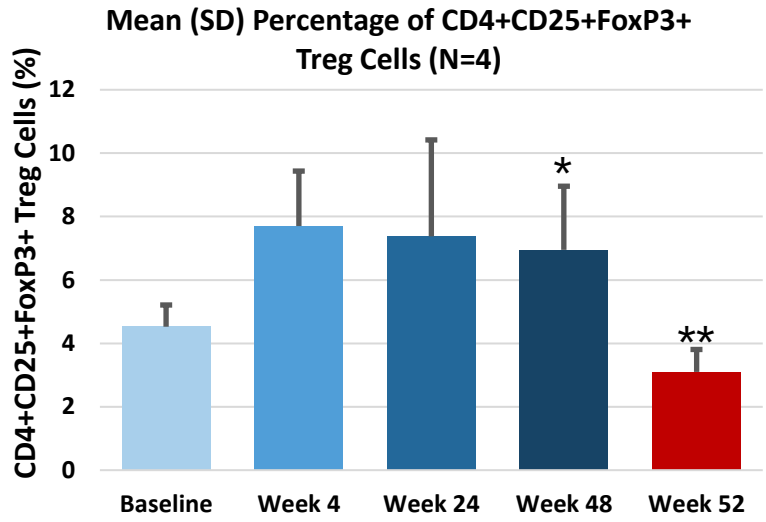
B: Baseline
n.s.: not significant (paired t test)
Conducted using commercially available products

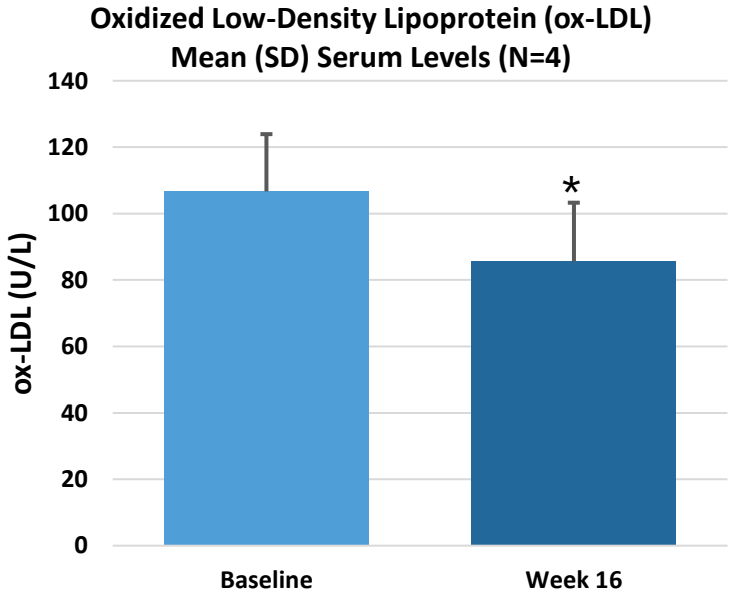
COYA 302:
Enhanced Biologic Activity

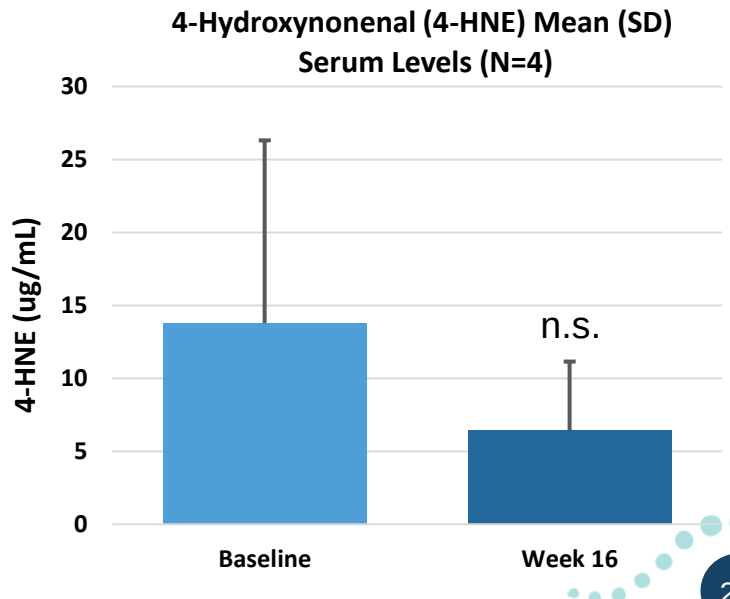
Key Takeaways

- ✓ **LD IL-2 + CTLA4-Ig significantly expands Treg suppressive function** as early as 4 weeks after initiation of treatment and maintained a significantly increased Treg function.
- ✓ **LD IL-2 + CTLA4-Ig increased Treg numbers as early as 4 weeks** after initiation of treatment and maintained a higher number over the course of treatment.
- ✓ **LD IL-2 + CTLA4-Ig enhanced suppression** of macrophage-mediated **oxidative stress and proinflammatory cytokine biomarkers** over 48 weeks









n.s.: not significant (paired t test)
*p <0.05
** p <0.01 (paired t test)
Conducted using commercially available products

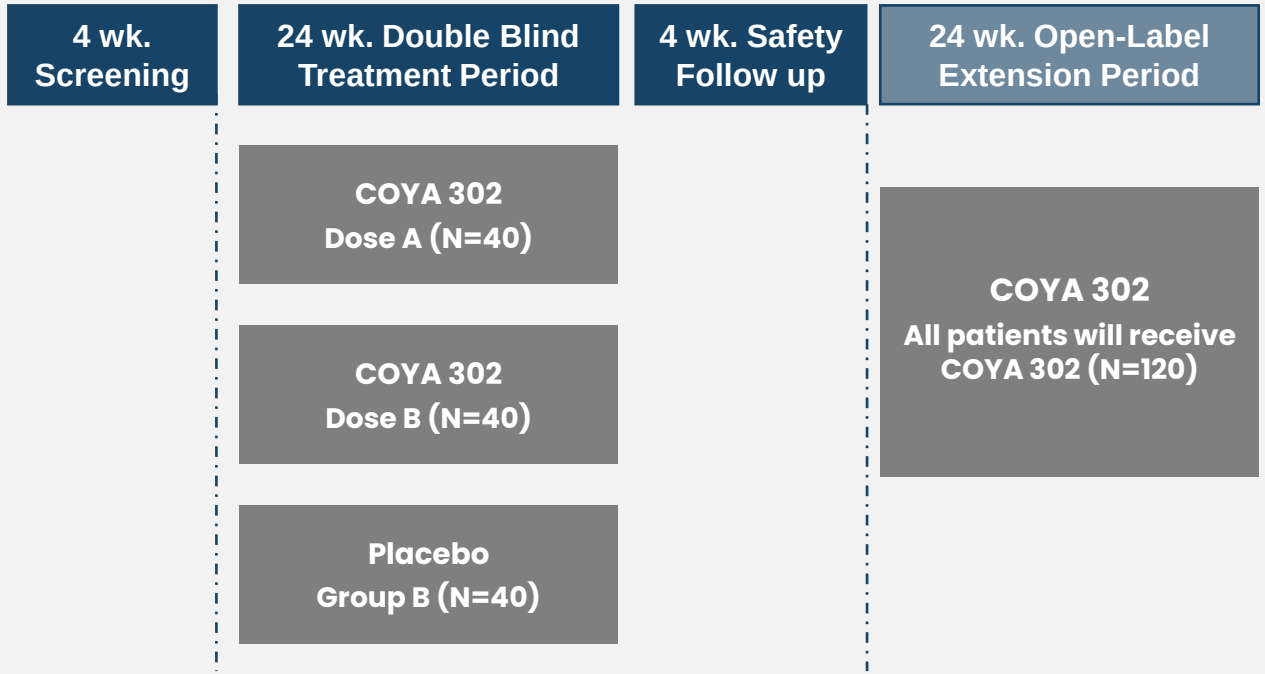
COYA THERAPEUTICS

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 ≤ 24 months from Screening
- ALSFR-R score ≥ 35 at Screening
- A score of at least 2 points in each ALSFRS-R item
- Forced vital capacity (FVC) ≥ 70% of predicted capacity for age, height, and gender at Screening
- Documented disease progression (by ALSFR-R score) for at least 16 weeks prior to Screening

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



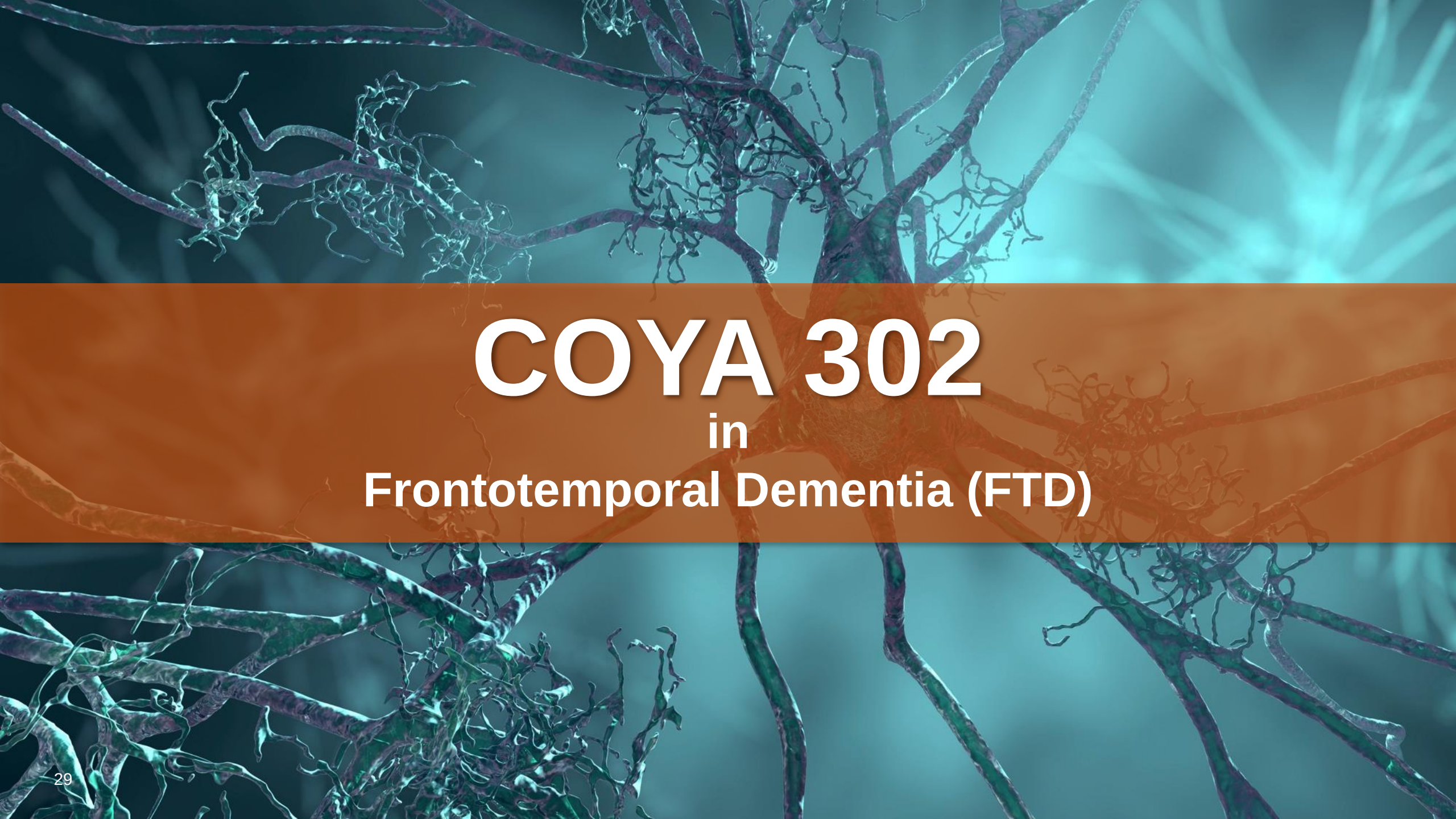
Primary Endpoint

Change in disease severity over time measured by ALSFRS-R total score from baseline to Week 24 vs. placebo

Study Objectives

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

COYA THERAPEUTICS



COYA 302

in

Frontotemporal Dementia (FTD)

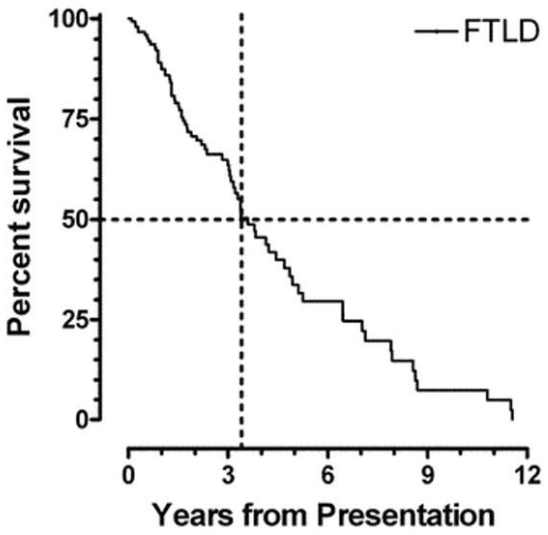
Alzheimer's Drug Discovery Foundation $5M Investment

- $5M investment for funding of Phase 2 FTD study

Alzheimer's Drug Discovery Foundation

Title: A Phase II, Randomized, Double-Blind, Placebo-Controlled, Multi-Center, 26-Week Study to Evaluate the Safety and Efficacy of COYA 302 for the Treatment of Nonfluent Variant Primary Progressive Aphasia (nfvPPA) Subtype of Frontotemporal Lobar Degeneration (FTLD)

Frontotemporal Disorder (FTD) is a Rare Disease but is One of Most Common Dementias in Younger People



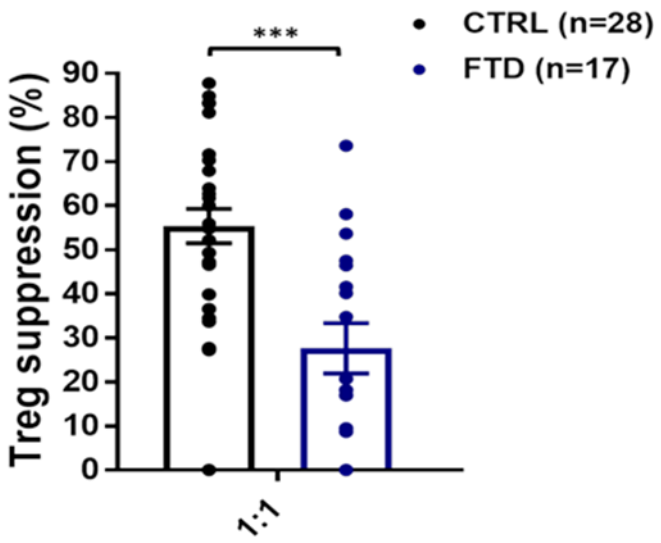
SYMPTOMS OF FTD

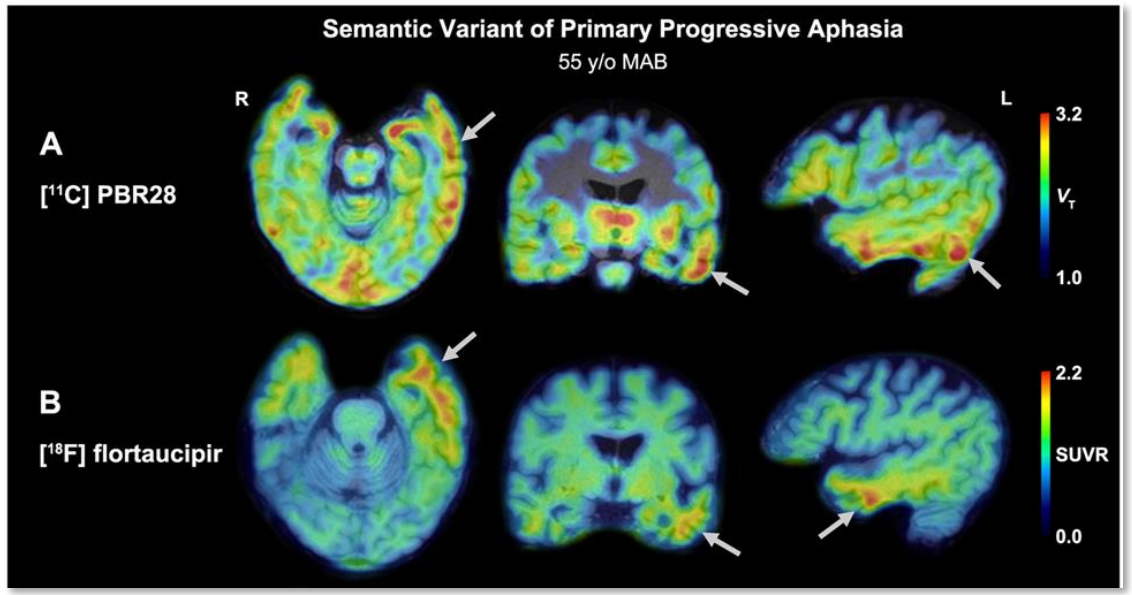
- Changes in personality, mood and social.
- Language, speech and communication problems.
- Deteriorating problem-solving skills
- Difficulty planning, organizing, staying focused or completing tasks.
- Poor financial judgement.
- Balance issues, frequent falls, trouble walking, poor coordination, tremors or shaking.

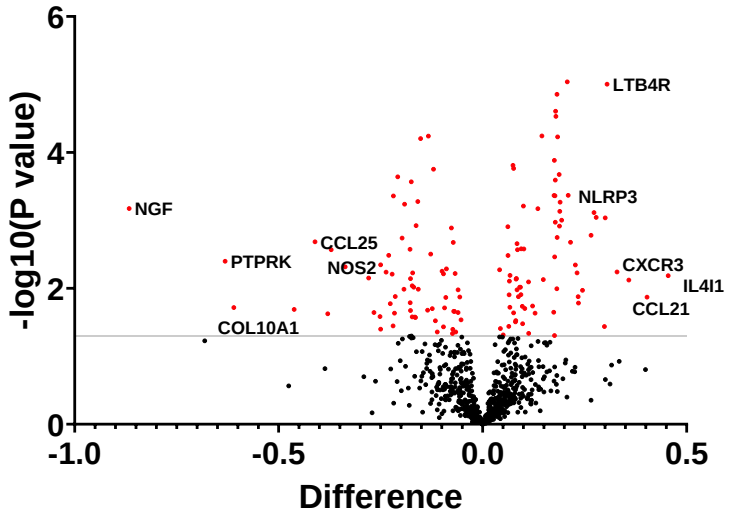
Frontotemporal disorder progresses to death faster than Alzheimer's disease, and, unfortunately, <u>there is no effective treatment</u>

COYA THERAPEUTICS

Exacerbated Systemic and Central Inflammatory Responses in FTD



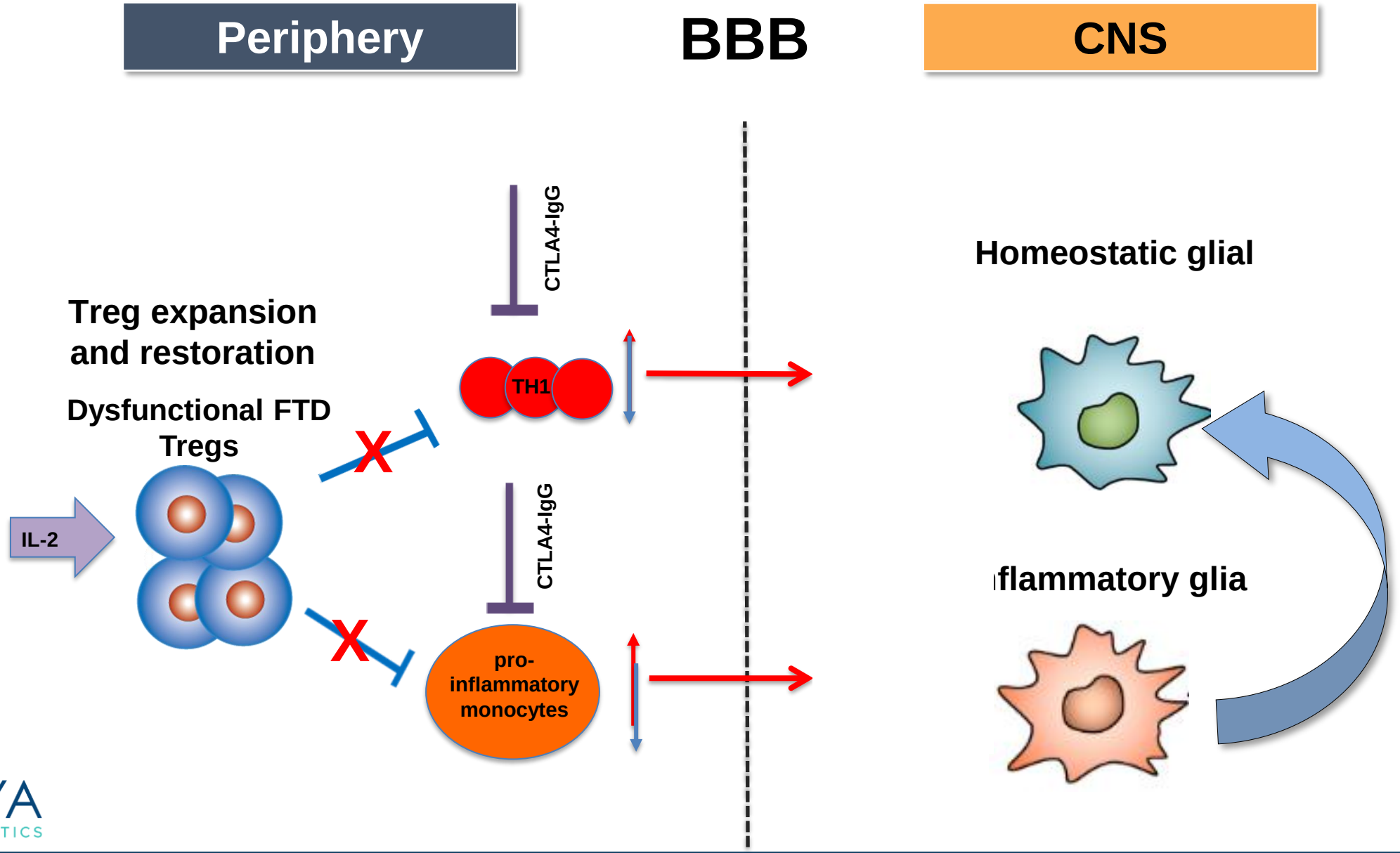






Internal Data

Targeting Inflammation in FTD to Slow Disease Progression



COYA THERAPEUTICS

COYA 302 FTD Phase 2a Study

Houston Methodist Center is a center of excellence in ALLFTD: a single infrastructure clinical data platform in FTD with collaborative decision making among 5 leading centers around the USA



Eligibility Criteria

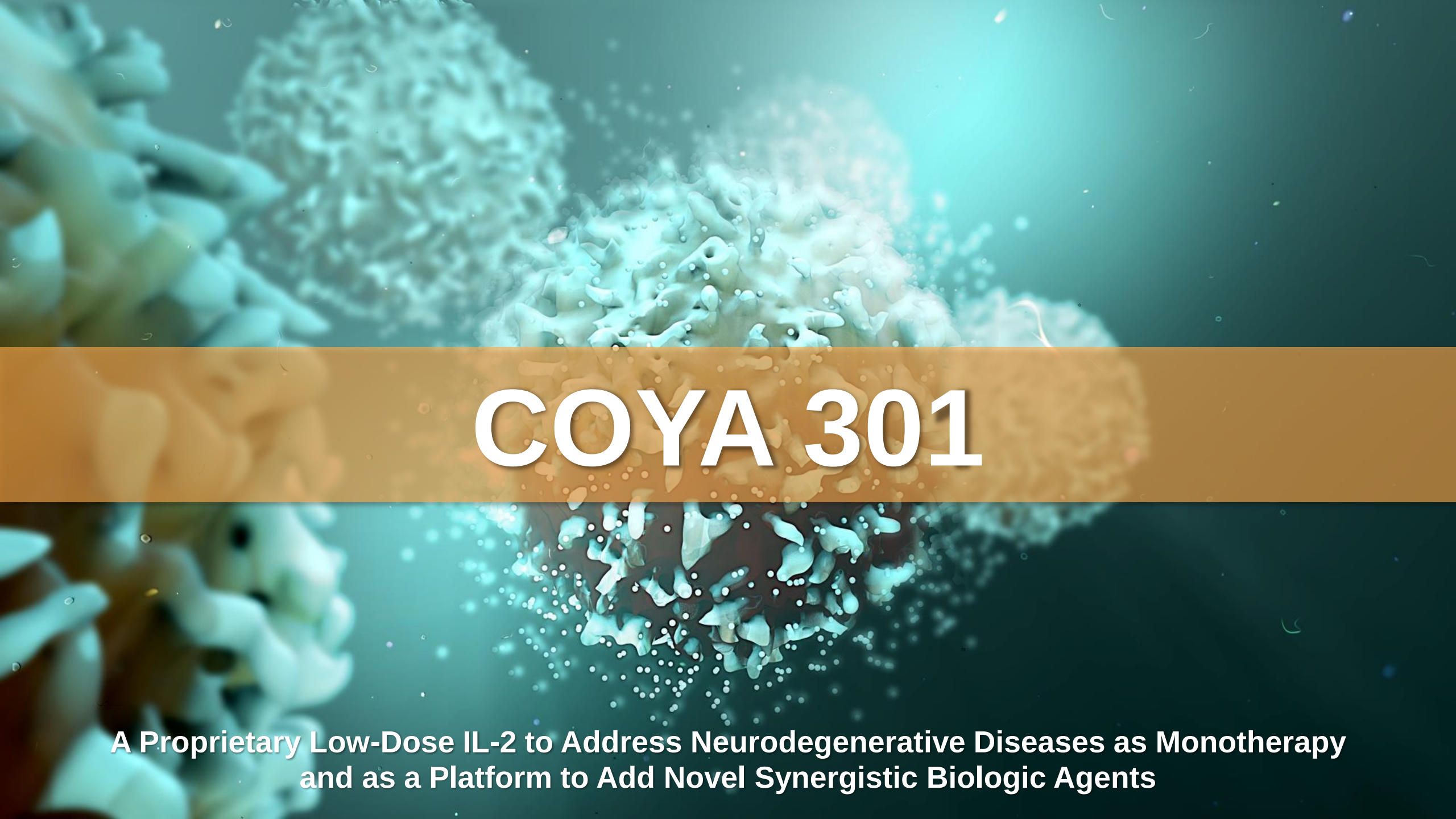
- Non-Fluent Primary Progressive Aphasia Subtype
- Global Clinical Dementia Rating - Frontotemporal Lobar Degeneration (CDR® plus NACC FTLD) score of 0.5 or 1

Primary Endpoints

- CDR+NACC-FTLD-SB*
- Neuropsychological tests
- NfL
- MRI Volume

* CDR® Dementia Staging Instrument PLUS National Alzheimer's Coordinating Center (NACC) Behavior and Language Domains for FTLD - sum of boxes

COYA THERAPEUTICS

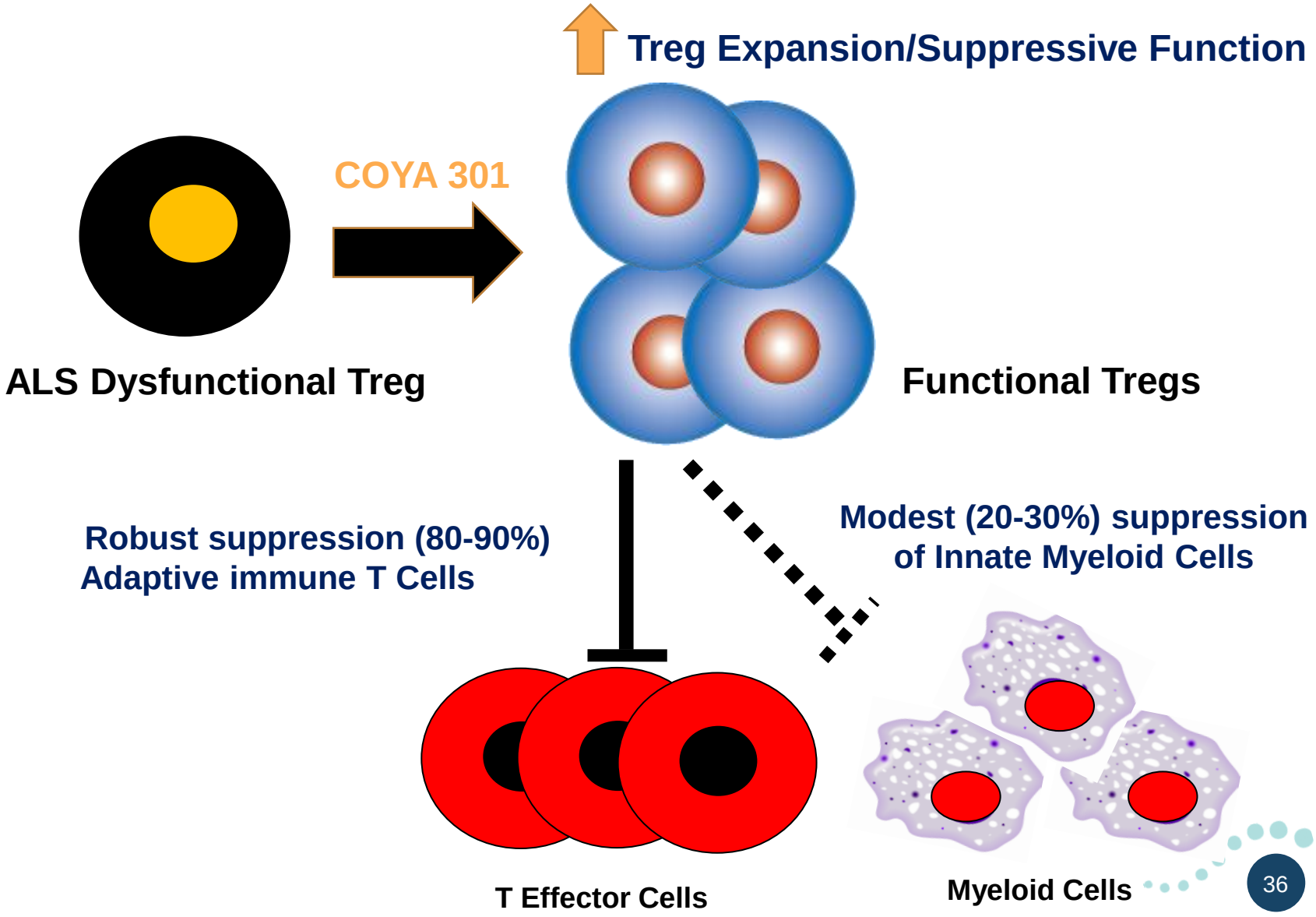


COYA 301

A Proprietary Low-Dose IL-2 to Address Neurodegenerative Diseases as Monotherapy and as a Platform to Add Novel Synergistic Biologic Agents

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

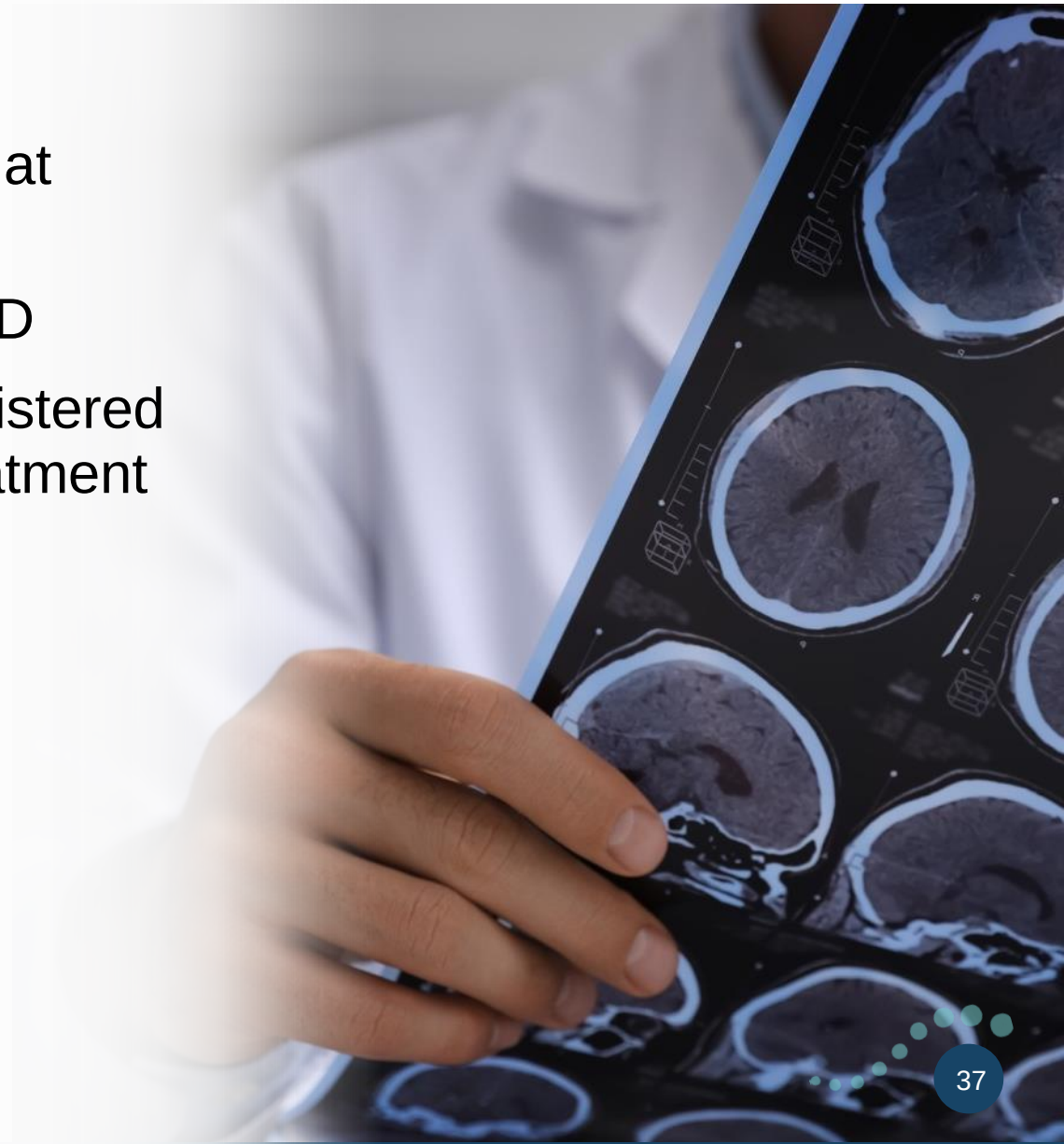
Dysfunctional Tregs are associated with neuroinflammation promoted by activated T effector cells and activated innate myeloid cells



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

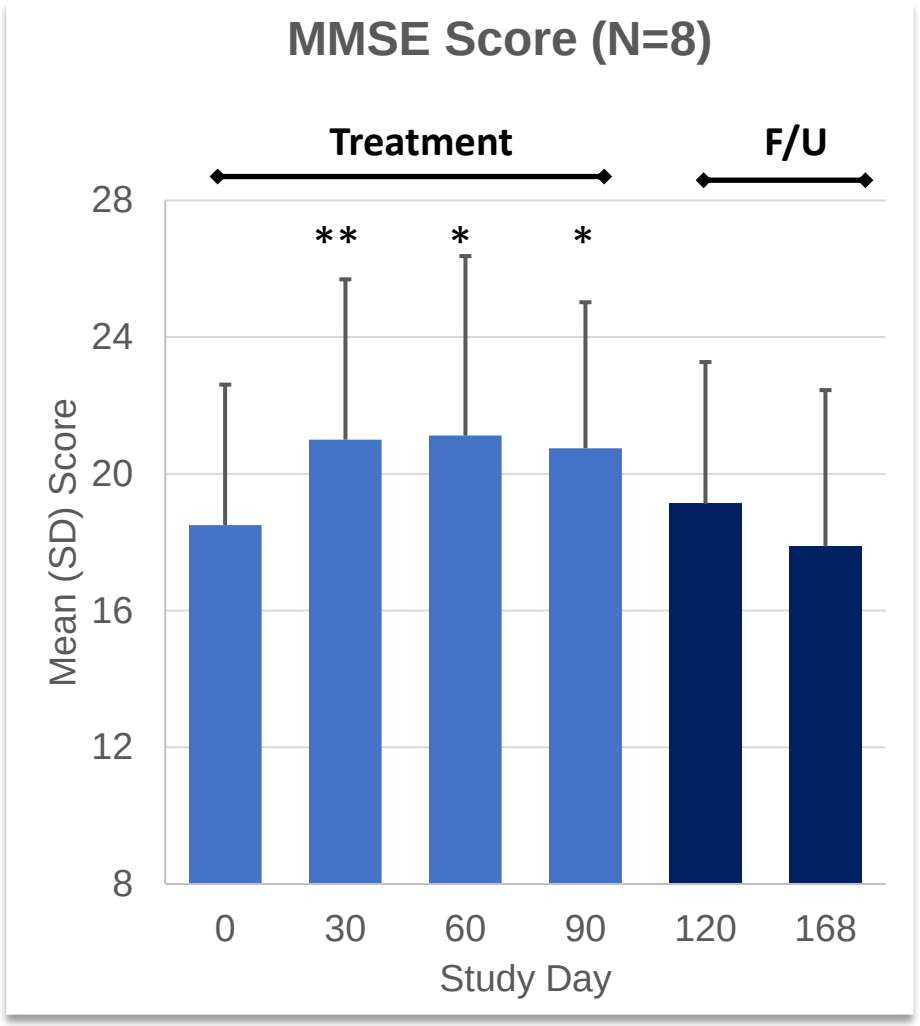
Overall Study Design

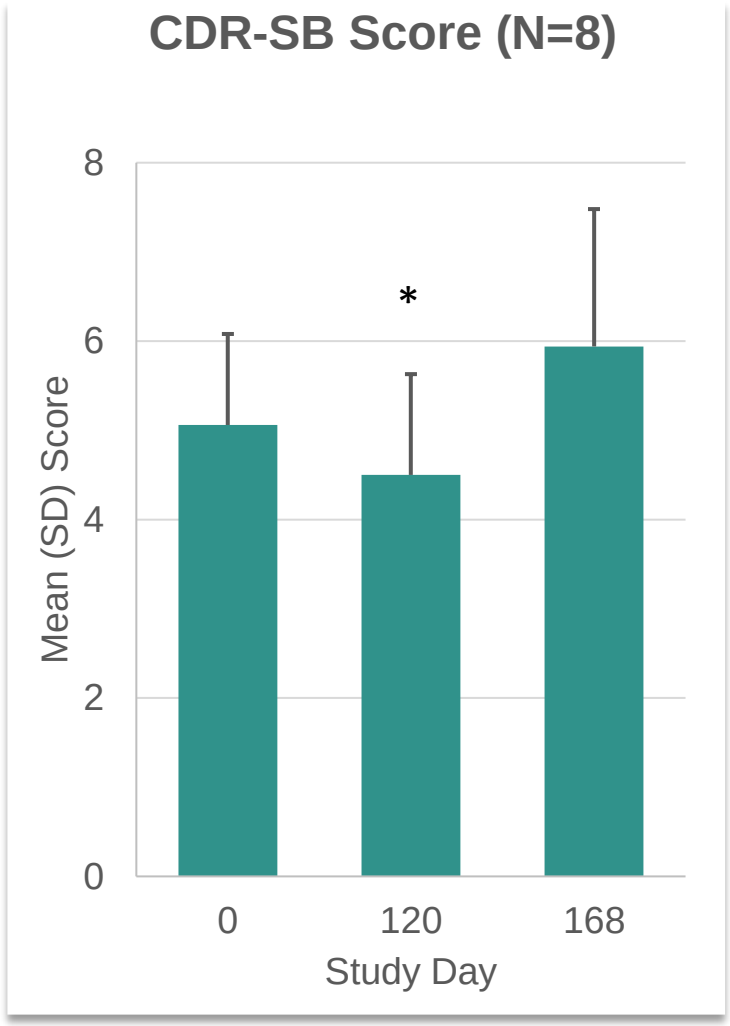
- Proof-of-Concept open-label study, conducted at Houston Methodist Hospital
- Population: 8 patients with mild-to-moderate AD
- Treatment: 4 monthly COYA 301 cycles administered subcutaneously, followed by 2-month post-treatment observation. The study was conducted with commercially available product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

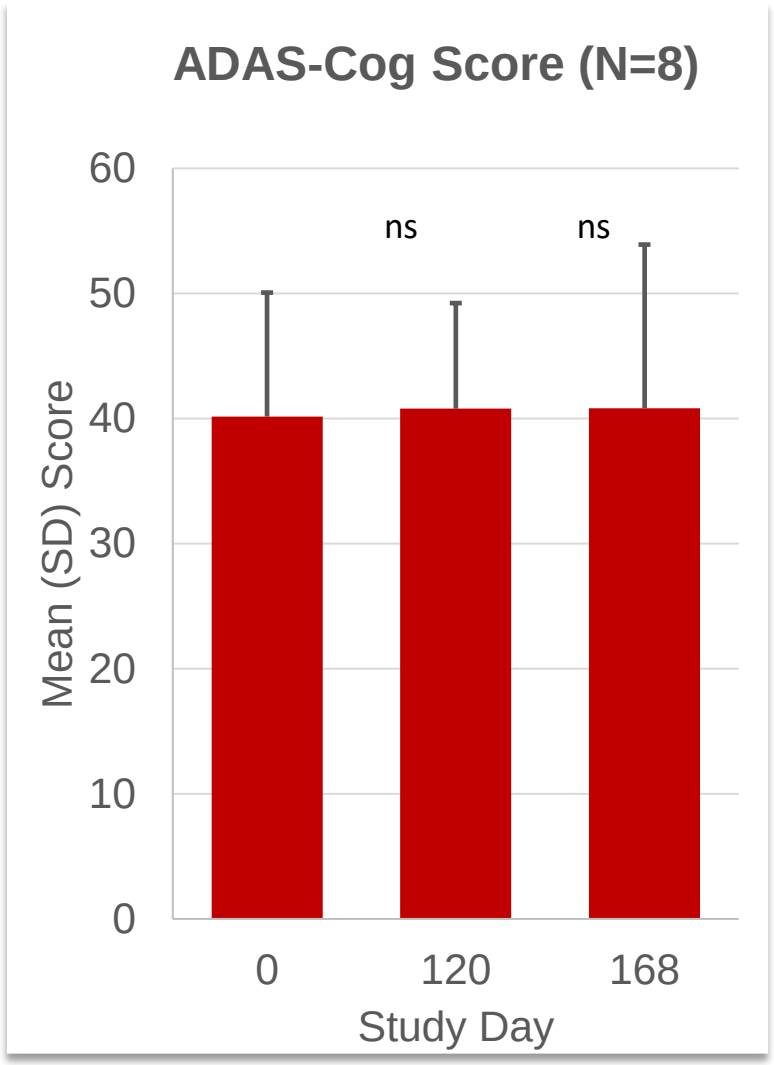


COYA THERAPEUTICS

COYA 301:
Improved or Halted Cognitive Decline in AD Patients







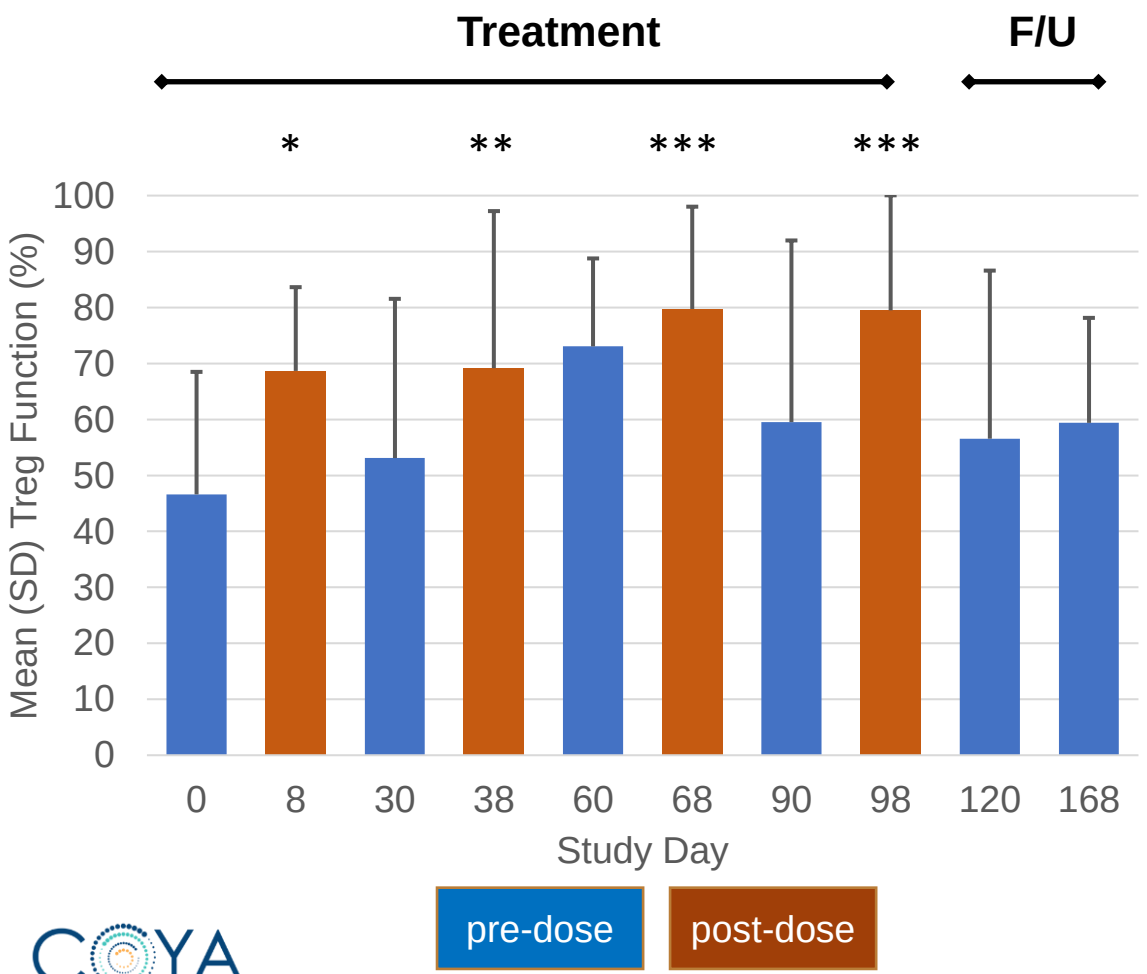
***p<0.05, **p<0.01 ns: not significant**

MMSE: Mini-Mental State Examination, ADAS-Cog: Alzheimer's Disease Assessment Scale-Cognitive Subscale
CDR-SB: Clinical Dementia Rating scale – Sum of Boxes

Conducted using commercially available product

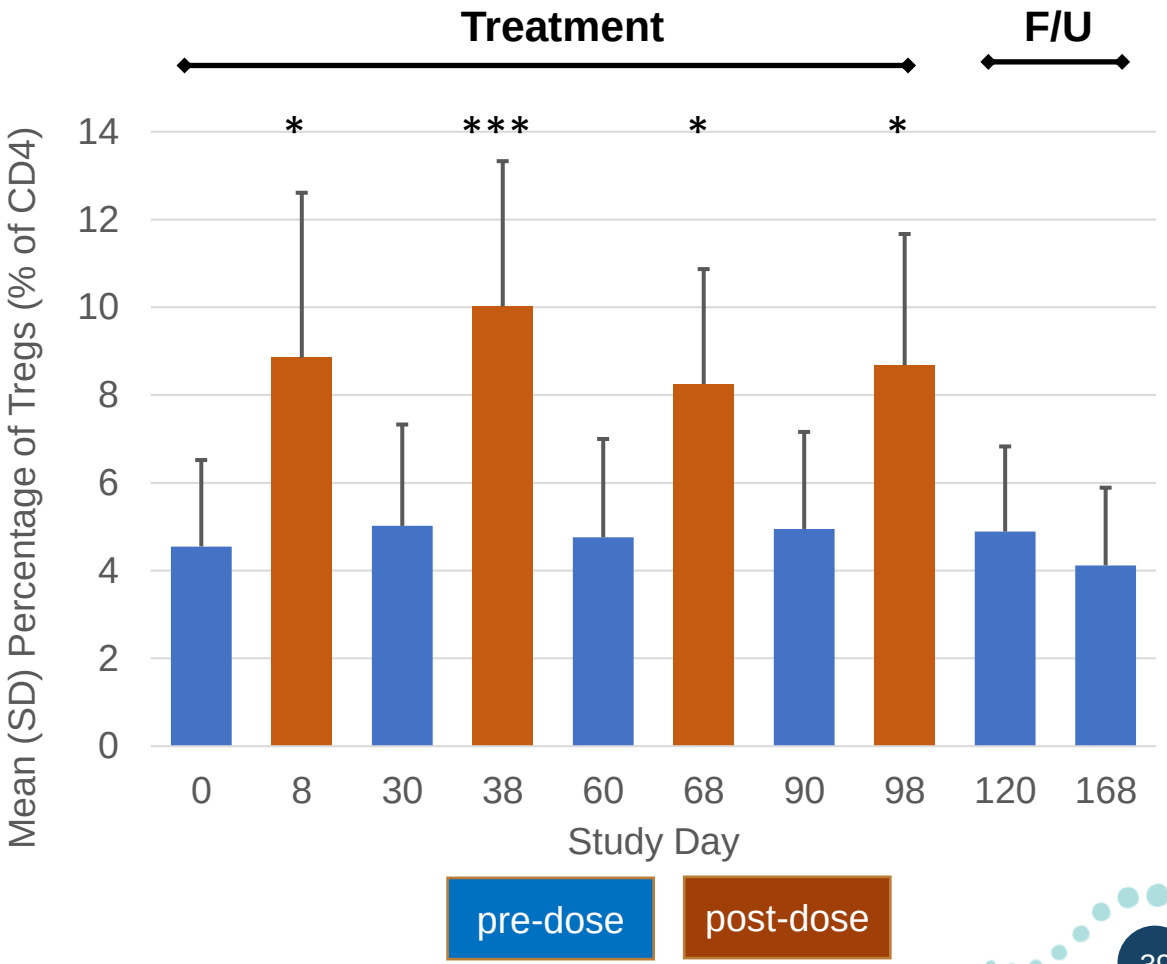
COYA 301:
Enhanced Treg Function and Numbers *in vivo* in AD Patients (N=8)

Statistically Significant Enhancement of Treg Suppressive Function



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

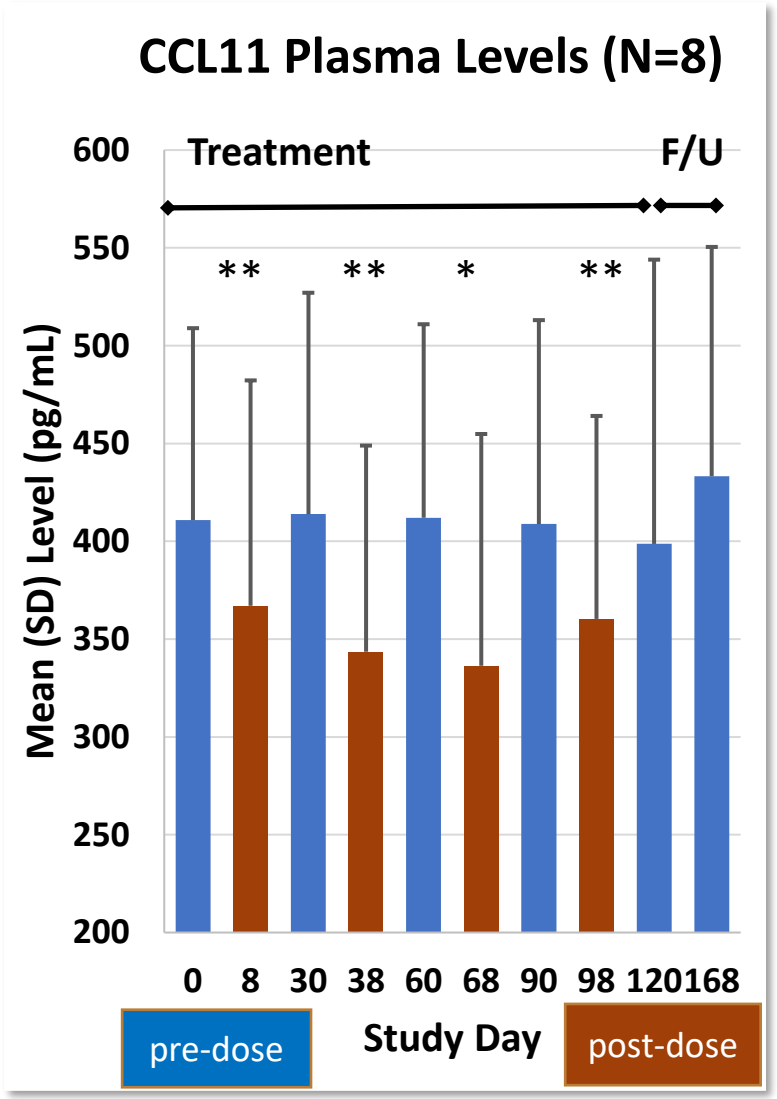
Statistically Significant Enhancement of Treg Numbers

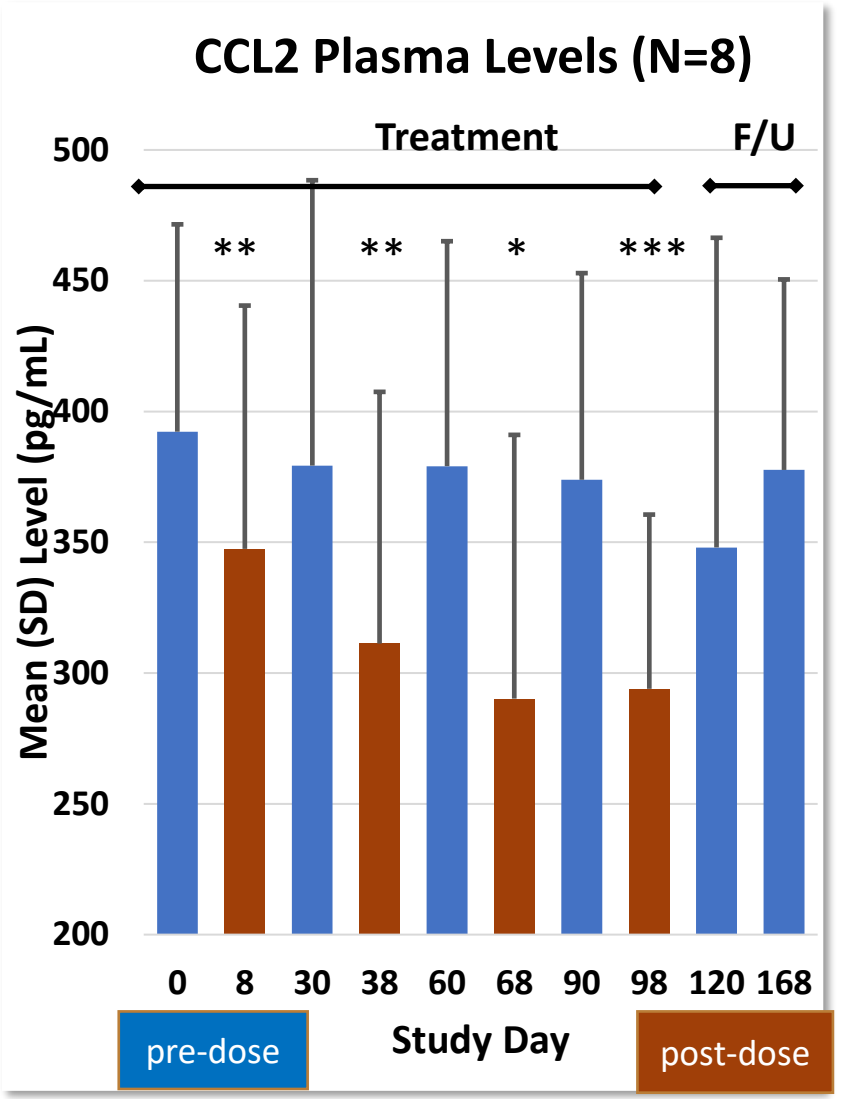


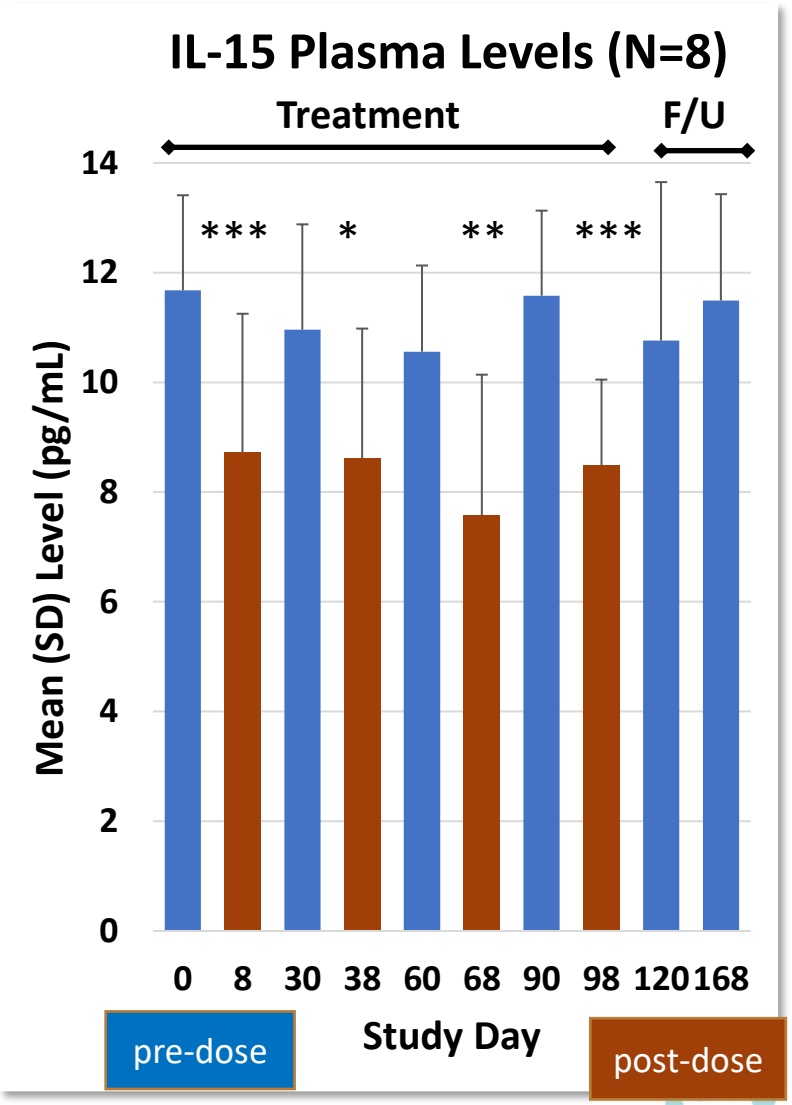
*p<0.05, ***p<0.001

Conducted using commercially available product

COYA 301: Significantly Lowered Plasma Proinflammatory Chemokines and Cytokines in AD Patients





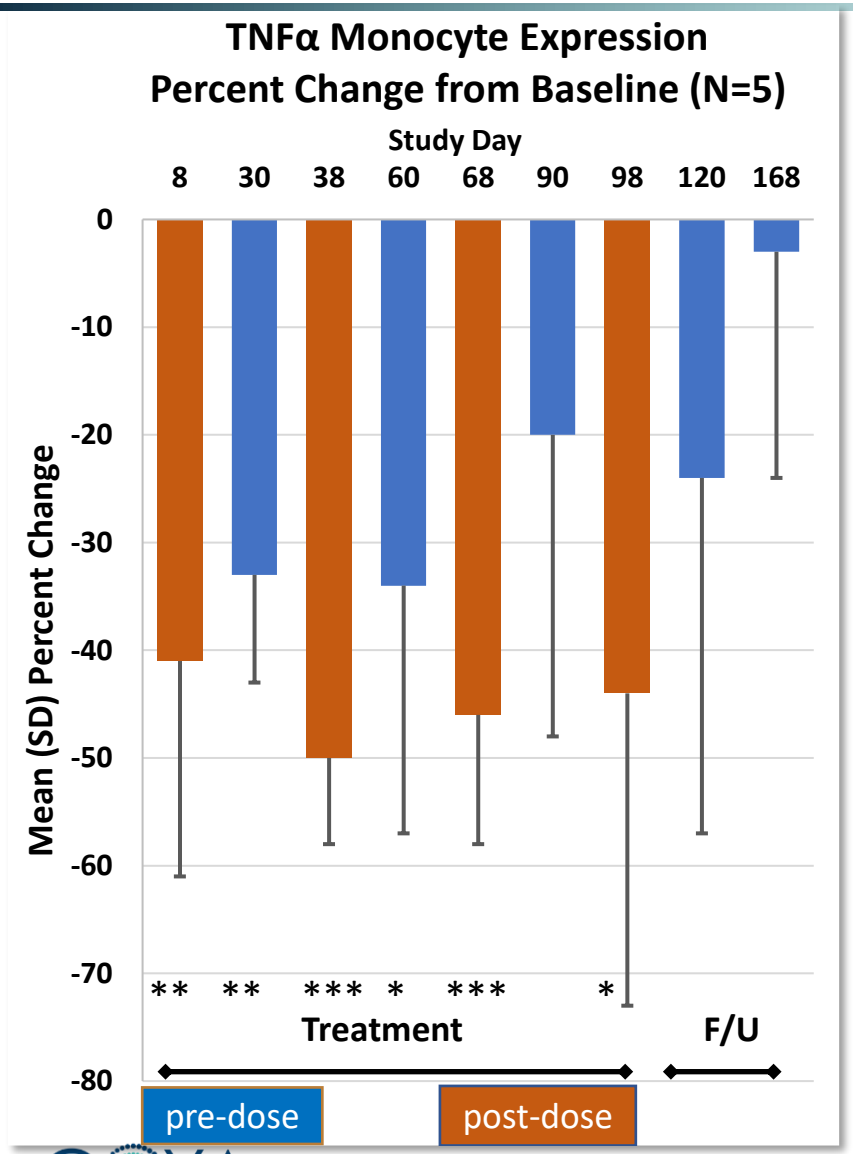


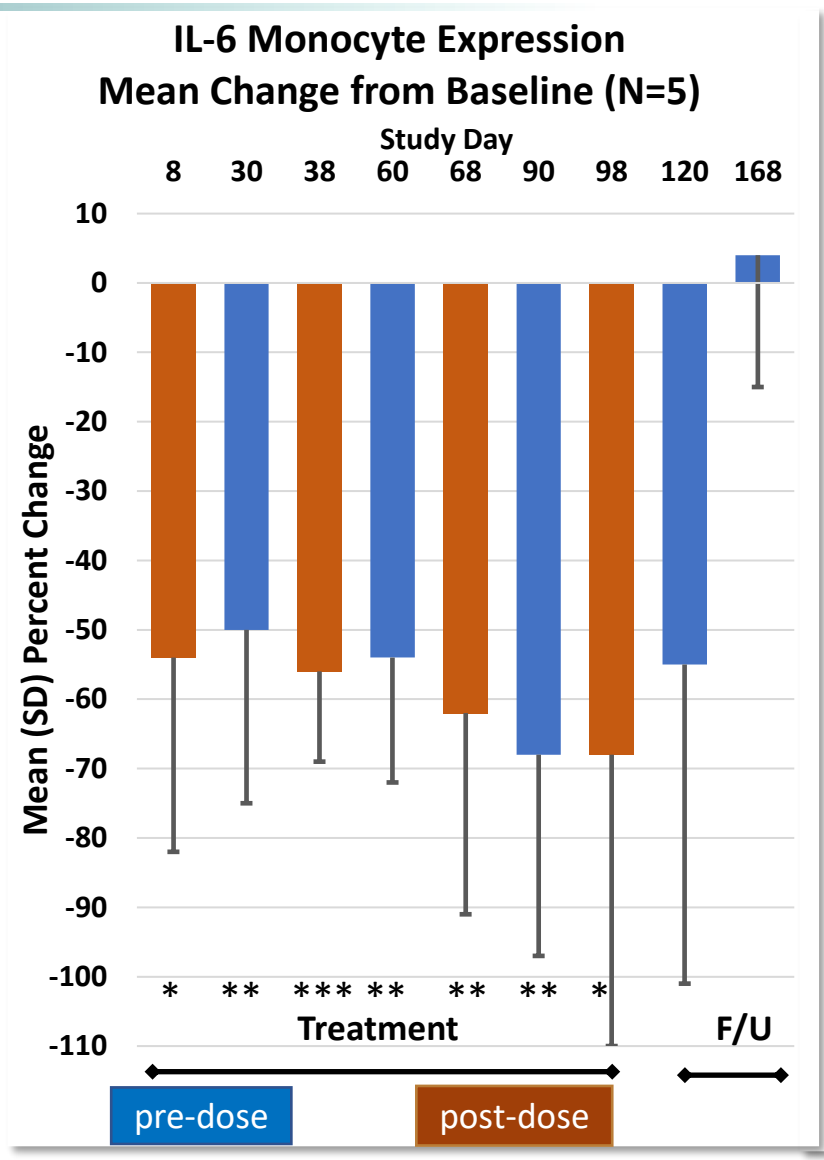
CCL11: chemokine C-C motif ligand 11 (eotaxin-1); CCL2: chemokine monocyte chemoattractant protein 1
IL-15: interleukin 15

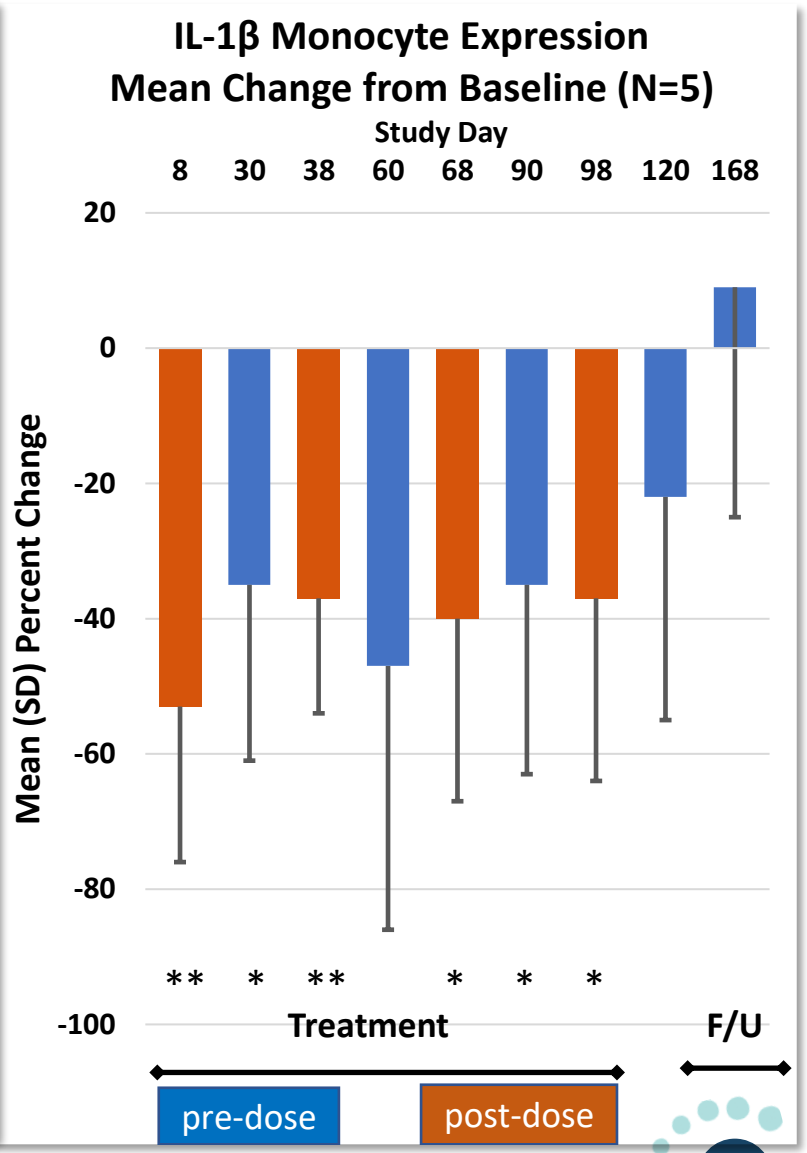
Conducted using commercially available product

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

COYA 301: Significantly Lowers Expression of Proinflammatory Cytokines in AD Patients







TNFα: tumor necrosis factor alpha; IL-6: interleukin 6; IL-1β: interleukin 1 beta
Conducted using commercially available product

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

Case Study of Brain Imaging of AD Patient Before And After LD IL-2 Treatment

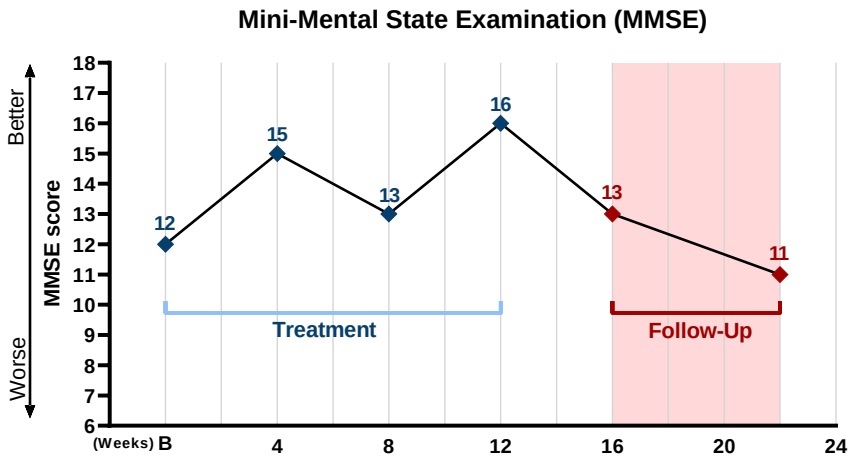
70-Year-Old Male

Baseline MMSE: 12

Positive PIB PET Scan

Positive Neurodegeneration MRI

Other Rx: Donepezil 10mg

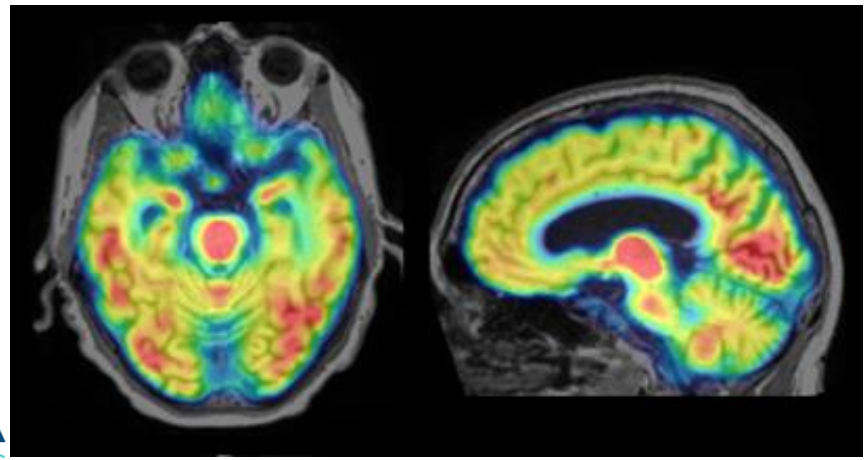


Neuroinflammation (TSPO) (^{11}C) ER-176 PET Scan at baseline and after 4-monthly cycles of low dose IL-2.

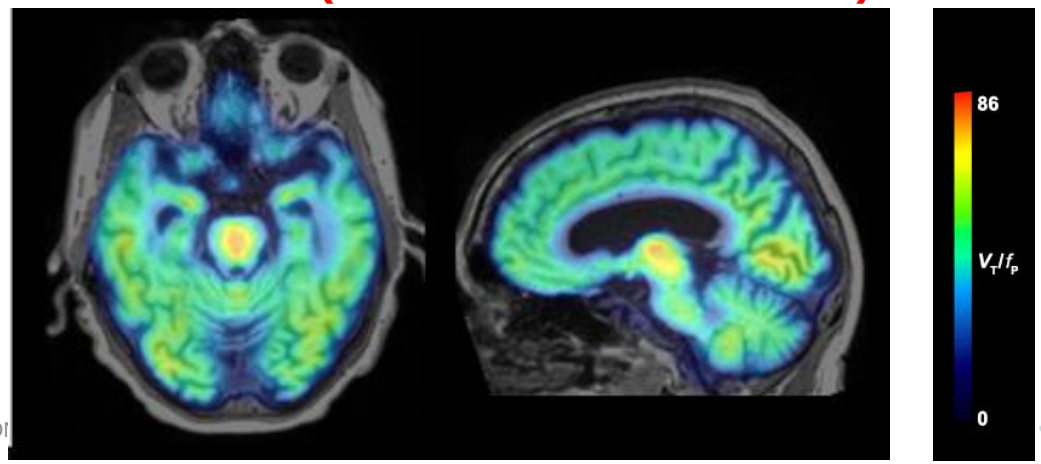
The second PET scan was done 2 weeks after last dose.

PET: Positron Emission Tomography
TSPO: translocator protein

PET Scan (Baseline)



PET Scan (2 weeks after last dose)



COYA THERAPEUTICS

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 deaths or other serious AE occurred over the course of the study



COYA THERAPEUTICS

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

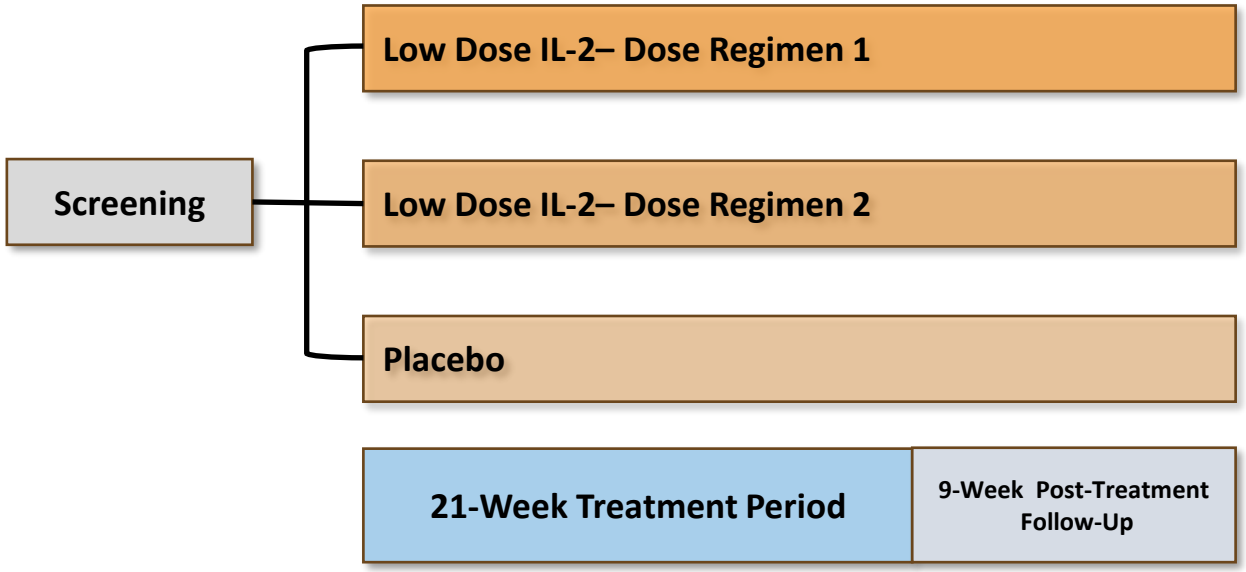
The encouraging results of the open-label, proof-of-concept study in AD (N=8) supported conducting the ongoing randomized, double-blind, controlled Phase 2 study in 38 patients with mild-to-moderate AD.

Study Objectives

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

Results to be presented at CTAD24

(October 29, 2024)



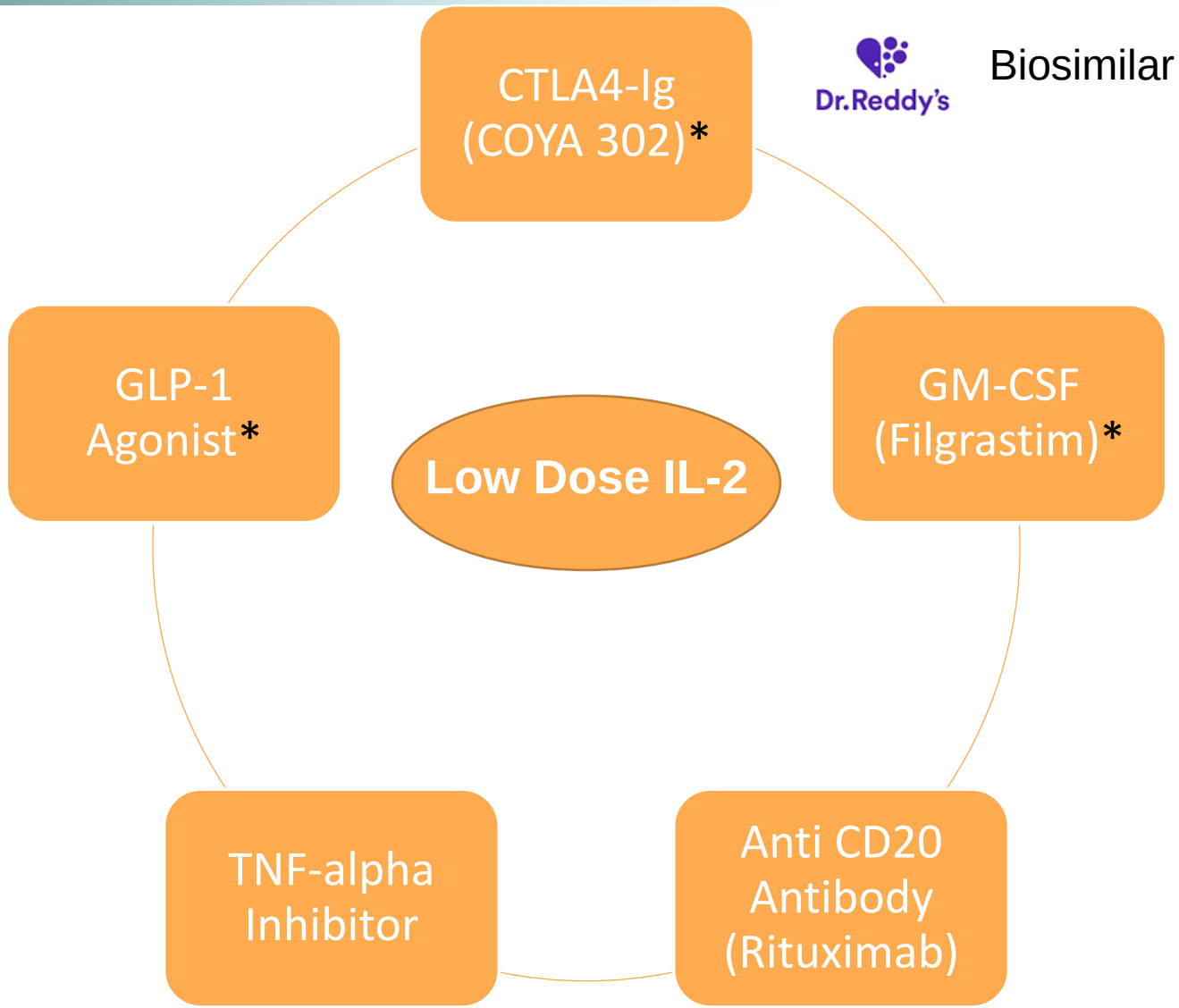
Dose Regimen 1: 1 million IU administered SC daily for 5 days, **every 4 weeks**
Dose Regimen 2: 1 million IU administered SC daily for 5 days, **every 2 weeks**

Study funded by the Gates Foundation and Alzheimer's Association

COYA THERAPEUTICS

Conducted using commercially available product

Low Dose IL-2 as a Backbone Treatment In Combination With Immunomodulatory Biologics



* Coya has IP filed on the combination

GLP-1 Receptor Agonists Combination with COYA 301

COYA Expanding Pipeline to Address Unmet Needs

- COYA 303 (COYA 301 + GLP-1 RA) may have additive/synergistic anti-inflammatory effect on multiple cell types
- Combination expands potential therapeutic areas in neurodegenerative, inflammatory, and metabolic conditions
- Proposed proprietary combination of COYA 301 and GLP-1 RA has potential to expand the GLP-1 RA market beyond current indications
- COYA IP around this combination provides value-creating opportunities



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