



vTv Therapeutics (VTVT)

May 2019

NASDAQ: VTVT

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Clinical stage pipeline of novel small molecule drug candidates targeting significant unmet medical needs: **Diabetes and Alzheimer's disease**



Positive phase 2 results in **type 2 diabetes (T2D)** with two novel oral candidates

Ongoing phase 2 study in **type 1 diabetes (T1D)** with TTP399

Topline results from Part 1 expected in **June 2019**



Conducting start-up activities for a clinical trial in subjects with **mild Alzheimer's disease and type 2 diabetes** that consists of sequential phase 2 and phase 3 studies operationally conducted under a single protocol

Screening expected to begin for phase 2 in **June 2019**



Significant, long-term financial sponsor in MacAndrews and Forbes

Distinguished Management Team



Steve Holcombe, B.Sc.
President, Chief Executive Officer



Jeff Kindler, J.D.
Executive Chairman



Rudy Howard, B.A., C.P.A.
Executive Vice President, Chief Financial Officer



Rob Andrews, Ph.D.
Senior Vice President, Chemistry



Robin Abrams, J.D.
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Senior Vice President, Biometrics and Regulatory



Carmen Valcarce, Ph.D.
Executive Vice President, Chief Scientific Officer



Sam Rollins, Ph.D., J.D.
Senior Vice President, Intellectual Property



Aaron Burstein, Pharm.D.
Senior Vice President, Clinical Development



Robust Pipeline of Novel Product Candidates

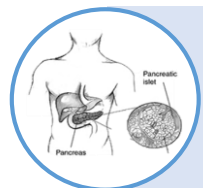


PROGRAM	INDICATION	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	PARTNER
Azeliragon (RAGE)	Alzheimer's Disease					
TTP399 (GKA)	Type 1 Diabetes					
TTP399 (GKA)	Type 2 Diabetes					
TTP273 (Oral GLP-1r)	Type 2 Diabetes					 华东医药 HUADONG MEDICINE Asia
HPP593 (PPAR-δ)	Orphan Indication					 Worldwide
HPP737 (PDE4i)	COPD					NEWSQARA 恒翼生物医药 Asia
Nrf2/Bach1 Program	Undisclosed					



Type 1 Diabetes Program

TTP399
Liver-Selective Glucokinase Activator (GKA)



T1D is an **autoimmune disease** when the pancreas stops producing insulin, the hormone that controls blood-sugar levels ⁽¹⁾



1.25 million people in the US suffer from T1D ⁽¹⁾



Insulin is the current standard of care administered by multiple **daily injections** or **insulin pumps**



Severe **hypoglycemia** and **diabetic ketoacidosis (DKA)** are common side effects of insulin treatment



No FDA-approved oral therapies improve glycemic control in T1D

The Need

“FDA recognizes there is an unmet need for patients with T1DM to help **achieve glycemic goals and improve quality of life and treatment satisfaction**.

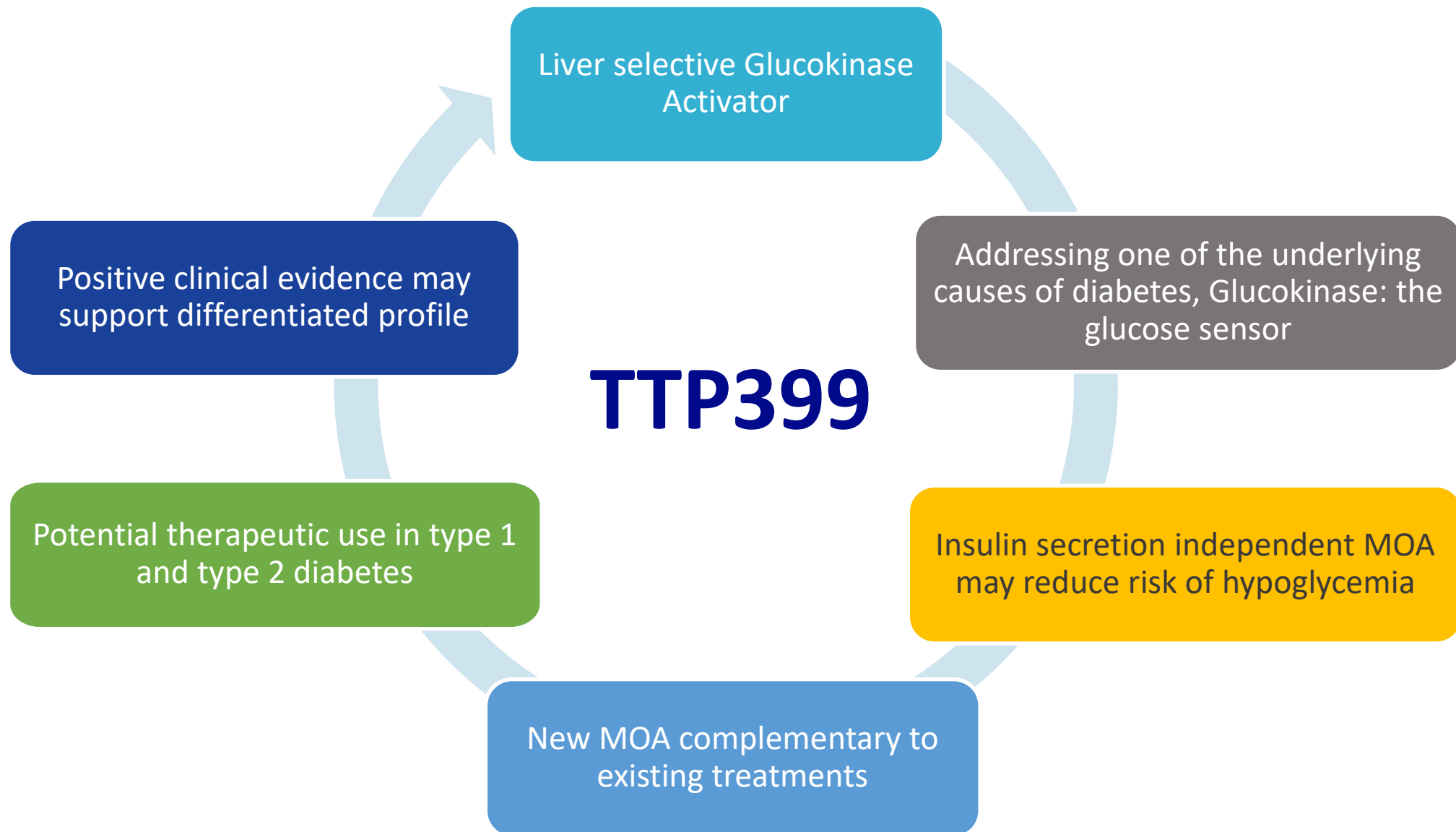
At the same time, the additional risk(s) [such as diabetic ketoacidosis (“DKA”)] incurred by an adjunct therapy need to be carefully considered relative to the benefits the therapy provides.” ⁽²⁾

- SGLT1/2 and SGLT2s recently approved in EU for T1D with **limitations**:
 - Approved for T1D patients **only with BMI ≥27**
 - Treatments **increase risk** of DKA, genital infections and amputations

(1)JDRF Type 1 Diabetes Facts

(2)[FDA Briefing Document, Endocrinologic and Metabolic Drugs Advisory Committee Meeting, January 17, 2019](#)

TTP399 – an Investigational, Oral, Small Molecule, Liver Selective Glucokinase Activator (GKA) for the Management of Diabetes



TTP399 – Strong Evidence Base from 12 Clinical Trials Supporting Development and Investment in T1D

Phase 1 Studies

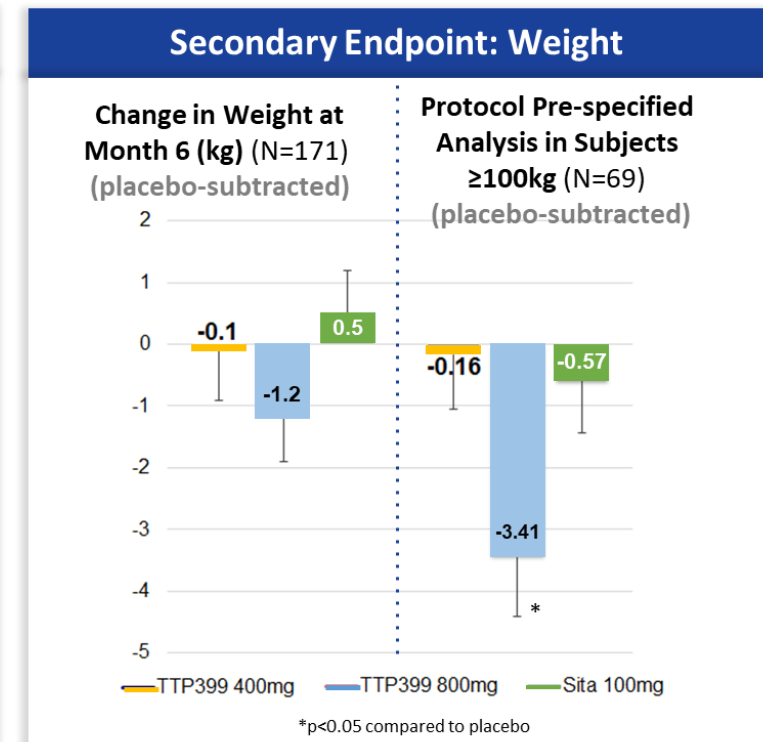
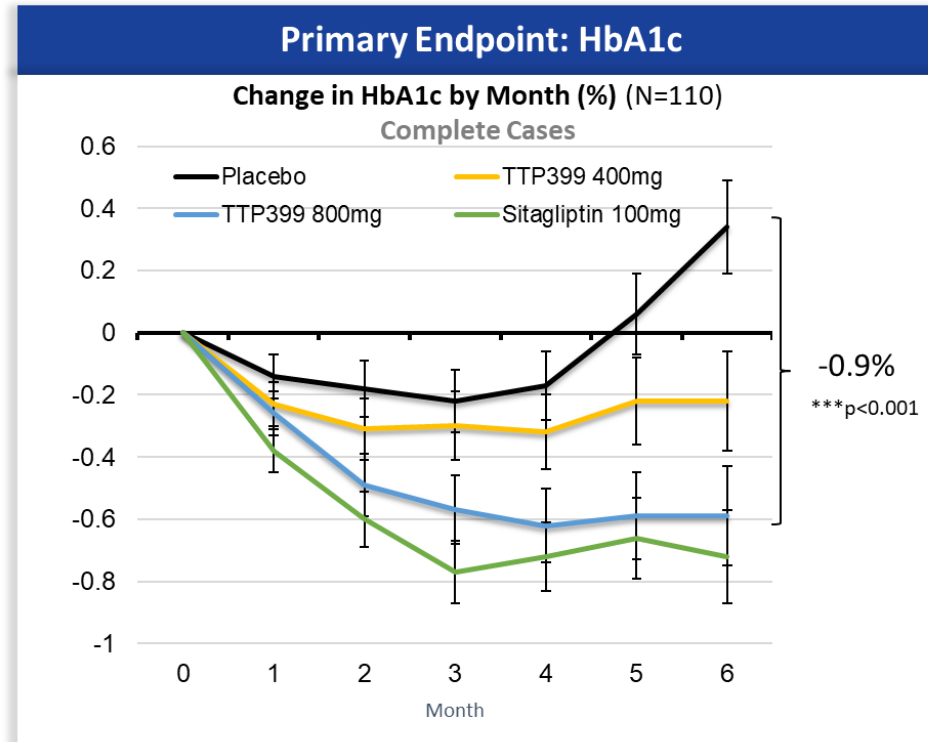
Nine phase 1 studies in healthy volunteers and subjects with T2D

Phase 2 Studies

Two phase 2 trials **completed** in T2D with one trial dosing up to 6 months

One phase 2 trial **ongoing** in T1D

TTP399-202 Phase 2b Study (AGATA)



- Sustained, meaningful reduction in HbA1c over 6 months in phase 2 study
- Well-tolerated, negligible incidences of hypoglycemia and hyperlipidemia, and no occurrences of DKA

TTP399-203 (Simplici-T₁): Adaptive Phase 1b/2 Study Trial Design

In Collaboration with JDRF



Phase 1 (Sentinels)

Study Design:

- Open-label
- **7 day** dose escalation up to 1200mg QD
- **5** adult subjects with T1D on CSII and CGM

March 2018

TTP399 was well tolerated

- **No** incidents of **severe hypoglycemia** or **DKA**
- Indications of **improved glycemic control**, while **reducing insulin dose**
 - Increase % time in range
 - Reduce % time in hyperglycemia without increasing % time in hypoglycemia



Phase 2-Part 1 (Learning Phase)

Study Design:

- Double-blind Placebo control
- **12 weeks** dosing 800mg QD
- **~20** adult subjects with T1D on CSII and CGM
- **Primary Endpoint:** change in HbA1c

June 2019

Results expected in June 2019



Phase 2-Part 2 (Confirming Phase)

Study Design:

- Double-blind Placebo control
- **12 weeks** dosing 800mg QD
- **~90** adult subjects with T1D (all comers)
- **Primary Endpoint:** change in HbA1c

Q1 2020

Results expected in Q1 2020

1. ClinicalTrials.gov Identifier: NCT03335371
2. Subjects with Continuous Subcutaneous Insulin Infusion (CSII) and Continuous Glucose Monitoring (CGM)





'Kristina'
T1D Patient
Wilmington, North Carolina

“Having lived with T1D for nearly all of my life, shots, finger pricks and managing my diet are all I've ever known. From a mental health perspective, the constant management of dosing and eating can quickly take a toll on me.

Having an **oral medication option to pair with insulin to help keep blood sugars in range** (even when deciding to indulge in cake or ice cream), and **one that does not have side-effects like DKA**, could truly change the way that I live.”

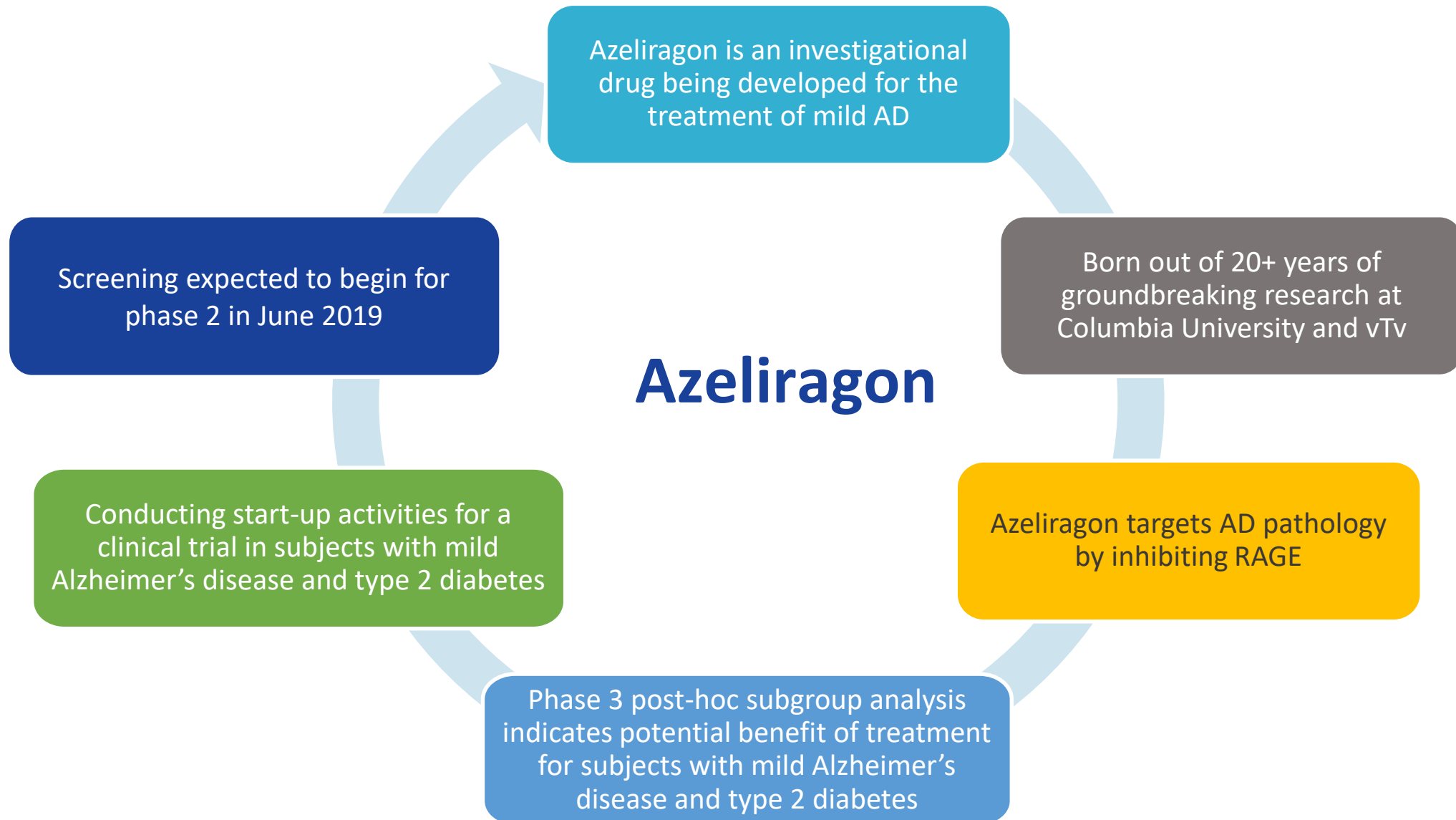


Alzheimer's Disease Program

AZELIRAGON

Antagonist of RAGE (Receptor for Advanced Glycation Endproducts)

A New Approach to Treating Alzheimer's Disease



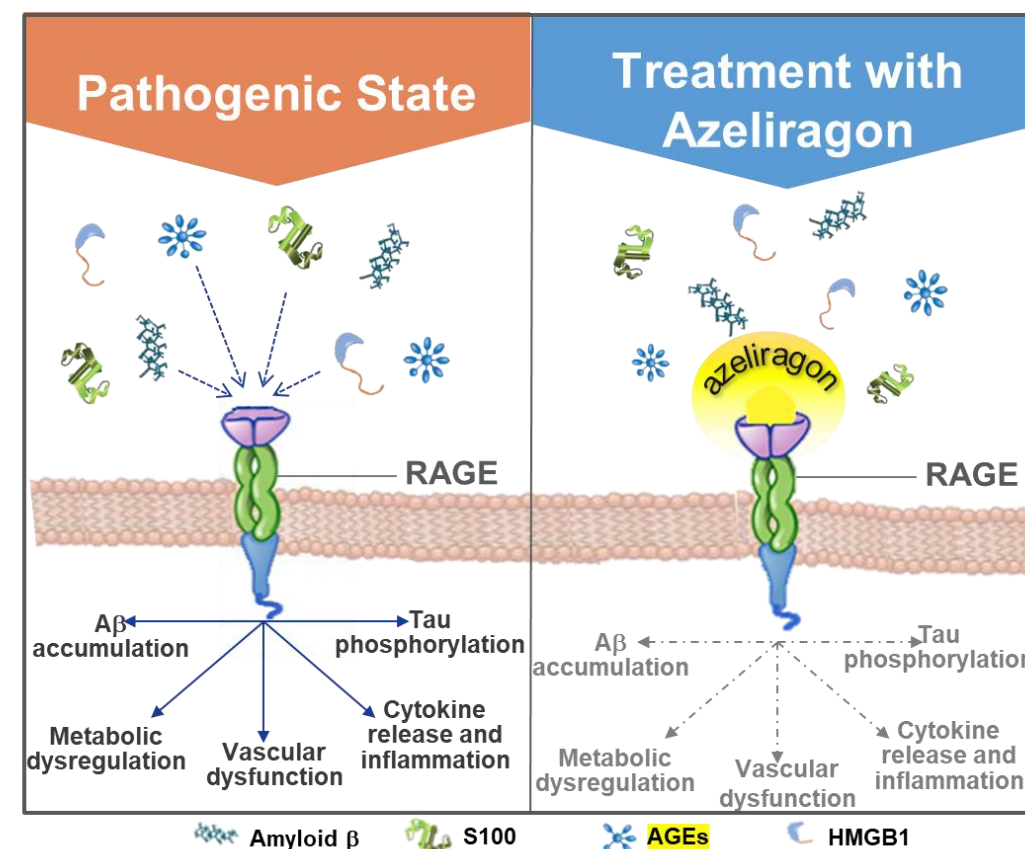
RAGE

- Receptor for Advanced Glycation Endproducts (RAGE) is expressed at low levels in healthy tissues (except skin and mucus membranes)
- **Increases** in the concentration of **RAGE ligands** (AGEs, HMGB1, S100 and Ab) **induce RAGE expression**
- **The interaction of AGEs (or other ligands) with RAGE** leads to sustained **cellular damage and inflammation**

RAGE in Alzheimer's Disease and Diabetes

- RAGE protein is increased in autopsied AD brains compared to controls with no AD⁽¹⁾
- Increases in RAGE protein and percentage of RAGE-expressing microglia parallel the severity of disease⁽¹⁾
- Patients with AD and diabetes show **increased hippocampal immuno-staining for RAGE protein**⁽²⁾
- **AGE** accumulation parallels the development of **cognitive impairment and dementia in individuals with diabetes**⁽³⁾

Azeliragon antagonizes RAGE, blocking ligands from binding to the receptor



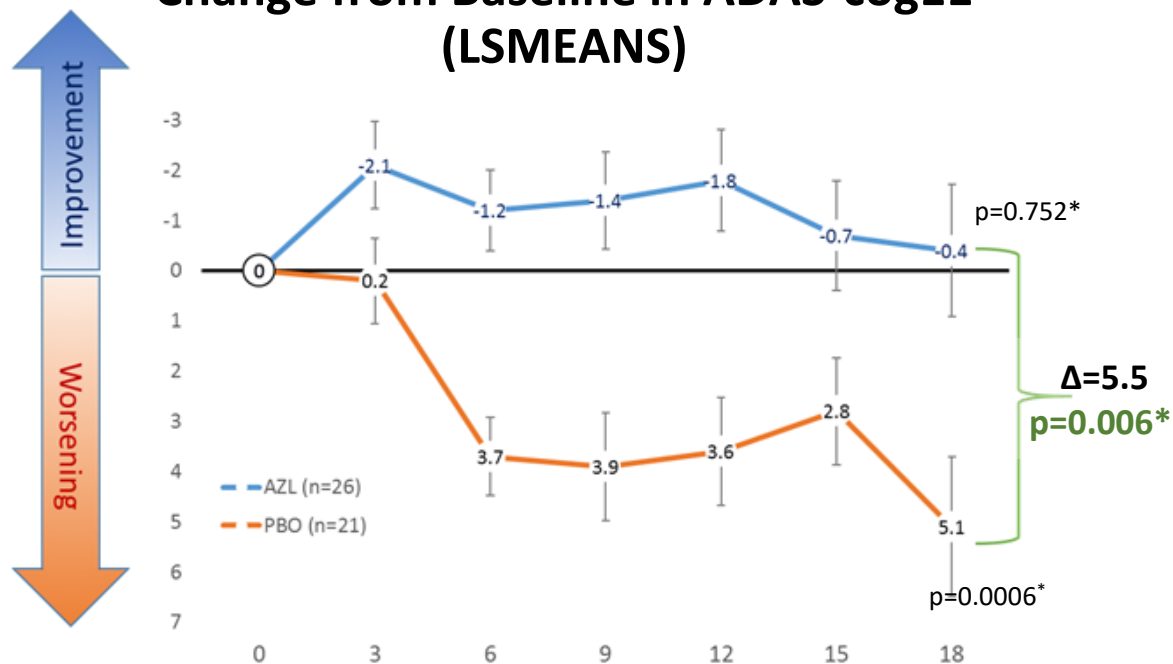
(1) Lue L-F. Curr. Drug Targets CNS Neurol. Disord. 2005 Jun;4 (3):249-66. (2) Valente T. Neurobiology of Disease 37 (2010) 67-76. (3) Dhananjayan et al. (2018) Advance Glycation, Diabetes and Dementia <https://doi.org/10.1016/B978-0-12-809454-9.00009-3>

Phase 3 Subgroup Results (A-Study): Azeliragon Delayed Decline in Cognition and Function in Patients with Presumed Increased RAGE Expression



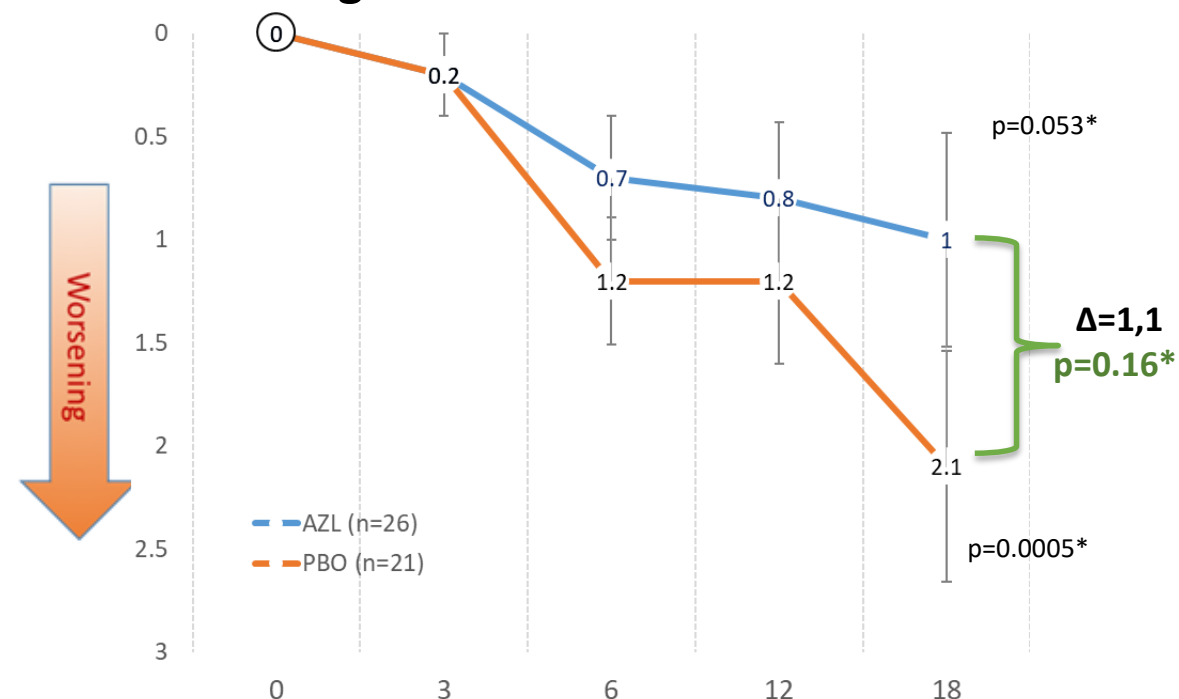
STEADFAST A-Study ADA-T2D Subgroup (FAS)

Change from Baseline in ADAS-cog11 (LSMEANS)



STEADFAST A-Study ADA-T2D Subgroup (FAS)

Change from Baseline in CDR-SB



- Cognitive improvement cannot be explained by improvement in glycemic control

Analysis of Patients with Diabetes (HbA1c $\geq 6.5\%$ at anytime during the study)

Results are LSMeans $\pm$ SE based on MMRM model.

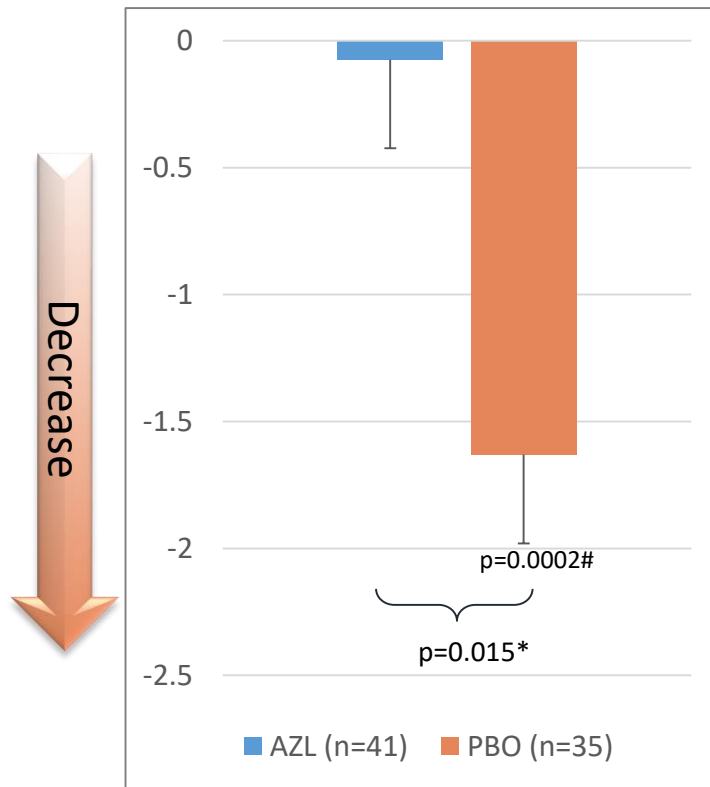
*All p values are nominal. FAS = Full Analysis Set

Data presented on March 30, 2019 at the 14th International Conference on Alzheimer's & Parkinson's Diseases held in Lisbon, Portugal

Change in MRI Brain Volume at Month 18 in the Diabetes Subgroup: Less Brain Atrophy in the AZL-treated Group

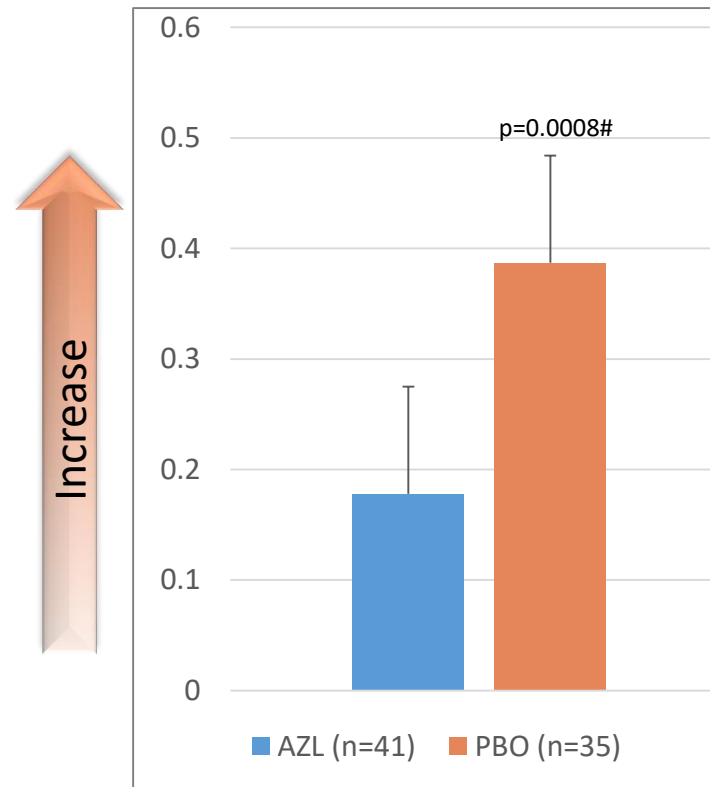
ADA-T2D Subgroup

Change in Whole Brain Volume (%)



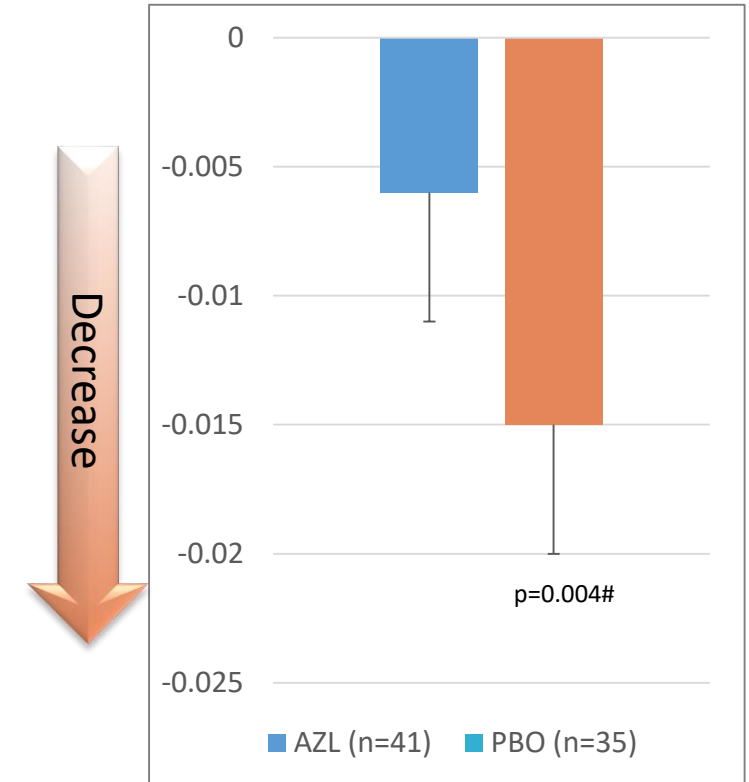
ADA-T2D Subgroup

Ventricular Enlargement (%)



ADA-T2D Subgroup

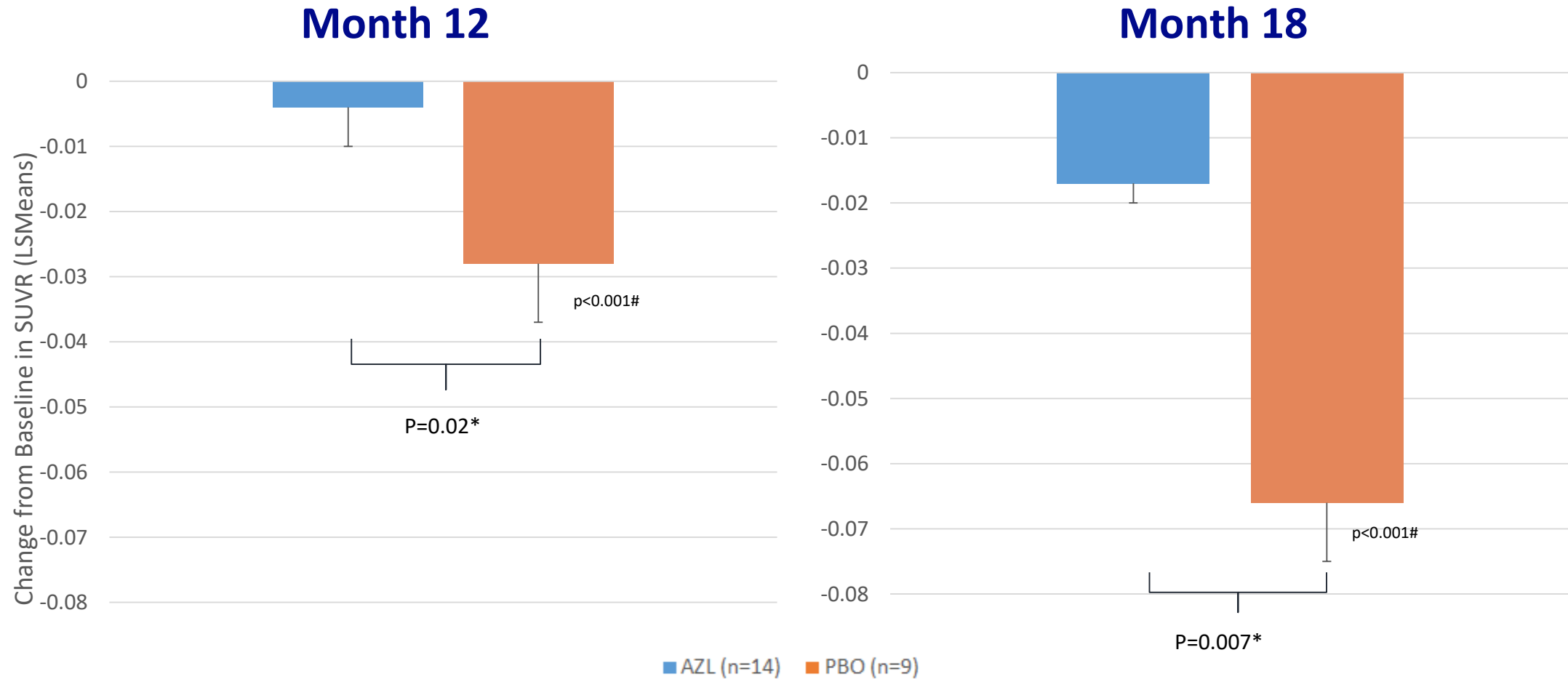
Change in Total Hippocampus Volume (%)



Analysis of Patients with Diabetes (HbA1c $\geq$ 6.5% at anytime during the study). **Results are change from baseline LSMeans $\pm$ SE ANCOVA adjusted for baseline, FAS.
#1-sample test nominal significance indicating worsening. *All p values are nominal

Data presented on March 30, 2019 at the 14th International Conference on Alzheimer's & Parkinson's Diseases held in Lisbon, Portugal

Change in FDG-PET SUVR in the Diabetes Subgroup: Less Reduction in Glucose Utilization in AZL-treated Group



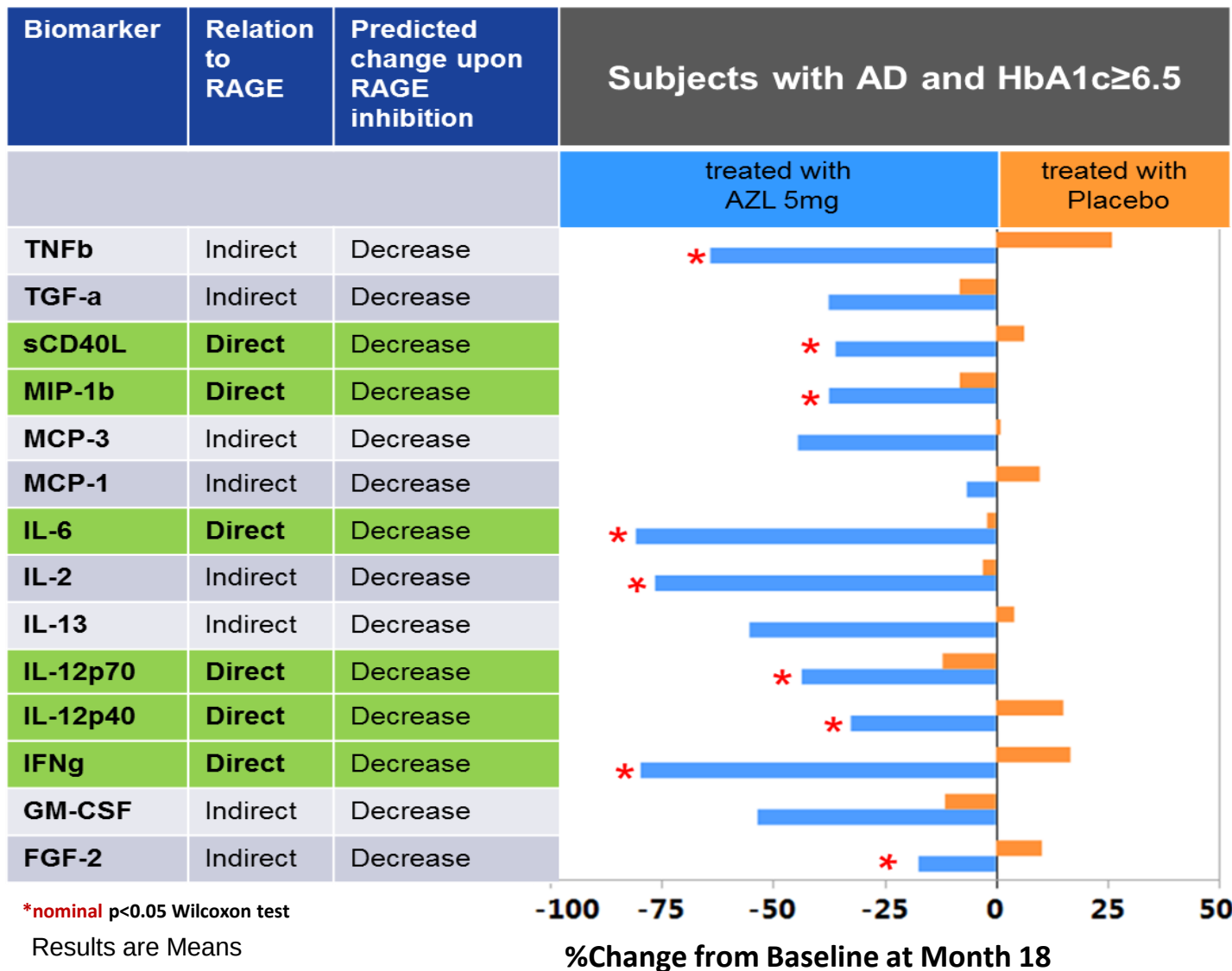
- SUVR composite (unweighted combination of frontal, anterior/posterior cingulate, lateral parietal, lateral temporal, and hippocampus)

Results are LSMeans $\pm$ SE based on MMRM model, FAS. AD-T2D=HbA1c $\geq 6.5\%$ at anytime during the study.

#1-sample test nominal significance indicating worsening. *All p values are nominal

Data presented on March 30, 2019 at the 14th International Conference on Alzheimer's & Parkinson's Diseases held in Lisbon, Portugal

Decreases in Inflammatory Biomarkers Consistent with RAGE Inhibition



Biomarker Profile

Azeliragon treatment significantly decreased the following markers linked to RAGE:

- IL6
- IL12
- INFg
- CD40L
- MIP-1
- IL2
- TNFb

Each of these markers is a major player in the neuroinflammatory pathway¹

¹Based on Ingenuity software predictions

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Study Objectives:

Phase 2:

- Proof of concept study to confirm the findings from the diabetes subgroup of the STEADFAST study

Phase 3:

- Demonstrate safety and efficacy with co-primary endpoints of cognition and function to support possible registration



Phase 2

(Part 1 / Proof of Concept)

- Double-blind, placebo control
- 5mg QD or placebo for 6 months
- ~100 adult subjects with mild Alzheimer's disease and HbA1c $\geq$ 6.5%
- Primary Endpoint: ADAS-cog14
- Secondary Endpoints: CDR-sb, FAQ, Amsterdam-IADL, MMSE

Study start expected June 2019

Results expected 4Q2020



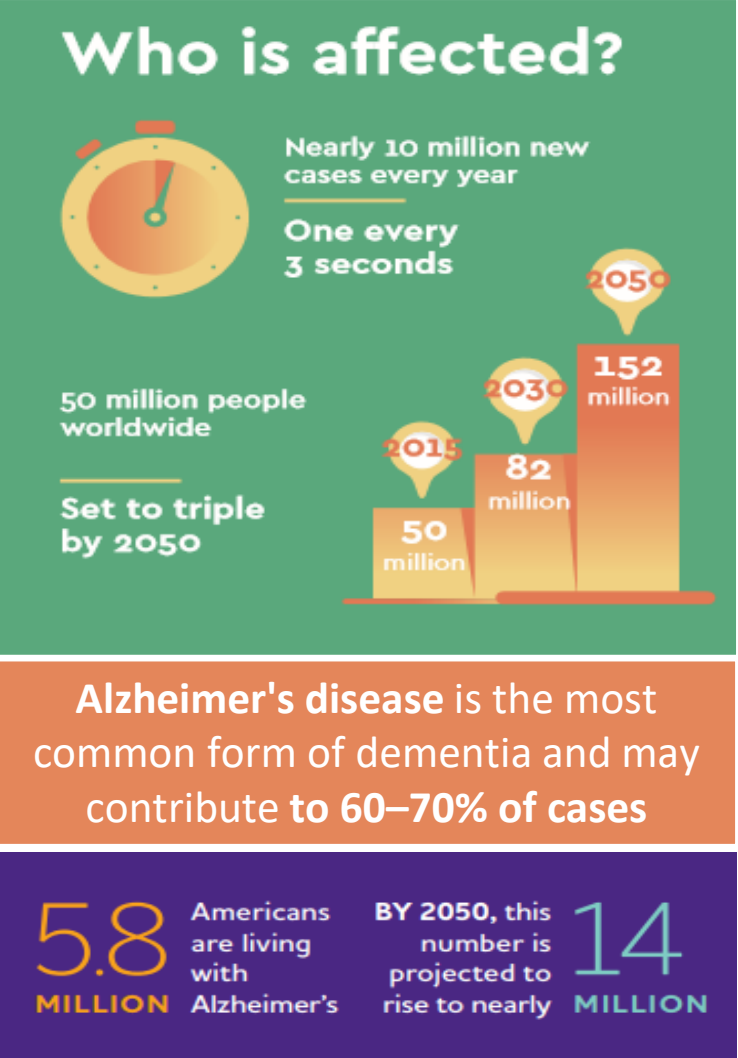
Phase 3

(Design may be adjusted based on Part 1 results)

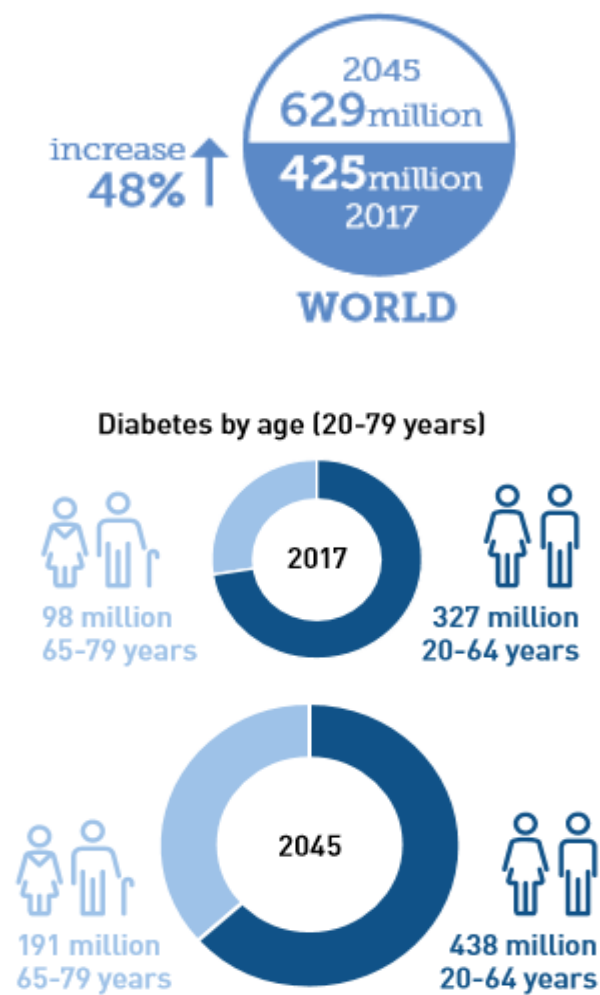
- Double-blind, placebo control
- 5mg QD or placebo for 18 months
- ~200 adult subjects with mild Alzheimer's disease and HbA1c $\geq$ 6.5%
- Co-primary Endpoints:
 - Cognition: ADAS-cog14
 - Function: TBD

Study start expected 1Q2021

Dementia and AD⁽¹⁾⁽²⁾



Diabetes⁽³⁾

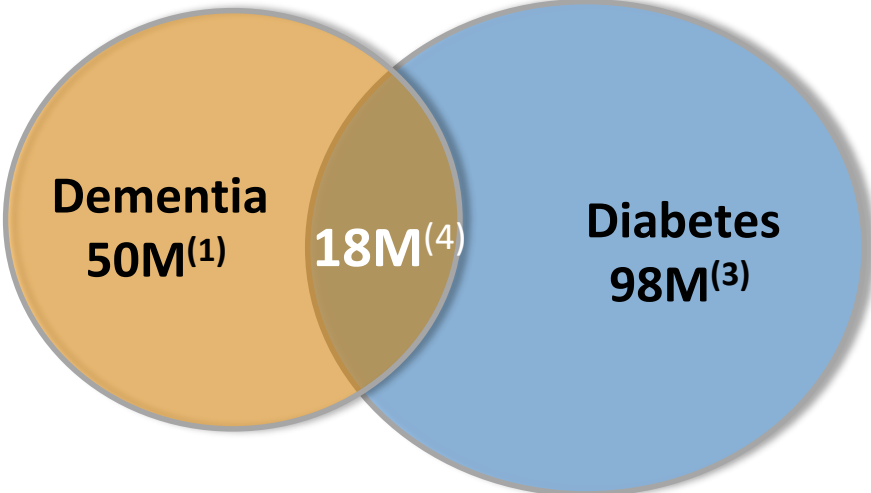


Diabetes & Dementia

Since the late '80s, case-control and prospective epidemiologic studies around the world have reported an association between T2D and dementia *Type 2 Diabetes and Dementia (2018)* <https://doi.org/10.1016/B978-0-12-809454-9.00001-9>

Number of People Living with Dementia

Number of People ≥65 Living with Diabetes



(1) Globally, number of people with dementia in 2017 (source: *Dementia, key facts, WHO, 2017*)
(2) 2019 Alzheimer's Disease Facts and Figures (source: Alzheimer's Association)
(3) Globally, number of people with diabetes 65–79 years of age (source: *IDF Diabetes Atlas 8th Edition*)
(4) Assumption based on 37% estimate of Medicare beneficiaries age 65 and older with dementia who also have diabetes in the US (Alzheimer's Association. 2018 Alzheimer's Disease Facts and Figures)

Next Steps

Conducting **start-up activities** for a clinical trial in subjects with mild AD and T2D that consists of sequential phase 2 and phase 3 studies operationally conducted under a single protocol



Market Opportunity

Nearly 40% of Medicare beneficiaries age 65 and older with dementia also have diabetes⁽¹⁾



Clinical Evidence

Results of STEADFAST subgroup analysis in subjects with Type 2 diabetes indicate a **potential benefit of treatment with azeliragon**



Underserved Population

No new treatments for AD/dementia amid growing senior population and rising diabetes pandemic

⁽¹⁾ Alzheimer's Association. 2018 Alzheimer's Disease Facts and Figures



Partnerships

Creating Value with Program Licenses

Type 2 Diabetes Unmet Needs in China

- Over 100 million people with diabetes*
- China's diabetes drug market projected to reach \$20B USD by 2025*
- Opportunity to introduce new drug classes to a market that has historically lagged behind in access to innovative drugs



Huadong Medicine Co., Ltd

- One of the largest pharmaceutical companies in China
- A strategic focus in diabetes; >20 candidates in development

GLP-1r Program Exclusive License Agreement in China and Other Pacific Rim Territories

- In December 2017, vTv granted an exclusive license to Huadong to develop, manufacture and commercialize vTv's GLP-1r agonist program in China and 15 other regions in the Pacific Rim excluding Japan
- Huadong will develop the GLP-1r program for type 2 diabetes in its territory
- vTv is eligible to receive future development and commercialization milestones as well as royalties on sales of approved products
- vTv will utilize the pre-clinical and clinical data generated by this collaboration to continue the development and to seek partners in ROW

*Morgan Stanley China Healthcare Report; Diabetes 2025: China's Antidiabetic Market Set to Triple (October 4, 2017)

COPD Market in China

- 8.6% (~100 million) COPD patients in China⁽¹⁾
- Annual sales of top 2 products (Seretide and Spiriva) greater than \$132M USD
- Total COPD market at \$4.5B USD



Newsoara Biopharma Co., Ltd.

- Newsoara was established in 2018 to in-license innovative drug candidates for development and commercialization with focus in China and/or Asia Pacific region
- Hangzhou TigerMed, a public company (stock ChiNext: 300347), is a significant investor in Newsoara
- CEO and founder Dr. Benny Li has more than 20 years of extensive drug research, development and regulatory experience with global leading pharmaceutical companies such as Takeda and Alcon

PDE4 Program Exclusive License Agreement in China and Other Pacific Rim Territories

- In May 2018, vTv granted an exclusive license to Newsoara to develop, manufacture and commercialize vTv's PDE4 Inhibitor program in China and 14 other regions in the Pacific Rim excluding Japan
- Newsoara will develop the PDE4 program for COPD and one other indication in its territory
- vTv is eligible to receive future development and commercialization milestones as well as royalties on sales of approved products
- vTv will utilize the pre-clinical and clinical data generated by this collaboration to continue the development and to seek partners in ROW

⁽¹⁾The Lancet Respiratory Medicine, 2018: DOI, April 09, 2018



Reneo Pharmaceuticals, Inc.

- San Diego-based clinical stage pharmaceutical company focused on the development of therapies for patients with genetically defined orphan diseases
- Founded by Mike Grey, an experienced VC and entrepreneur with deep biotech experience, and a strong team who have worked together and collaborated on previous successful programs
- Funded by multi-national investor group including Pappas, Rivervest, Lundbeckfonden Ventures and New Enterprise Associates

PPAR- δ Program Worldwide Exclusive License Agreement

- In December 2017, vTv granted an exclusive worldwide license to Reneo to develop, manufacture and commercialize vTv's PPAR- δ program
- Reneo will develop the program in orphan diseases associated with deficits in cellular metabolism and energy production
- vTv holds an equity interest in Reneo and is eligible to receive future development and commercialization milestones as well as royalties on sales of approved products

Discovering and Developing Innovative Therapies for Substantial Markets



vTv is a small and nimble company that has integrated innovative science with clinical drug discovery in challenging areas like **Diabetes and Alzheimer's disease**



vTv has a novel pipeline of programs including its **liver-selective GKA** for type 1 and type 2 diabetes and its **RAGE program** for mild Alzheimer's disease and type 2 diabetes



vTv has a track record of **strategic partnerships** with leading biopharmaceutical companies, academic institutions and patient advocacy groups