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Intranasal Fully Human Anti-CD3 mAb (“FORALUMAB”) Therapy to Enable Breakthroughs in Neuroinflammatory and Neurodegenerative Diseases



Nasdaq: TLSA

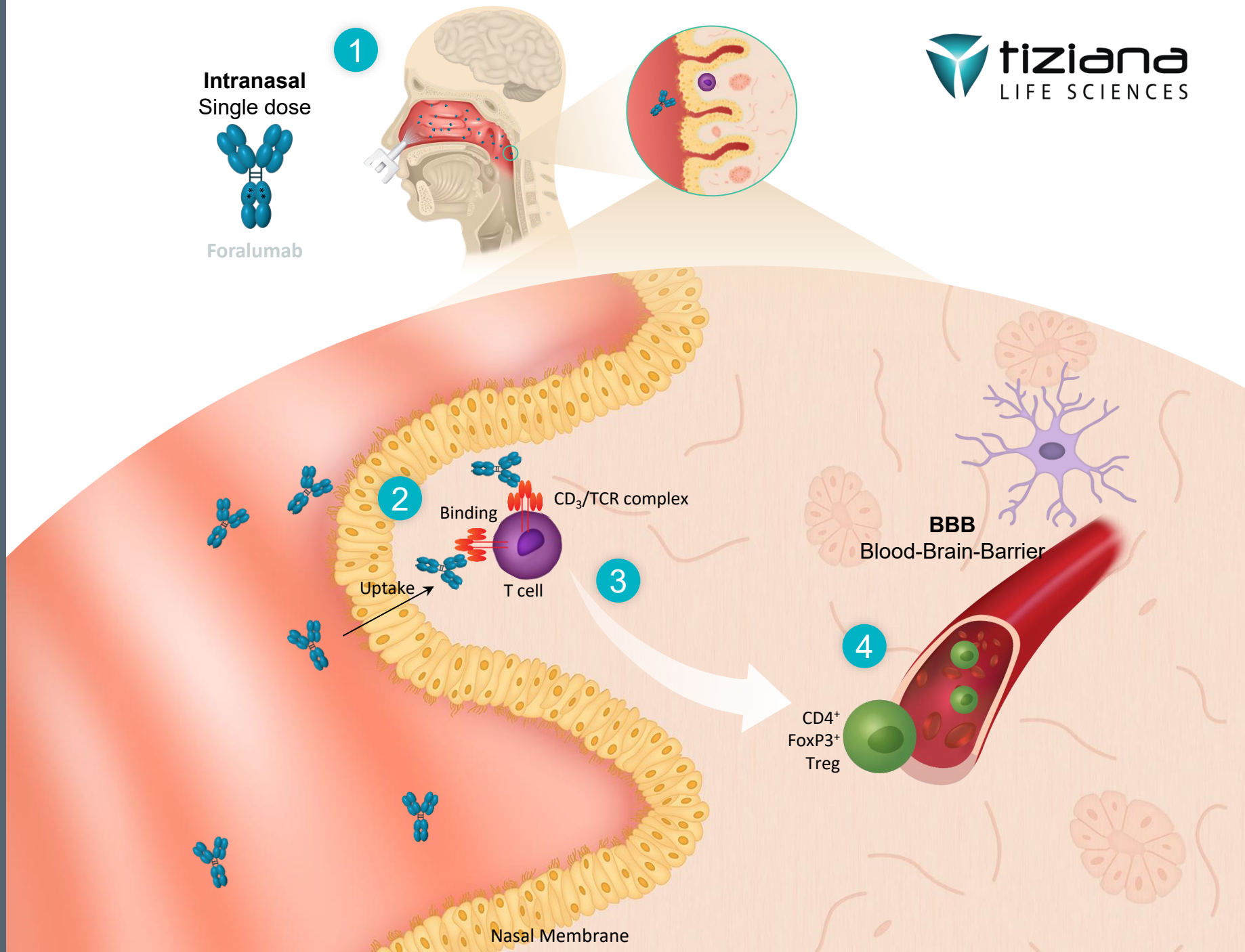
Foralumab: Mechanism of Action[1,2]

Patient inhales the antibody intranasally

Binding of foralumab to the T-cell receptor complex in cervical lymph node

Tregs are then created and activated

These created Tregs then cross the blood brain barrier and regulate the activated innate immune system (microglia).



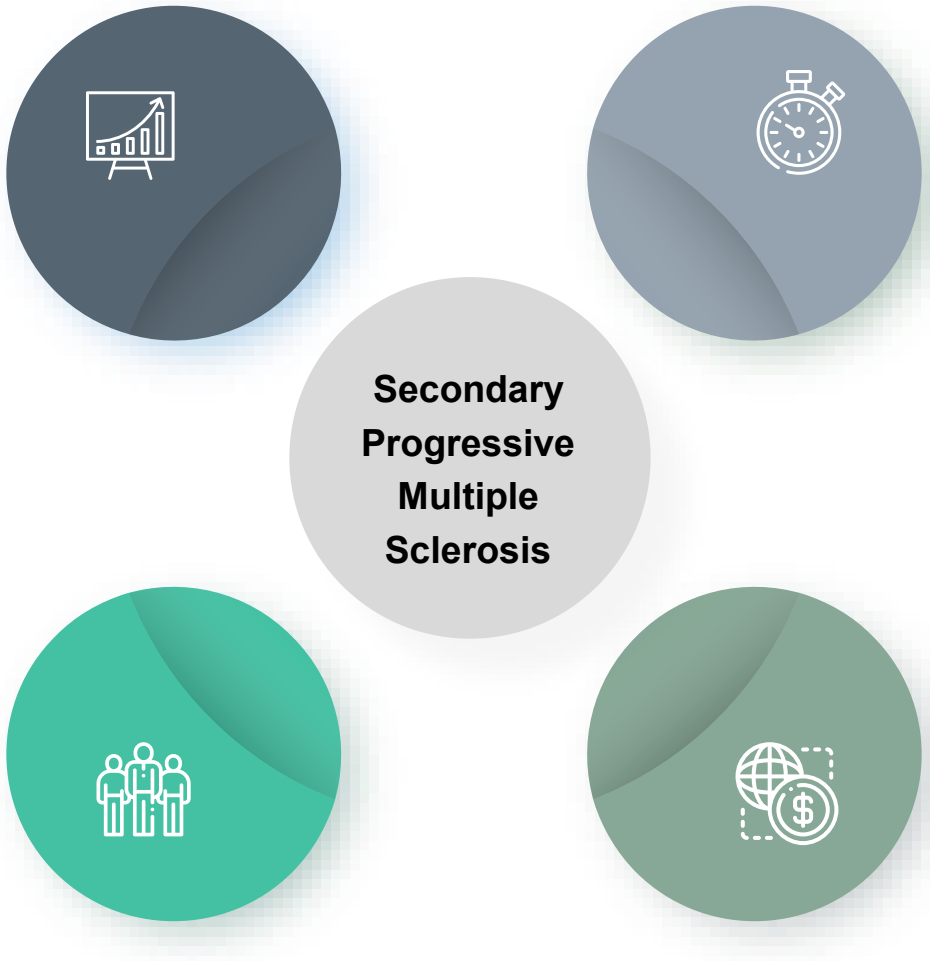
[1] https://www.pnas.org/doi/10.1073/pnas.2220272120
[2] https://www.pnas.org/doi/10.1073/pnas.2309221120

Non-active Secondary Progressive Multiple Sclerosis (na-SPMS)



Non-Active Secondary Progressive Multiple Sclerosis is an Attractive Market

Approximately 25% of Relapsing Remitting MS (RRMS) patients are estimated to progress to SPMS*



There are currently no effective treatments for Non-Active (non-relapsing) SPMS

Patients who have progression independent of relapses (PIRA) are underserved

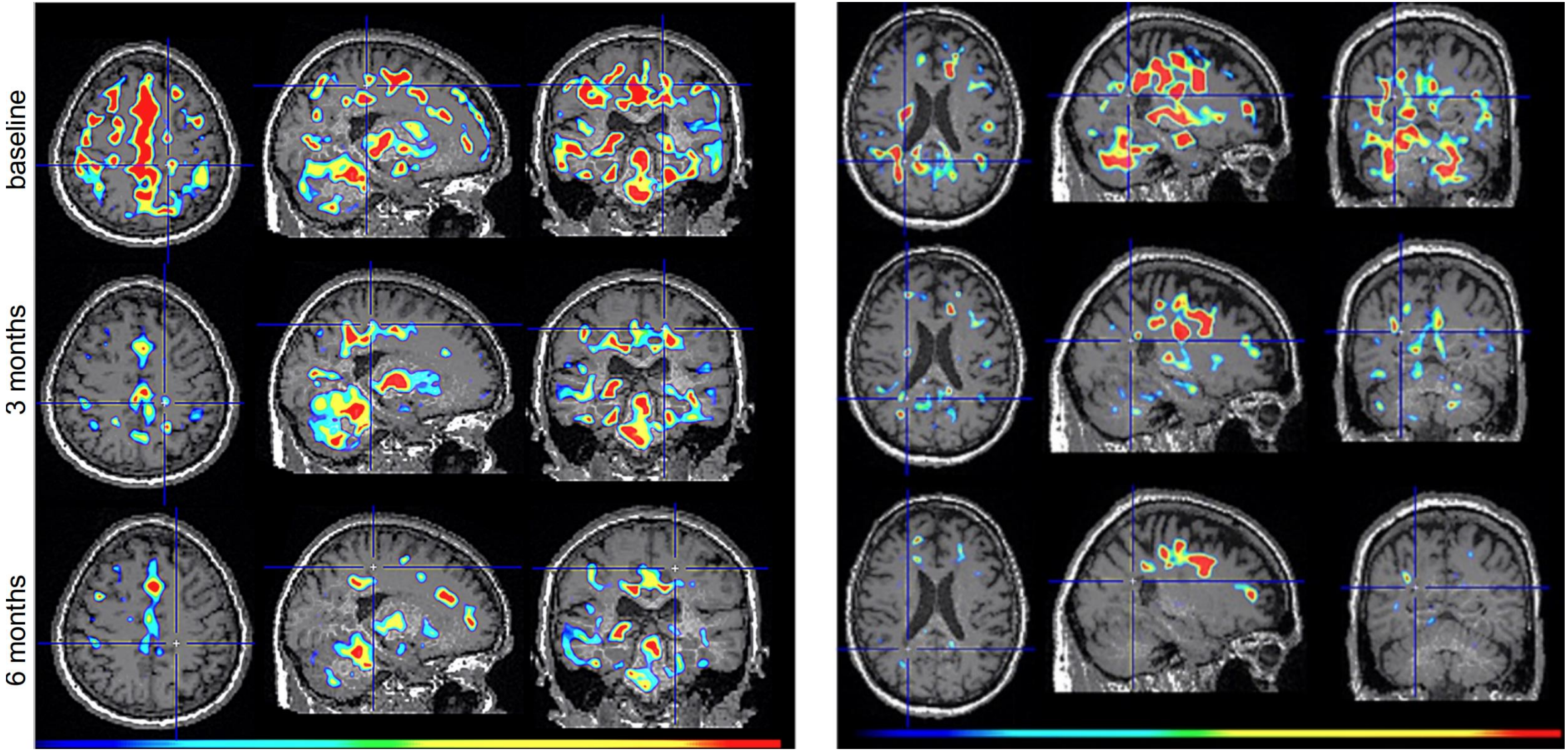
Global Multiple Sclerosis therapeutic market size $25.9 billion (2023) CAGR of 5.9% from 2024 - 2030

Global Ocrevus (Roche) sales estimated to be over $9.1 billion#

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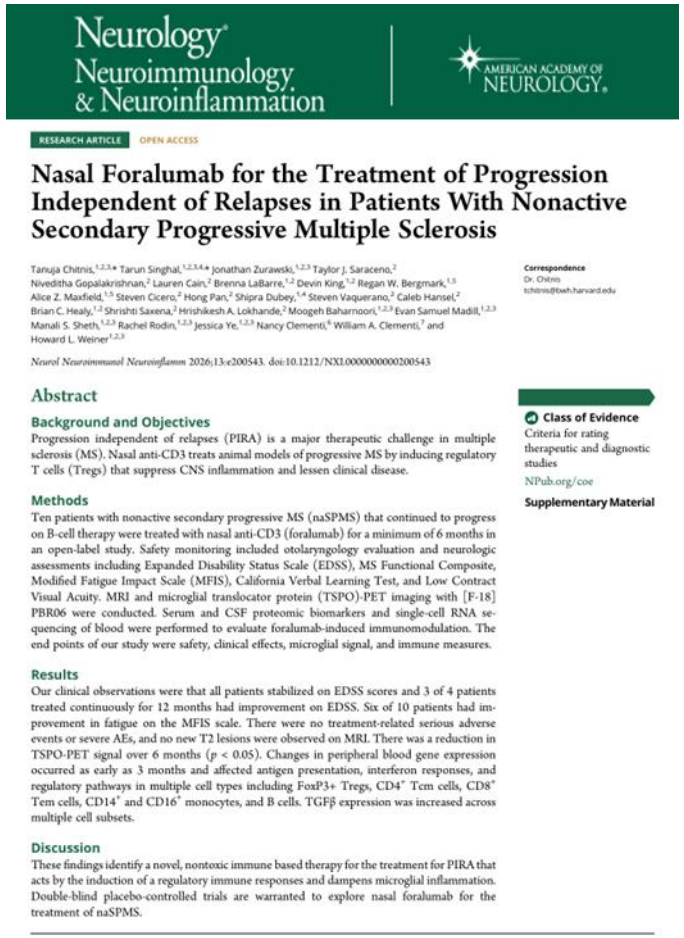
Sources: *Vasanthaprasad et al. BMC Neurology (2022) 22:301 **Tjalf Ziemssen, et. al Neurol Neuroimmunol Neuroinflamm. 2023 Jan; 10(1): e200064; #Ocrevus global sales reported by Roche as CHF 8.4 billion CHF in 2023

Intranasal Foralumab Reduces Neuroinflammation



Improvement or Stabilization in all na-SPMS Expanded Access Patients

- Clinical improvements or stabilization was reported across most of the group, as measured by Fatigue scores (MFIS) and EDSS
- Fatigue scores improved in 11/14 patients
- Clinically meaningful improvement in MFIS seen in 9/14 patients (64%)
- TSPO-PET shows significant reduction in microglia activation after 6 months of treatment ($p<0.05$)
- 75% of patients treated continuously for 12 months showed improvement in EDSS scores
- Paper Published in Neurology in 2026



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RESEARCH ARTICLE OPEN ACCESS

Nasal Foralumab for the Treatment of Progression Independent of Relapses in Patients With Nonactive Secondary Progressive Multiple Sclerosis

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Abstract

Background and Objectives

Progression independent of relapses (PIRA) is a major therapeutic challenge in multiple sclerosis (MS). Nasal anti-CD3 treats animal models of progressive MS by inducing regulatory T cells (Tregs) that suppress CNS inflammation and lessen clinical disease.

Methods

Ten patients with nonactive secondary progressive MS (naSPMS) that continued to progress on B-cell therapy were treated with nasal anti-CD3 (foralumab) for a minimum of 6 months in an open-label study. Safety monitoring included otolaryngology evaluation and neurologic assessments including Expanded Disability Status Scale (EDSS), MS Functional Composite, Modified Fatigue Impact Scale (MFIS), California Verbal Learning Test, and Low Contract Visual Acuity. MRI and microglial translocator protein (TSPO)-PET imaging with [F-18] PBR06 were conducted. Serum and CSF proteomic biomarkers and single-cell RNA sequencing of blood were performed to evaluate foralumab-induced immunomodulation. The end points of our study were safety, clinical effects, microglial signal, and immune measures.

Results

Our clinical observations were that all patients stabilized on EDSS scores and 3 of 4 patients treated continuously for 12 months had improvement on EDSS. Six of 10 patients had improvement in fatigue on the MFIS scale. There were no treatment-related serious adverse events or severe AEs, and no new T2 lesions were observed on MRI. There was a reduction in TSPO-PET signal over 6 months ($p < 0.05$). Changes in peripheral blood gene expression occurred as early as 3 months and affected antigen presentation, interferon responses, and regulatory pathways in multiple cell types including FoxP3+ Tregs, $CD4^+$ Tem cells, $CD8^+$ Tem cells, $CD14^+$ and $CD16^+$ monocytes, and B cells. TGFβ expression was increased across multiple cell subsets.

Discussion

These findings identify a novel, nontoxic immune based therapy for the treatment for PIRA that acts by the induction of a regulatory immune responses and dampens microglial inflammation. Double-blind placebo-controlled trials are warranted to explore nasal foralumab for the treatment of naSPMS.

Class of Evidence
Criteria for rating therapeutic and diagnostic studies
NPub.org/coe

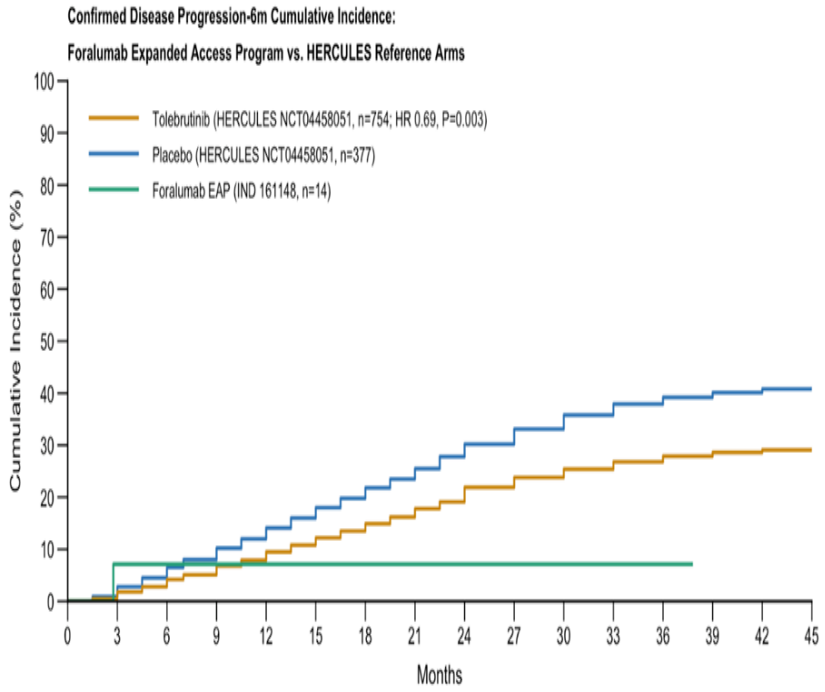
Supplementary Material

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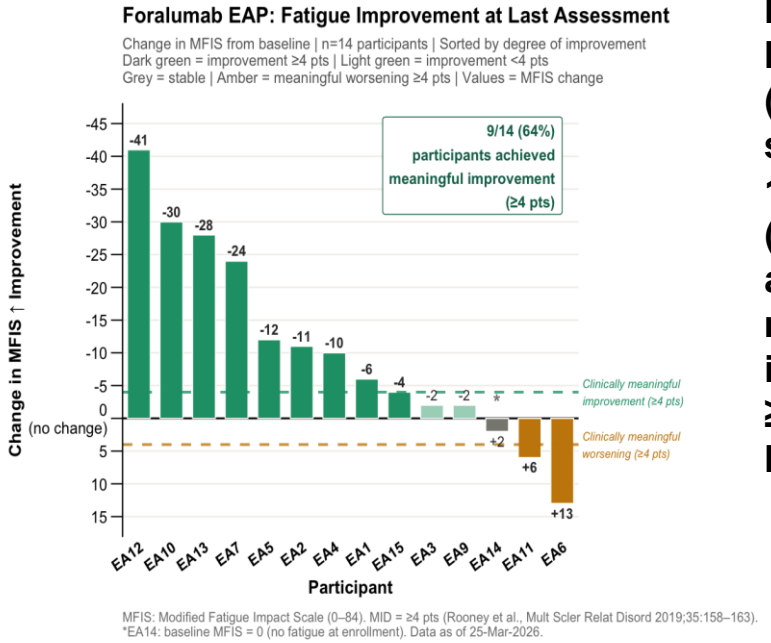
https://www.neurology.org/doi/10.1212/NXI.0000000000200543

Favourable Trends Seen in Stability of Disability and Clinically Meaningful Improvements in Fatigue.

- EDSS Stabilization: Favorable trend toward disease stabilization (i.e., reduced Confirmed Disability Progression (CDP)
- Fatigue Improvement: 64% of patients achieved a clinically meaningful improvement of ≥4 points in their MFIS score



Foralumab Expanded Access Program vs Hercules Reference Arms" compares the cumulative incidence of disability progression events in the foralumab EA cohort against the placebo and tolebrutinib arms from the Phase 3 HERCULES non-relapsing SPMS trial

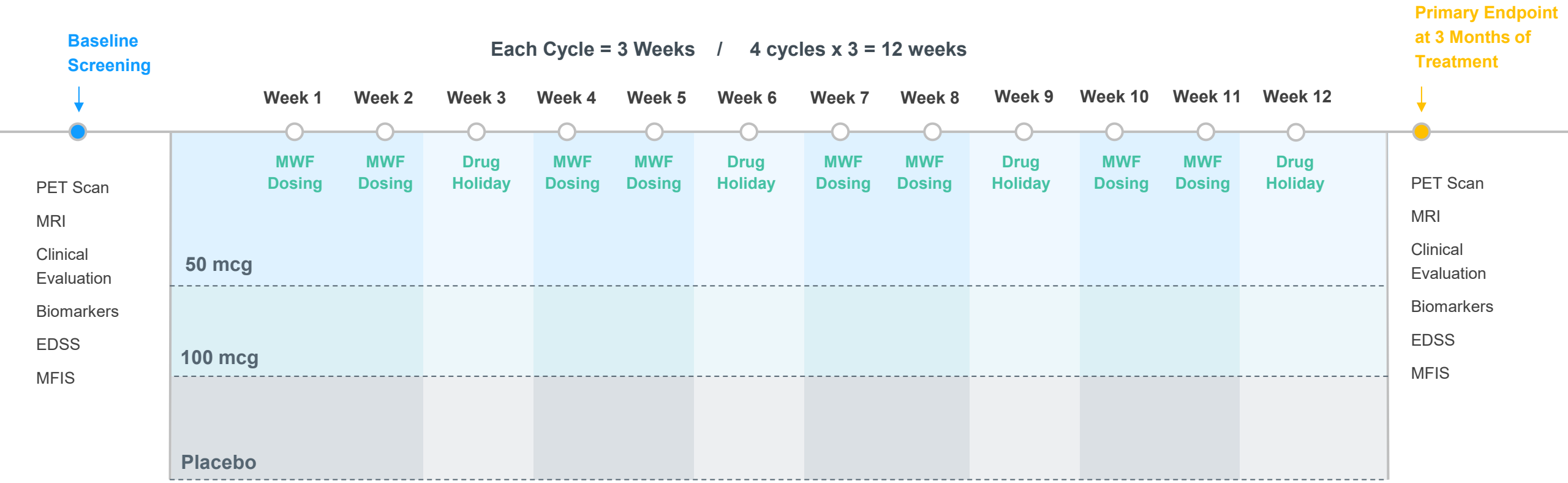


Modified Fatigue Impact Scale (MFIS) Score shows 9 out of 14 participants (64%) achieved a clinically meaningful improvement of ≥4 points on the MFIS

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Non-Active Secondary Progressive MS: Phase 2a Study Design:

Intranasal Foralumab Dosing (n=48); Double-Blind, Placebo-Controlled



Sites Enrolled:

HARVARD MEDICAL SCHOOL
BRIGHAM AND WOMEN'S HOSPITAL
Jefferson Thomas Jefferson University
Yale UNIVERSITY
UNIVERSITY OF MASSACHUSETTS AMHERST 1863
JOHNS HOPKINS UNIVERSITY
University at Buffalo
Cornell University

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Multiple System Atrophy (MSA)



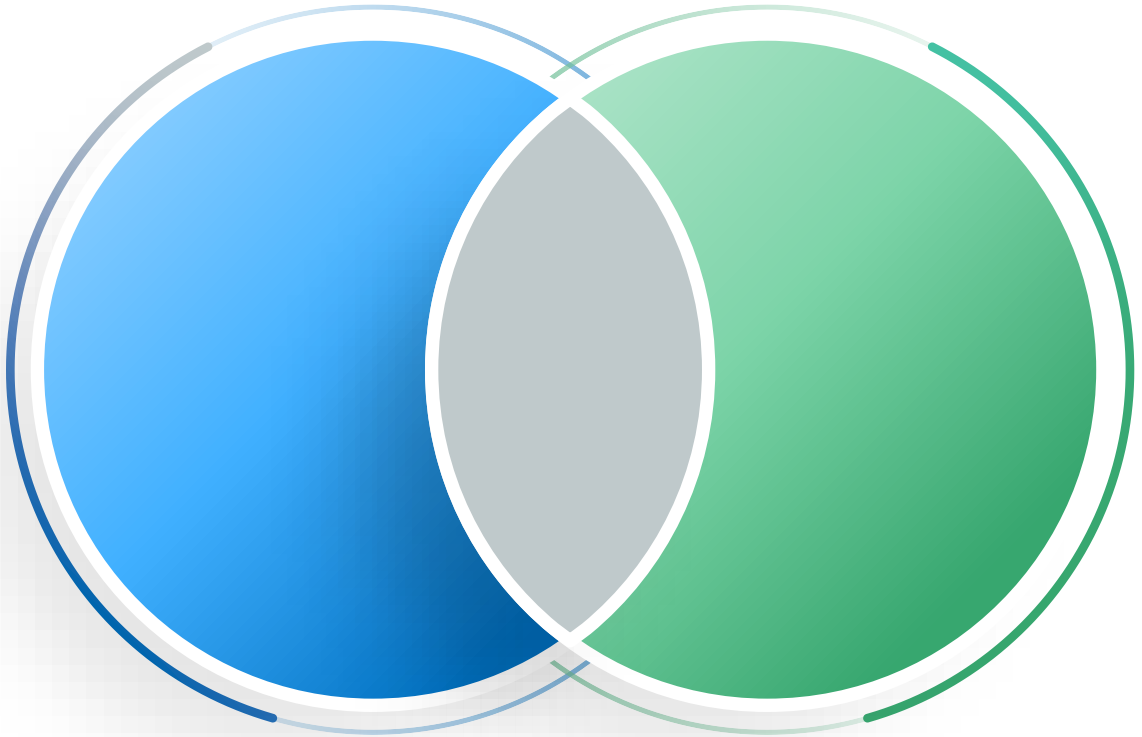
Multiple System Atrophy (MSA) Phase 2a Clinical Trial

MSA is a rapidly progressive neurological disorder. It is caused by degeneration or atrophy (shrinking) of nerve cells in several (or multiple) areas of the brain.

Classified as Orphan disease by the FDA

No FDA approved treatments available

Similar symptoms to Parkinson's disease so often misdiagnosed



FDA Approved IND Q3 2025

First patient dosed in August 2025 and will assess microglial activation and MSA clinical outcome measures

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Early Symptomatic & Moderate Alzheimer's Disease (AD)



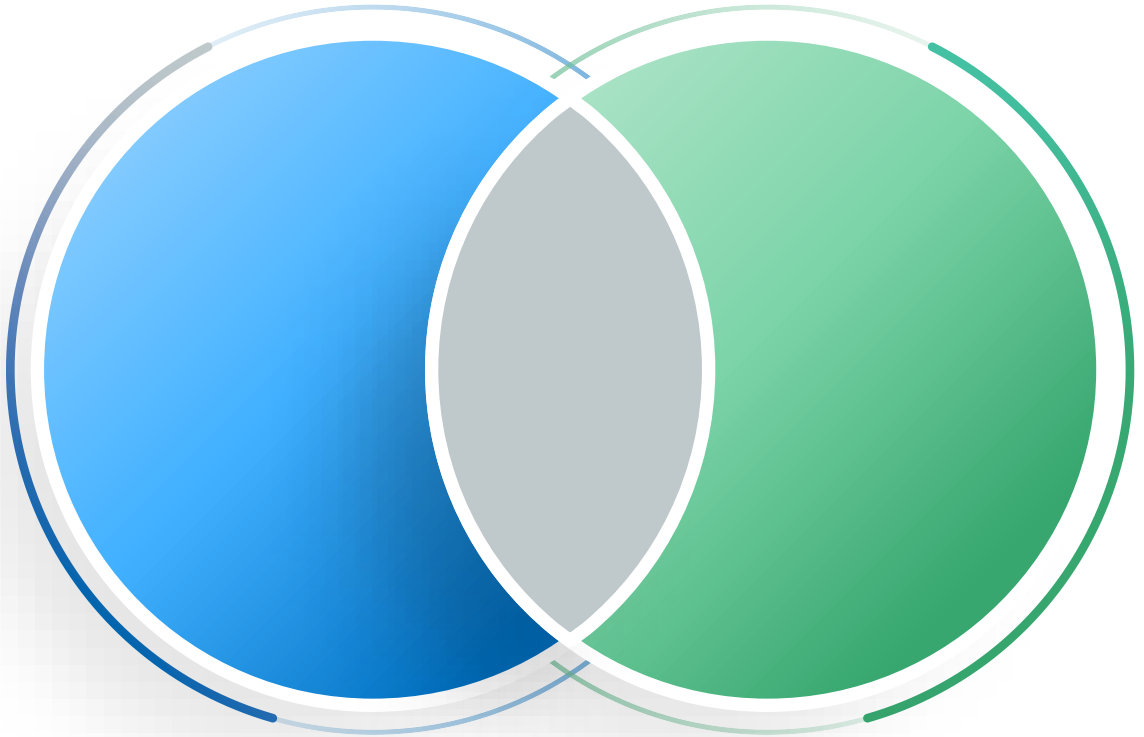
Alzheimer's Disease Program is Advancing and Equally Exciting

Awarded $4 Million Grant from National Institutes of Health (NIH), National Institute on Aging to Study Anti-CD3 in Alzheimer's Disease

NIH
National Institutes of Health

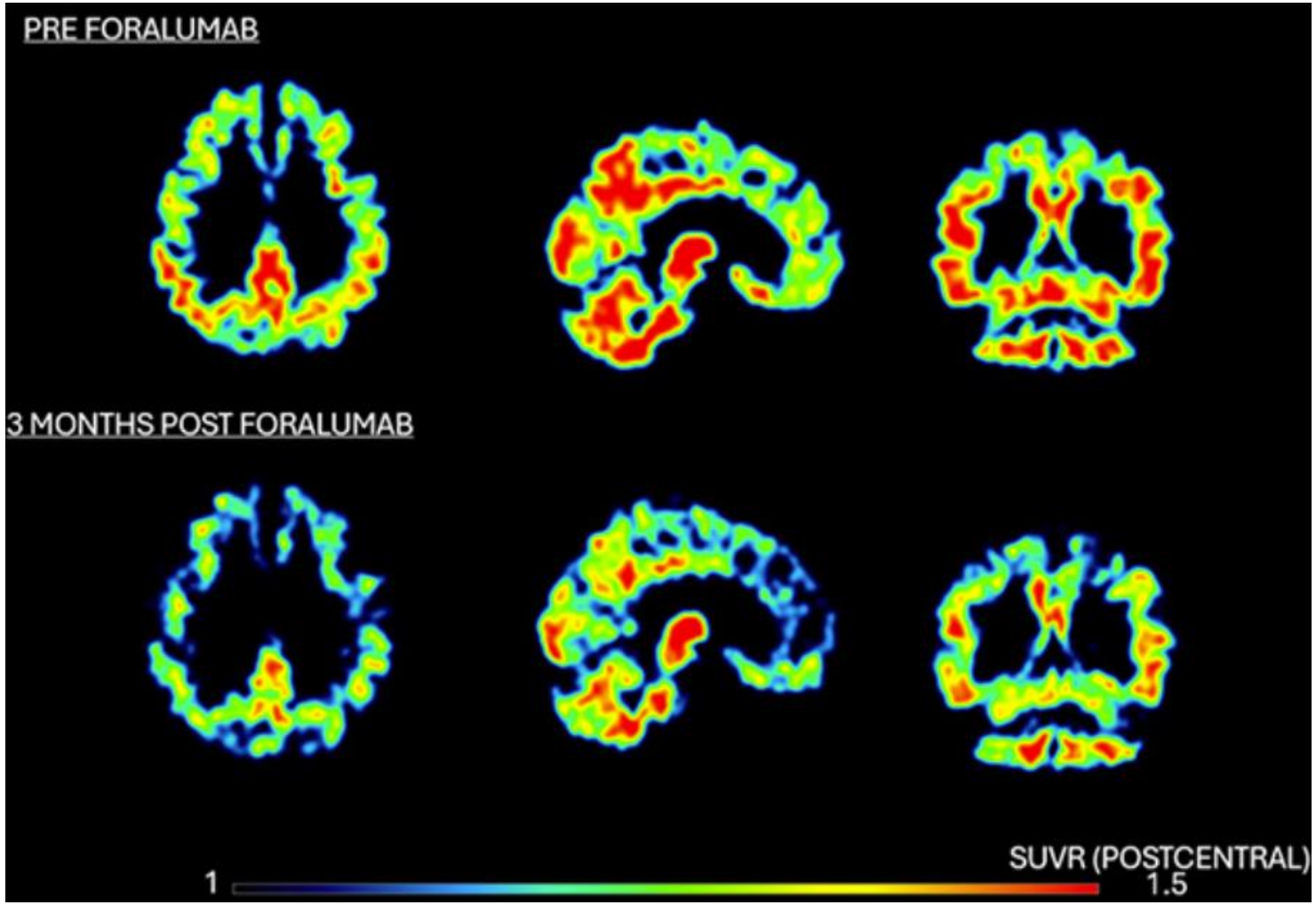
Letter to Proceed received for IND to conduct a Phase 2 study of intranasal foralumab in Alzheimer's disease patients

Phase 2 trial for Early Symptomatic Alzheimer's Disease started Dec 2025 and will assess microglial activation as part of combination therapy with recently approved drugs



Expanded Access program granted by FDA to treat Moderate Alzheimer's Disease began dosing in December 2024

Moderate Alzheimer's Disease Expanded Access Study



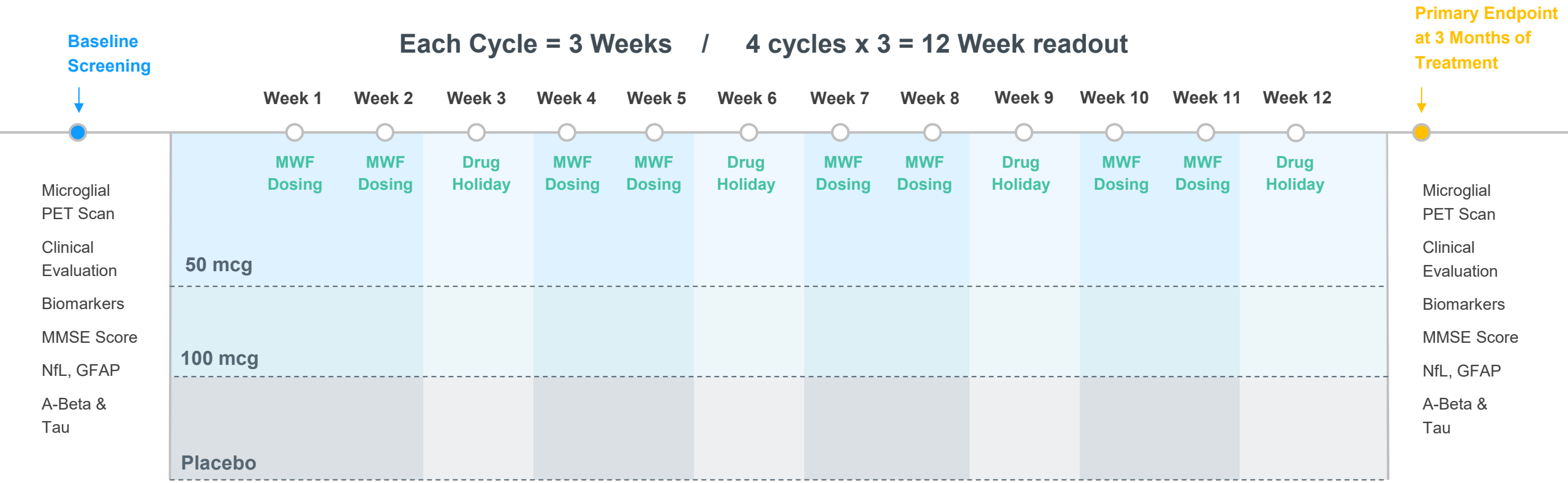
- 78-Year-Old Moderate Alzheimer's patient treated for 3 months with intranasal foralumab
- PET Scan shows significant reduction of microglia activity following 3 months of treatment

- Data presented at AD/PD in April 2025
- Data Published in the Journal of Clinical Nuclear Medicine in May 2025

https://journals.lww.com/nuclearmed/Fulltext/9900/dampening_of_microglial_activation_with_nasal.1721.aspx

Early Symptomatic Alzheimer's Disease: Phase 2a Study Design:

Intranasal Foralumab Dosing (n=32); Double-Blind, Placebo-Controlled, 2 Treatment Arms: 12 x 50mcg, 12 x 100mcg, 8 x Placebo.



Amyotrophic Lateral Sclerosis (ALS)



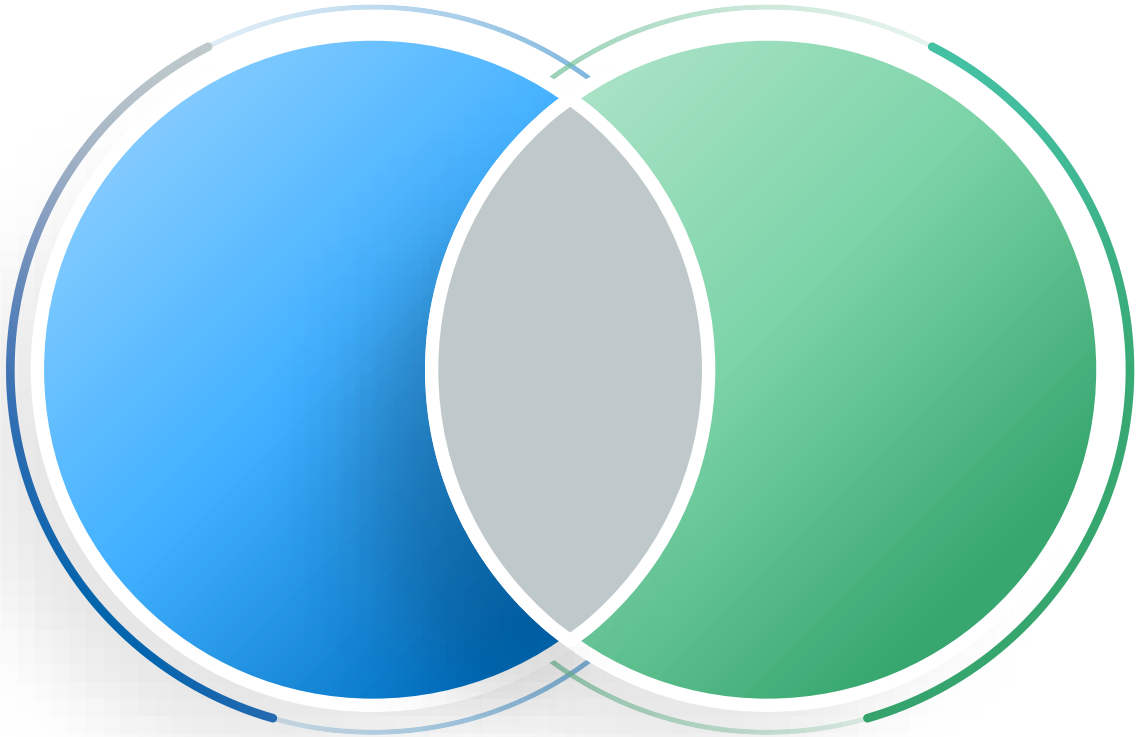
ALS Phase 2 Study Supported by The ALS Association

Grant Awarded from The ALS Association to Study Intranasal Foralumab in ALS patients in a 20 Patient, Dose Ranging, Phase 2 Clinical Trial

Global Market size of $790m

CARG of 5.8% from 2024-2030

$1.38bln by 2035

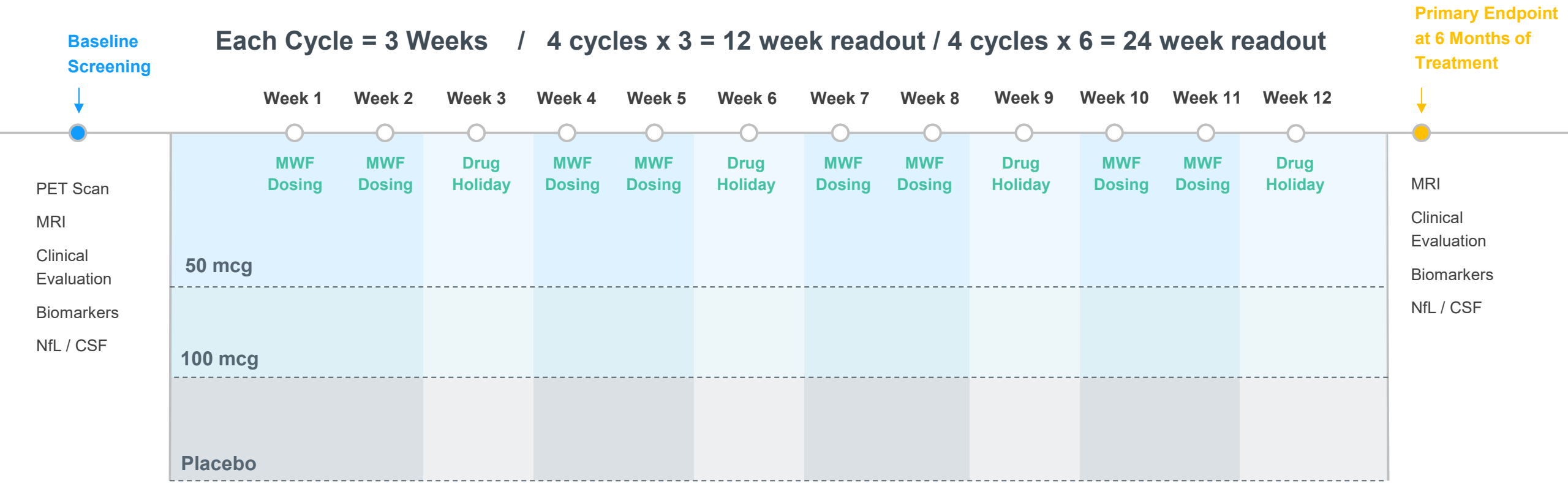


IND Filed March 2025

Phase 2 trial planned to start H1 2026 and will assess microglial activation

ALS: Phase 2a Study Design:

Intranasal Foralumab Dosing (n=24); Randomized, Placebo Controlled Trial



Intranasal Foralumab Pipeline



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