Preliminary Safety and Efficacy Results from the Phase 2 PIONEER Trial of T3D-959 in Mild to Moderate Alzheimer's Patients

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Disclosures

- John Didsbury is a shareholder in T3D Therapeutics, Inc.

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Introduction

- T3D Approach - Treating Alzheimer's (AD) as a brain-specific form of diabetes (Type 3 Diabetes") where aberrant metabolism is causing brain "starvation" leading to loss of brain functions.

- New drug candidate T3D-959 – Acting to:
  1. Correct dysfunctional glucose energy metabolism
  2. Correct dysfunctional lipid metabolism inherent in AD brains. Addressing the 3rd pathological hallmark of AD; "Adipose Inclusions" described by Alois Alzheimer in 1906.
  3. Target multiple abnormalities instead of just one (e.g. plaques or tangles)

- PIONEER Phase 2 trial is a double-blind, placebo-controlled study with cognitive, functional, and biomarker endpoints

- PIONEER is aimed at validating earlier, positive pre-clinical and exploratory clinical studies to demonstrate safety and efficacy in treating mild to moderate AD patients.

Conclusions

At this juncture where PIONEER is 92% enrolled with topline results projected for 2Q2023:

- T3D-959 appears to be safe and well tolerated through 32,000+ treatment days.
- Evidence of a possible treatment effect with improvement of cognition as assessed by ADAS-cog11, even with placebo data included with the 3 drug treatment groups average.
- Evidence of a possible treatment effect with reduced decline of function as assessed by ADCS-CGIC, even with placebo data included with the 3 drug treatment groups average.
- Evidence of a possible treatment effect with improvement of executive function as assessed by DSCT, even with placebo data included with the 3 drug treatment groups average.

PIONEER Safety Update – 237 Randomized Subjects (as of 24 June 2022):

Number (%) of subjects with adverse events

	All adverse events	Related or possibly related adverse events
Any adverse event	**70 (29.5%)**	**8 (3.4%)**
Any serious adverse event	**9 (3.8%)**	**0**
Adverse event resulting in discontinuation	**4 (1.7%)**	**0**
Death	**1 (0.4%)**	**0**
Adverse events with incidence > 1%		
COVID-19	**12 (5.1%)**	**0**
Diarrhea	**9 (3.8%)**	**3 (1.3%)**
Urinary tract infection	**9 (3.8%)**	**0**
Fall	**6 (2.5%)**	**0**
Headache	**5 (2.1%)**	**1 (0.4%)**
Dizziness	**3 (1.3%)**	**0**

Conclusions and Implications:

High safety will enable ‘959 use in combination with other drugs

Aricept Market Approval Data: ADAS-cog11 - 24 Week Study

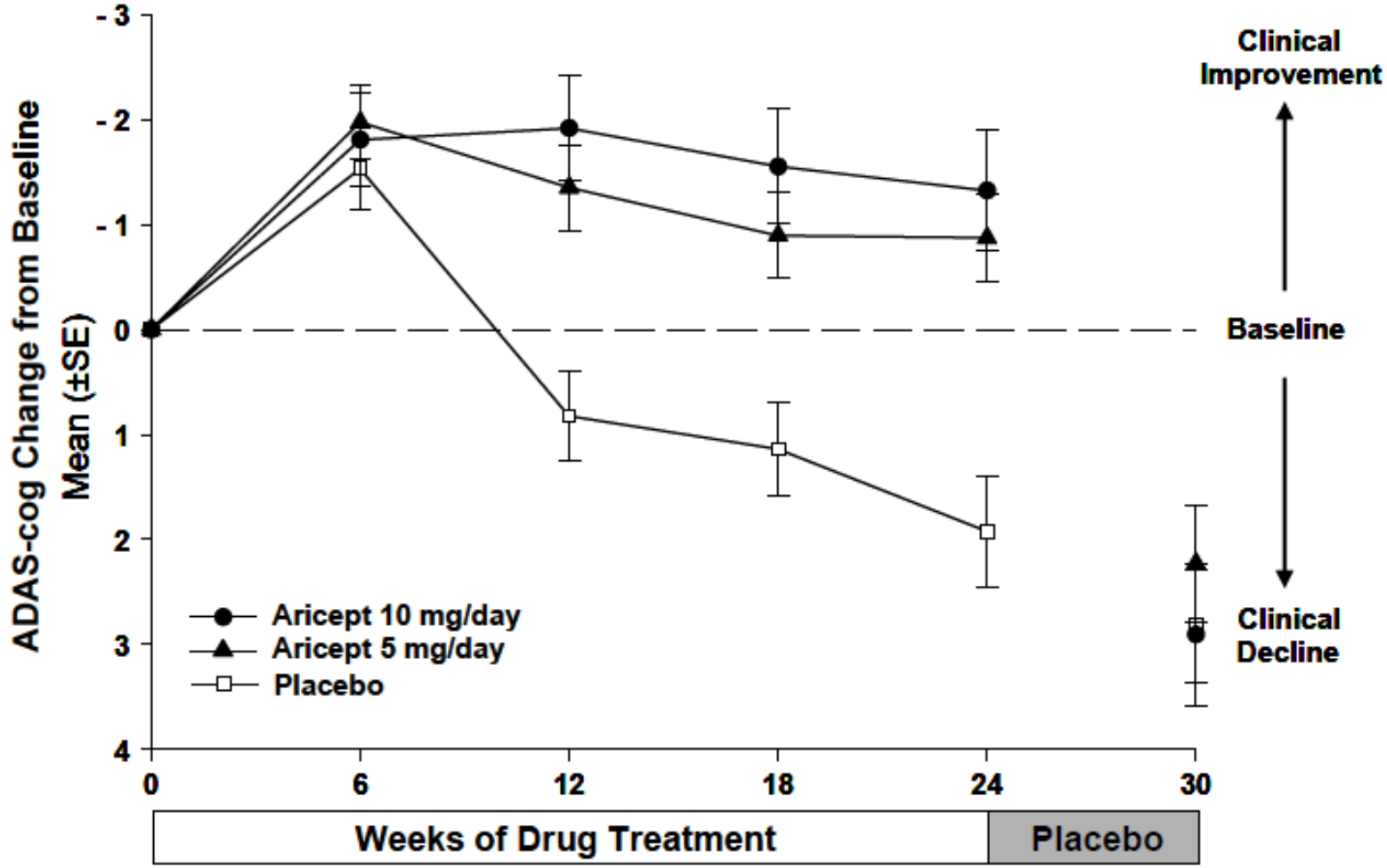


Figure 1. Time-course of the Change from Baseline in ADAS-cog Score for Patients Completing 24 Weeks of Treatment.

Mild Moderate AD (MMSE= 10-26) 150-153 patients per arm

Conclusions and Implications:

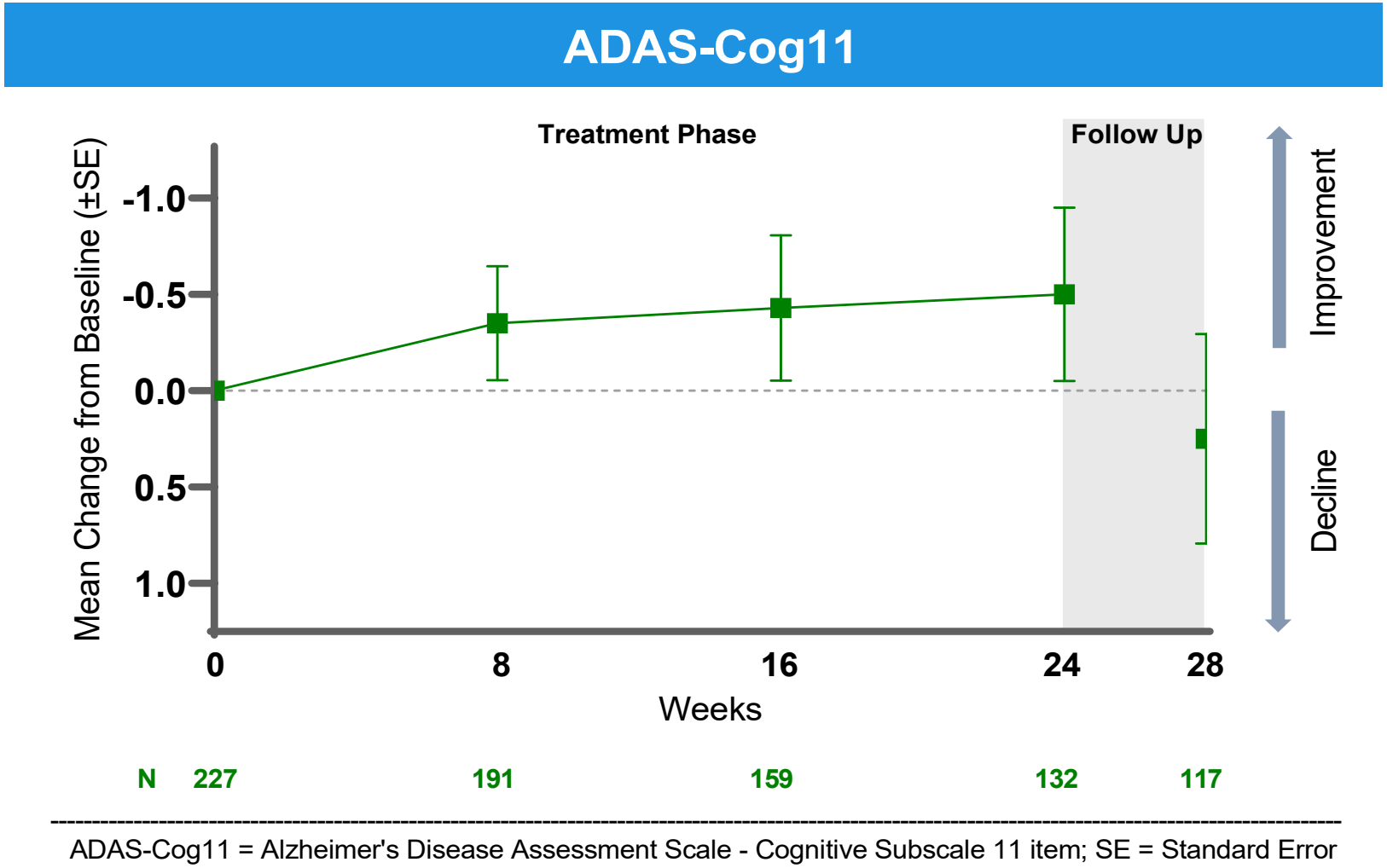
Aricept (donepezil) improves cognition

The market leading, gold standard for cognition and function improvement in AD patients

Benchmark for new AD drugs

Reference: Aricept Package Insert

PIONEER Study: ADAS-Cog11, All Data Pooled (as of 24Jun22)



ADAS-Cog11 = Alzheimer's Disease Assessment Scale - Cognitive Subscale 11 item; SE = Standard Error

Conclusions and Implications:

Encouraging results showing improvement in cognition, even before subtracting out placebo data

Aricept Market Approval Data & PIONEER (All data pooled)

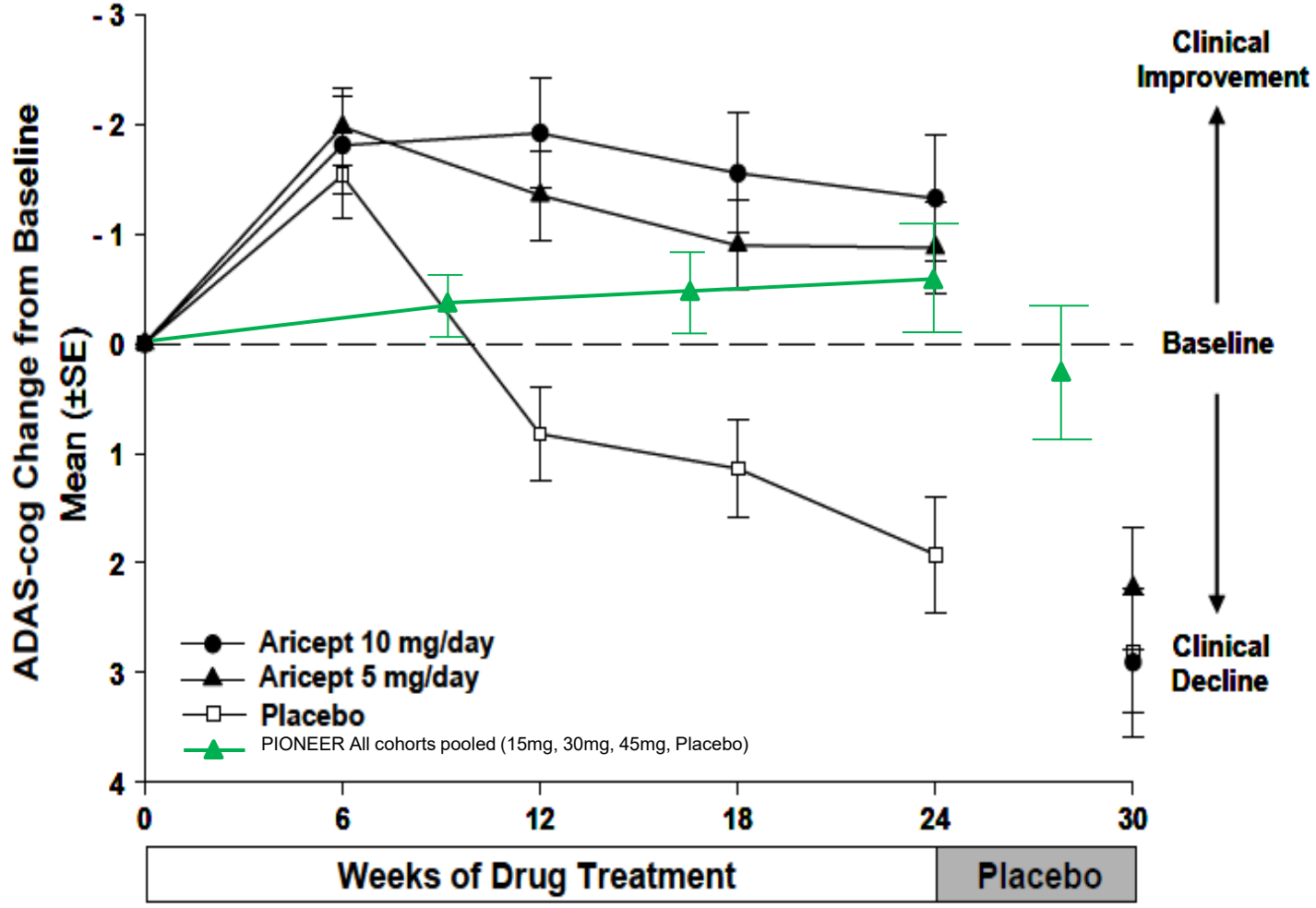


Figure 1. Time-course of the Change from Baseline in ADAS-cog Score for Patients Completing 24 Weeks of Treatment.

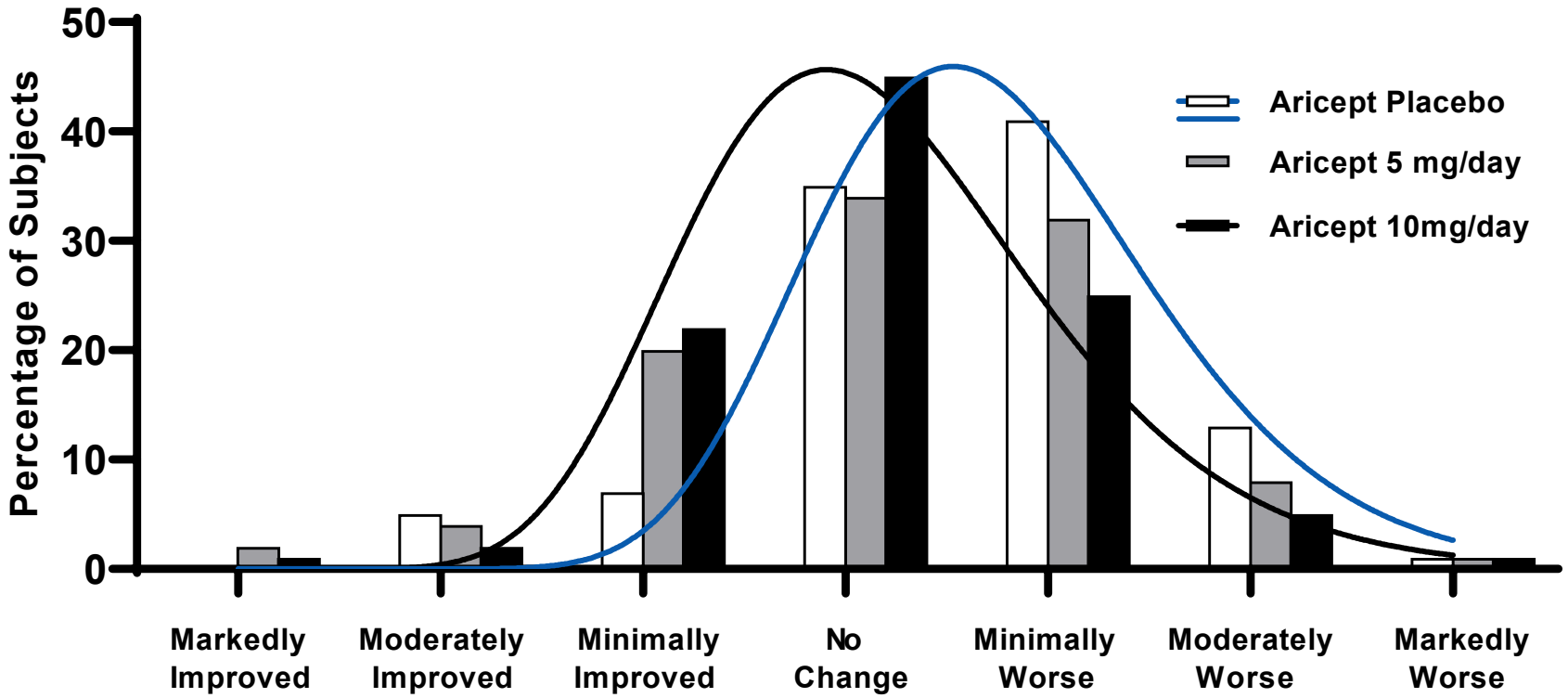
Conclusions and Implications:

Encouraging results benchmarked to Aricept showing improvement in cognition

Improvement in '959 cohorts likely to be greater when placebo data is subtracted out upon unblinding the study

Aricept Market Approval Data: CIBIC+ - 24 Week Study

CIBIC+ Aricept 10 mg QD vs. Placebo



Conclusions and Implications:

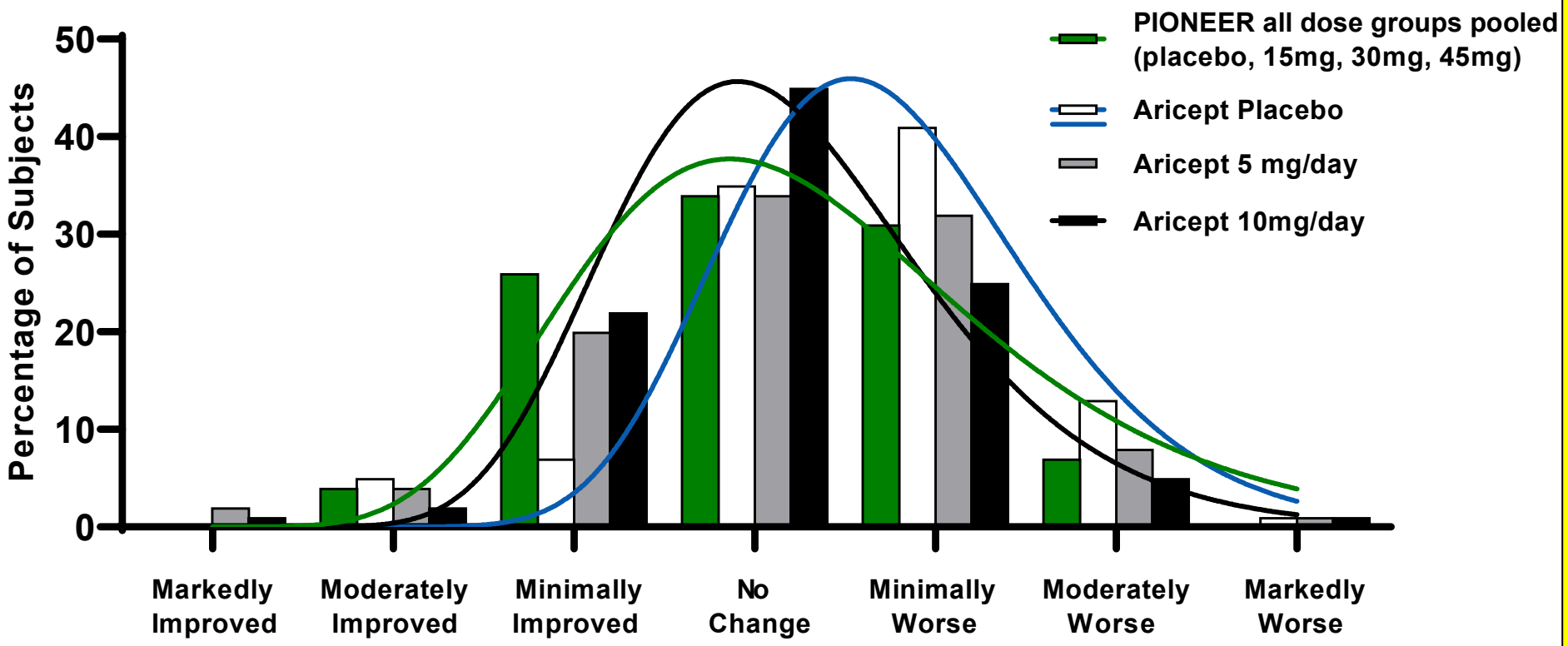
Aricept (donepezil) improves function

Benchmark for new AD drugs

Reference: Aricept Package Insert

Aricept Market Approval Data & PIONEER (All Data Pooled)

PIONEER CGIC vs. Aricept CIBIC+



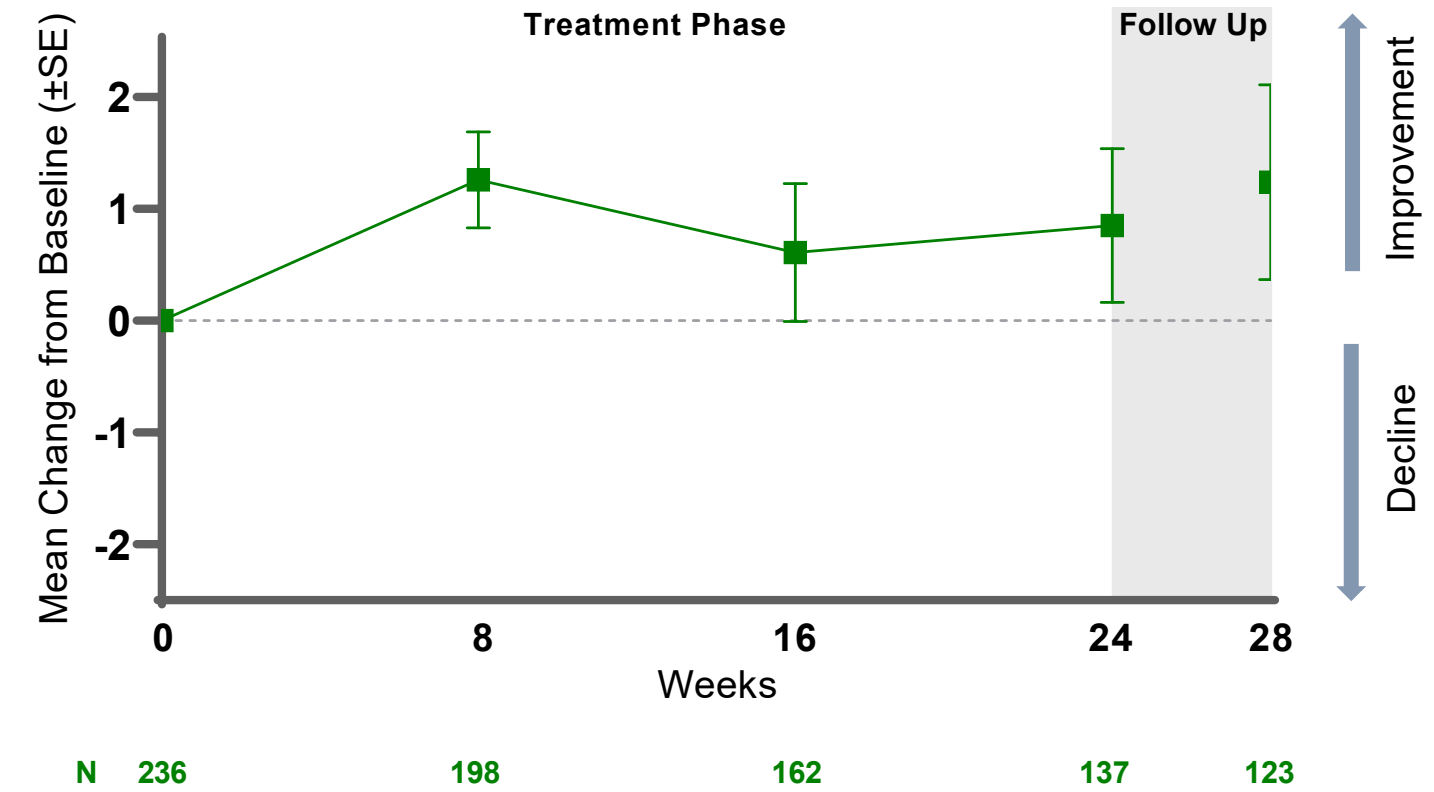
Conclusions and Implications:

Encouraging results showing potential improvement in function

Improvement in '959 cohorts likely to be greater when placebo data is subtracted out upon unblinding the study

PIONEER Study: DSCT, All Data Pooled (as of 24Jun22)

DSCT



DSCT= Digit Symbol Coding Test; SE = Standard Error

Conclusions and Implications:

Encouraging results showing improvement in executive function, even before subtracting out placebo data

Summary:

- Clinical stage lead product T3D-959 in Phase 2 with multiple positive indicators of a treatment effect in mild to moderate AD patients.

  Average scores for all treatment groups combined (including placebo and three drug strength arms) showing;
  - *Improvement on ADAS-cog11 (cognition)*
  - *Improvement on DSCT (executive function)*
  - *Reduced decline in CGIC (global function)*

- Excellent safety profile

- The PIONEER Study is 92% enrolled

- Topline results projected for 2Q 2023

- An Innovative Approach that Challenges Current Paradigms.

Appendix Materials:

PIONEER Trial Design:

- A Phase 2 randomized, double-blind, placebo-controlled design clinical trial.
- Evaluating three dose levels (15 mg, 30 mg, 45 mg) of T3D-959 vs. placebo in 256 subjects (64/arm) with mild-to-moderate Alzheimer's Disease (MMSE 14-26, CDR-Global 0.5-2.0 and CDR-SB $\geq$ 3.0).
- Subjects stratified by gender and ApoE4 genotype, assigned to one of four dose groups (1:1:1:1 ratio) in a randomized fashion.
- Study medication taken orally once daily for 24 weeks.
- Follow-up visit four weeks after the end of treatment (week 28 visit).
- 33 US clinical trial sites.

PIONEER Outcome Measures:

Primary

- Cognition – ADAS-cog11
- Function - ADCS-CGIC
- Safety and Tolerability

Secondary

- Executive Function – DSCT
- Amyloid Plaque Burden – Biomarker – Plasma Aβ42/40 ratio

Exploratory

- Apathy – NPI
- Expressive Language
- Physical Activity
- Brain Glucose Metabolism – FDG-PET scans
- Blood Biomarkers – Neurodegeneration, Tauopathy, Inflammation, Metabolism

T3D-959 Product Profile – Competitive Differentiators

- Potential to improve cognition and function [based on current (July 2022) blinded grouped PIONEER data]
- Oral delivery – no injections, no i.v. infusions
- Cachexia treatment potential (major cause of AD deaths)
- Type 2 diabetes and pre-diabetes treatment potential (37% of AD patients are diabetic)
- Language disorder treatment potential – Aphasia (based on P2a trial observations)
- Can potentially be combined with any other AD drug (based on known safety profile to date)
- Shelf storage of drug (stable long term, no refrigeration required)
- Lower cost to patients than biological therapies (e.g., antibodies)