The Azeliragon Elevage Study: Study Update and Preliminary Data on Baseline Characteristics of Participants with Mild Alzheimer's Disease and Type 2 Diabetes Randomized in Part 1

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Disclosures

Ann Gooch, Leslie Humphries, Imogene Dunn, Carmen Valcarce and Aaron Burstein

- Full time employees of vTv Therapeutics LLC

Louis Kirby

- Paid consultant for vTv Therapeutics LLC

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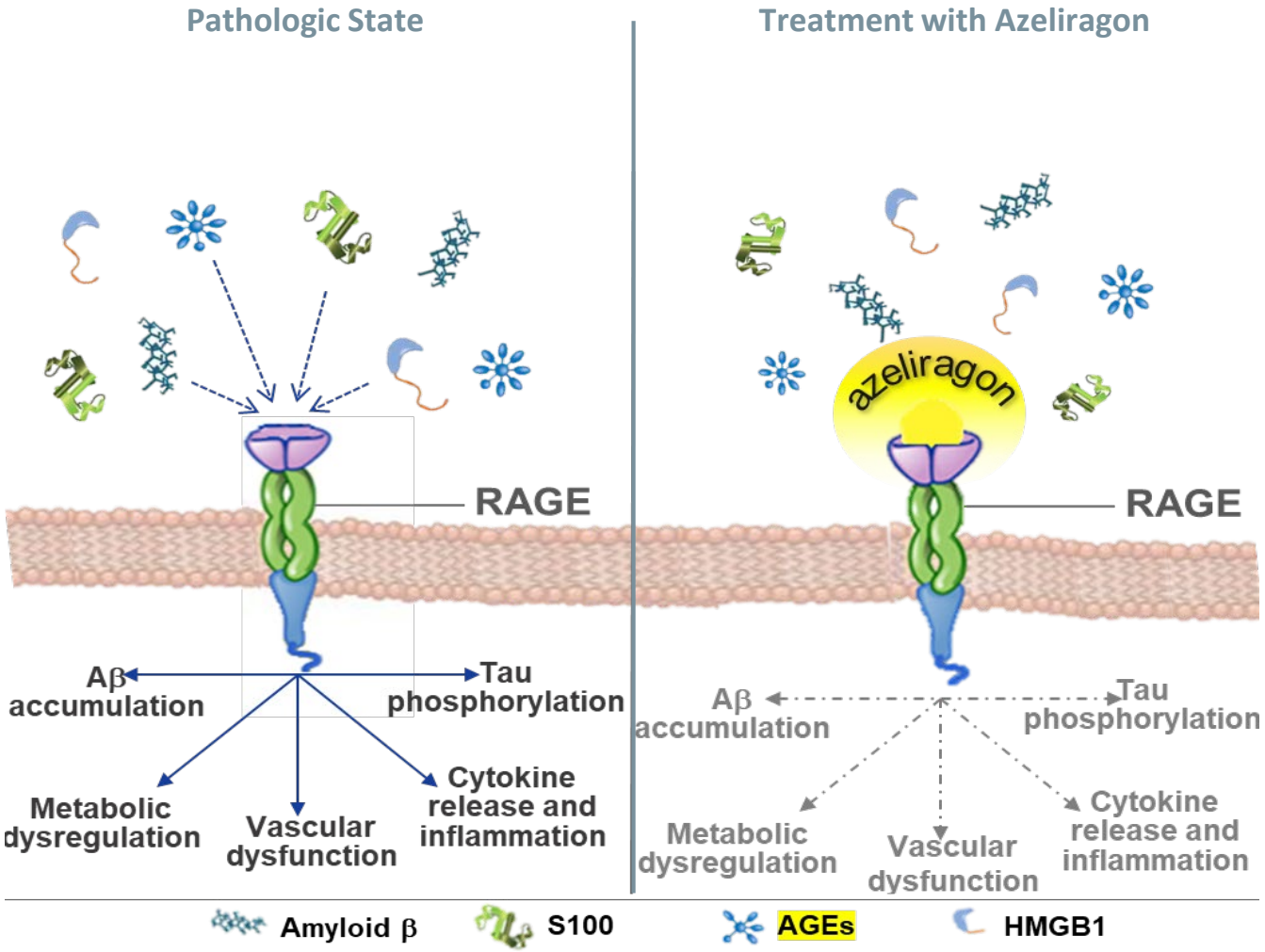
Receptor for Advanced Glycation Endproducts (RAGE) and Azeliragon

- RAGE is pattern recognition receptor with diverse ligands
- RAGE expression is usually low in the majority of healthy adult tissues
- Upregulated under pathologic conditions (e.g., AD, Diabetes)
- Azeliragon antagonizes RAGE, blocking ligands from binding to the receptor and blunting resultant downstream pathological events



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STEADFAST Study in Mild Alzheimer's Disease

- Two Phase 3 randomized, double-blind, placebo-controlled, parallel group, 18-month trials (A-Study and B-Study)
- 880 subjects with probable mild AD
  - 2011 NIA-AA criteria, Screening MMSE 21-26, CDR-global 0.5-1
- Successfully demonstrated safety and tolerability of azeliragon 5 mg/day
- Failed to demonstrate statistically significant benefit of azeliragon on co-primary endpoints of ADAS-cog and CDR-sb in mild AD

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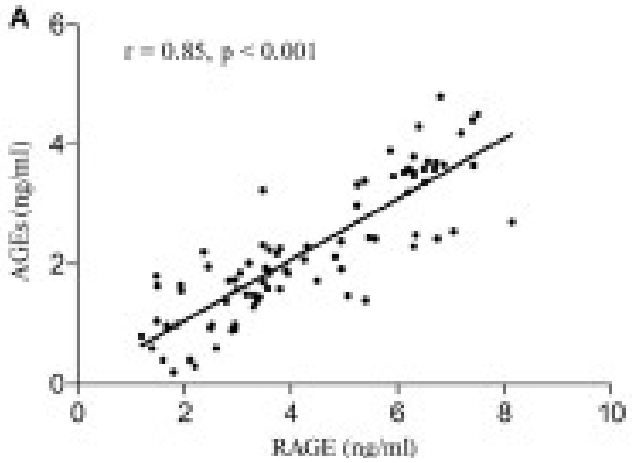
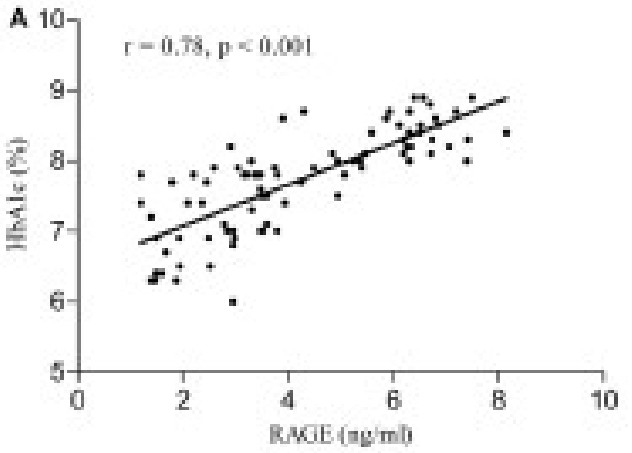
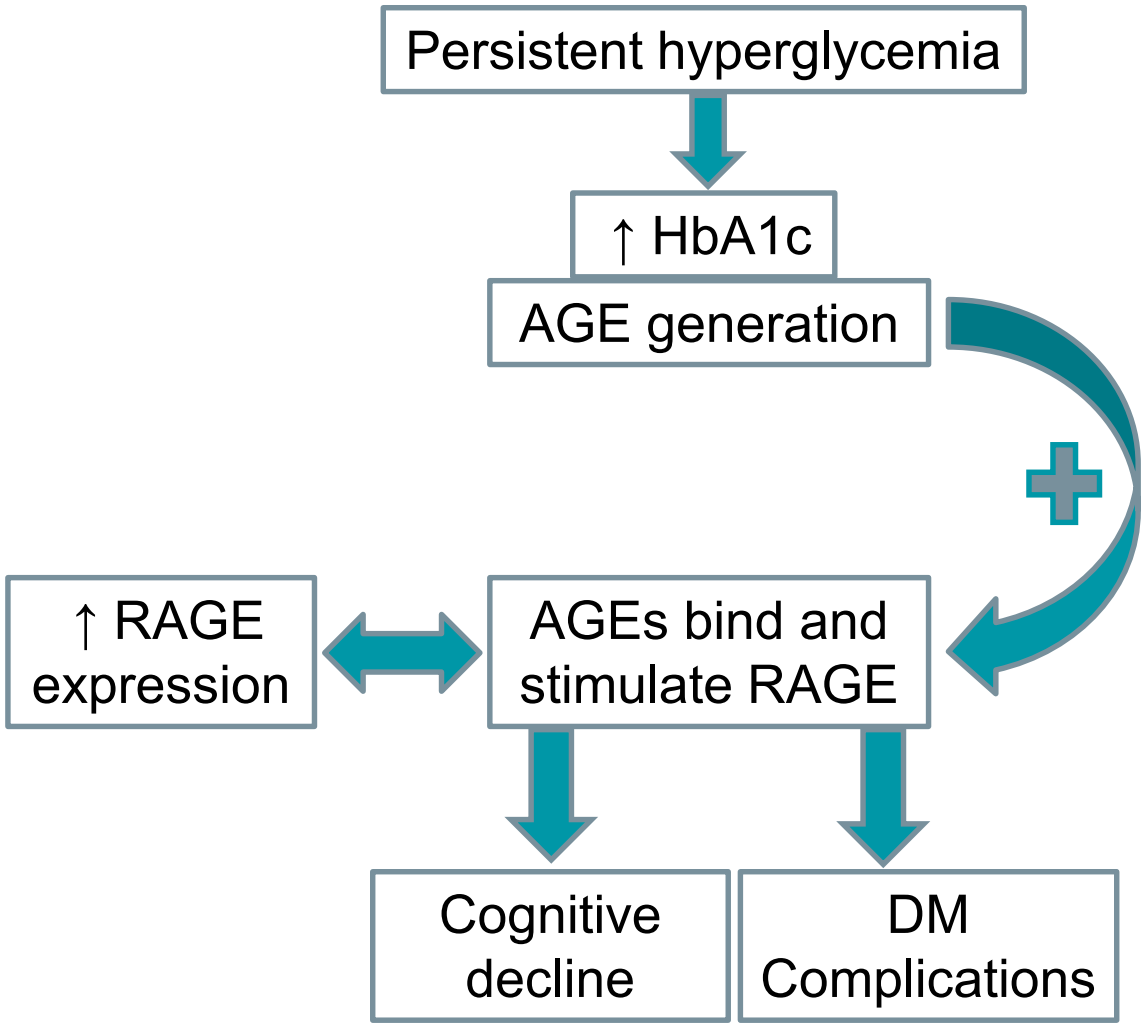
HbA1c: a surrogate for increased RAGE expression

Correlation of RAGE with AGEs in group of diabetic elderly patients with MCI



Correlation of HbA1c with RAGE in group of diabetic elderly patients with MCI





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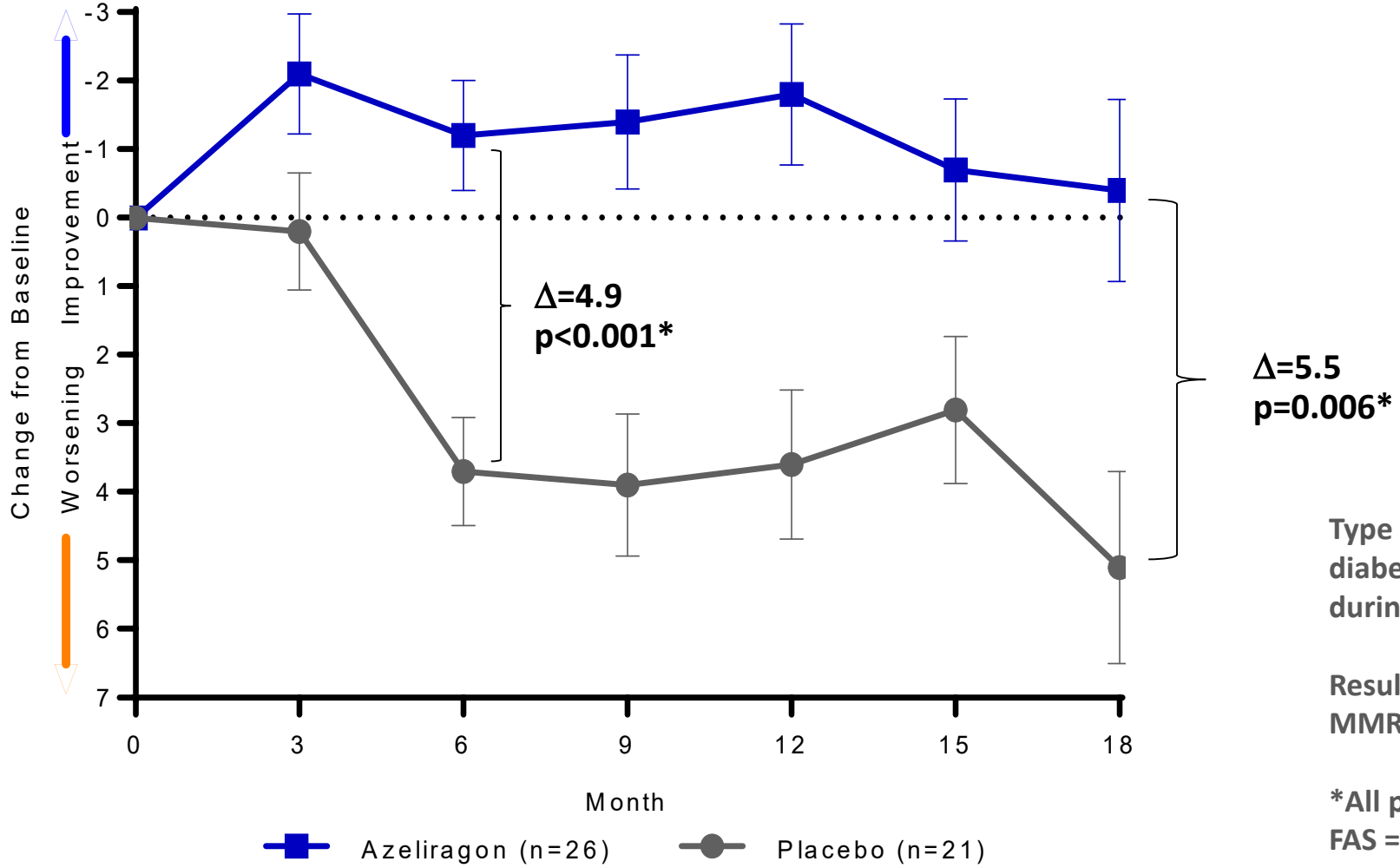
1. Gorska-Ciebiada M, Saryusz-Wolska M, Borkowska A, Ciebiada M and Loba J (2015) C-reactive protein, advanced glycation end products, and their receptor in type 2 diabetic, elderly patients with mild cognitive impairment. Front. Aging Neurosci. 7:209. doi: 10.3389/fnagi.2015.00209
2. Zheng, F., Yan, L., Yang, Z. et al. HbA1c, diabetes and cognitive decline: the English Longitudinal Study of Ageing. Diabetologia 61, 839–848 (2018). https://doi.org/10.1007/s00125-017-4541-7

Cognitive Benefit in Diabetes Subgroup of STEADFAST A - Study

ADAS-cog11



Type 2 Diabetes: Patients with diabetes (HbA1c ≥ 6.5% at any time during the study)

Results are LSMeans ± SE based on MMRM model.

*All p values are nominal.
FAS =Full Analysis Set

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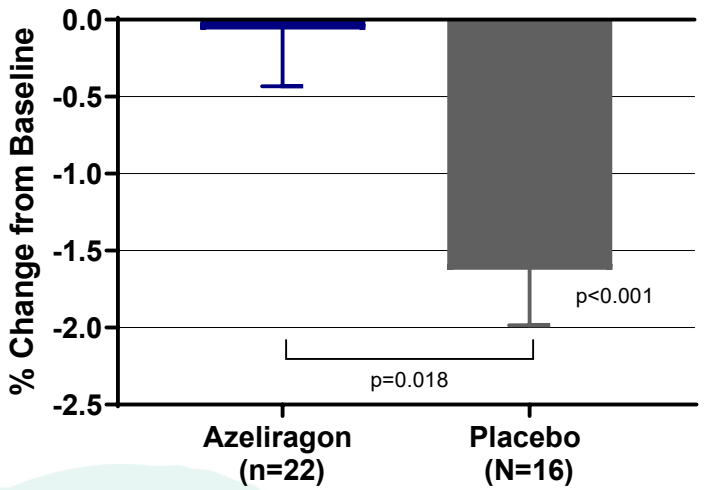
Brain MRI, FDG-PET and Plasma Inflammatory Biomarker Results Support Biological Effect in Dementia with Diabetes

Less Brain Atrophy

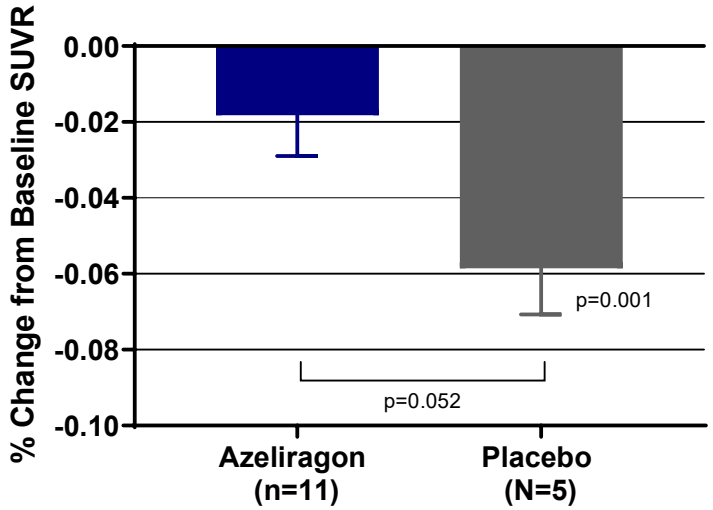
Whole Brain

Month 18



Less Reduction in Brain Glucose Utilization*

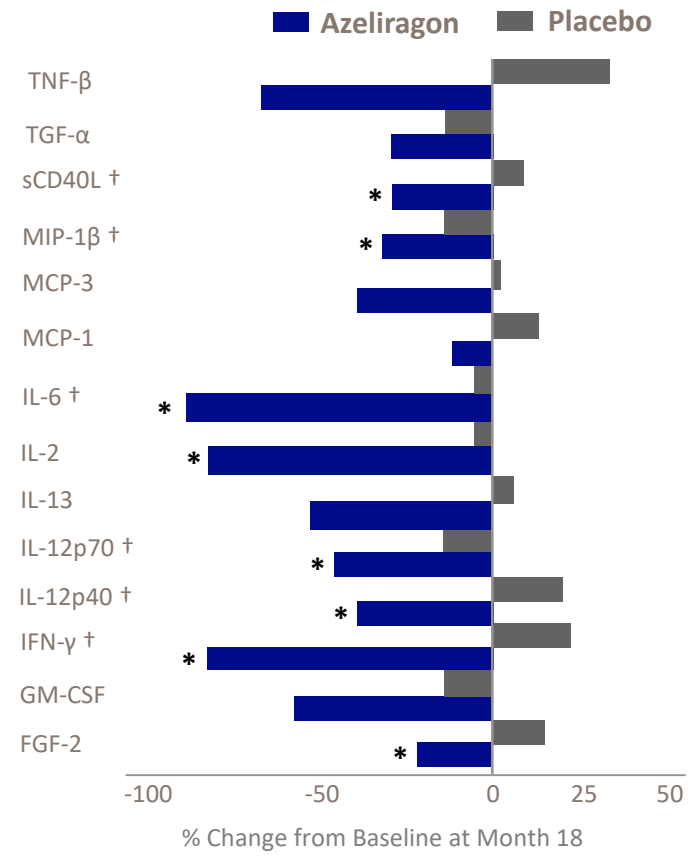
Month 18



*FDG-PET SUVR composite (unweighted combination of frontal, anterior/posterior cingulate, lateral parietal, lateral temporal, and hippocampus)

Reduction in Plasma Inflammatory Biomarkers

Month 18



Results are Medians

* Nominal p<0.05 Wilcoxon test

† Biomarkers with direct relationship to RAGE

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Elevage Study Objectives

- Strategic Objective
  - Replicate STEADFAST post-hoc subgroup analysis in Phase 2 POC study before embarking on expanded Phase 3 study
  - Part 1 results used to potentially adapt Part 2

- Part 1 Study Objectives
  - Primary - Evaluate effect of 6 months of treatment with oral azeliragon on cognitive performance in subjects with mild AD and impaired glucose tolerance
  - Secondary
    - Evaluate efficacy of azeliragon treatment on measures of function and activities of daily living
    - Evaluate the efficacy of azeliragon treatment on complications of diabetes
    - Evaluate the safety and tolerability of 6 months of azeliragon treatment
    - Evaluate effect of azeliragon on biomarkers and markers of inflammation

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Elevage Study

Studies	Part 1 – Proof of concept	Part 2 – Phase 3 confirmatory
Design	6-month, randomized, double-blind, placebo-controlled Phase 2 study	18-month, randomized, double-blind, placebo-controlled Phase 2 study
Sample Size **Geography**	100 (Planned); 43 (Actual) United States and Canada	200 TBD
Population	Mild Alzheimer's disease • Clinical dx of probable AD (2011 NIA-AA criteria) • MMSE 21-26, CDR global 0.5 or 1, ADAScog14 ≥ 10 Impaired glucose tolerance • HbA1c 6.5-9.5%	
Dose Regimen	• Azeliragon 5 mg or placebo once daily; randomized 1:1	
Primary Endpoint	• Change from Baseline in ADAScog14 at Month 6	• Change from Baseline in ADAScog14 at Month 18 • Change from Baseline in CDR-sb at Month 18
Secondary Endpoints	• CDR-sb, FAQ, Amsterdam-IADL, eGFR	• FAQ, Amsterdam-IADL, MMSE, eGFR, whole brain volume

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Demographics

Statistic	STEADFAST T2D Subgroup N=47	Elevage-Part 1 N=43
Country, n (%)		
Canada	4 (8.5)	11 (25.6)
USA	43 (91.5)	32 (74.4)
Ethnicity, n (%)		
Hispanic or Latino	10 (21.3)	2 (4.7)
Not Hispanic or Latino	37 (78.7)	41 (95.3)
Race, n (%)		
White	42 (89.4)	41 (95.3)
Black or African American	3 (6.4)	2 (4.7)
Asian	1 (2.1)	0
American Indian or Alaska Native	1 (2.1)	0
Sex, n (%)		
Female	9 (19.1)	20 (46.5)
Male	38 (80.9)	23 (53.3)
Age: Mean (SD)	76.8 (7.44)	76.7 (6.1)

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Baseline Characteristics - Body Measurements

Statistic	STEADFAST T2D Subgroup N=47	Elevage-Part 1 N=43
Height (cm), Mean (SD)	171.4 (9.29)	167.8 (10.0)
Weight (kg), Mean (SD)	82.9 (14.16)	81.6 (14.6)
BMI (kg/m2), Mean (SD)	28.2 (3.73)	28.9 (4.4)

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Baseline Characteristics – AD & T2D

Statistic	STEADFAST T2D Subgroup N=47	Elevage-Part 1 N=43
ApoE status, n (%)		
Heterozygous	21 (44.7)	20 (46.5)
Homozygous	2 (4.3)	2 (4.7)
Non-carrier	24 (51.1)	21 (48.8)
Education, n (%)		
High School	13 (27.7)	14 (32.6)
Other (trainings, certifications)	6 (12.8)	3 (7.0)
Some college	10 (21.3)	7 (16.3)
Associate's Degree	3 (6.4)	3 (7.0)
Bachelor's Degree	11 (23.4)	11 (25.6)
Master's Degree	3 (6.4)	5 (11.6)
Doctoral Degree	1 (2.1)	0
Background AD Medication, n (%)		
Memantine	16 (34.0)	16 (37.2)
Acetylcholinesterase inhibitor	45 (95.7)	37 (86.0)
Both	14 (29.8)	10 (23.3)
HbA1c at Baseline, Mean (SD)	6.6 (0.64)	7.2 (0.67)

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Baseline Characteristics - Scales

Statistic	STEADFAST T2D Subgroup N=47	Elevage-Part 1 N=43
MMSE, Mean (SD)	23.7 (2.62)	23.4 (2.55)
ADAScog11, Mean (SD)	15.5 (5.13)	17.4 (6.16)
CDR Global, n (%)		
0.5	27 (57.4)	23 (53.5)
1	20 (42.6)	20 (46.5)
CDR Sum of Boxes	4.1 (1.77)	4.5 (1.84)

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Conclusions

- Elevage Part 1 has closed enrollment
- Preliminary results suggest that the Elevage study population has baseline characteristics similar to the diabetes subgroup from the STEADFAST Study and reflect the main eligibility criteria shared across both studies.
- Elevage Part 1 study results targeted for 2Q 2021.

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We sincerely appreciate all the patients, families, investigators and staff for their participation in the Elevage study.

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