Alzheon ALZ-801 Data Presented in Oral Session at CTAD on Role of Amyloid Oligomers in Alzheimer's Disease

Therapeutic Inhibition of Toxic Beta Amyloid Oligomers Can Intervene Early in Amyloid Aggregation Cascade

Two Additional Posters at CTAD Support Advancement of ALZ-801 to Phase 3 Study as Oral Precision Medicine to Treat Alzheimer's Disease

FRAMINGHAM, Mass., November 2, 2017 – Alzheon, Inc., a clinical-stage biopharmaceutical company focused on developing new medicines for patients suffering from Alzheimer's disease (AD) and other neurological and psychiatric disorders, announced that an oral presentation, entitled *Amyloid Beta Oligomers in Alzheimer's Disease: A Missing Piece of the Alzheimer's Puzzle,* will review the status of the field and highlight the discovery by Alzheon scientists of a novel anti-oligomer therapeutic mechanism, as well as evidence from other research and drug development programs, for targeting of pathogenic amyloid oligomers in AD. This oral presentation will be made today by Jeffrey Cummings, MD, Director, Cleveland Clinic Lou Ruvo Center for Brain Health in Las Vegas and Professor of Neurology at the Cleveland Clinic, at the 10th Annual Clinical Trials on Alzheimer's Disease (CTAD) congress being held November 1-4 in Boston.

"We are seeing the emergence of new insights on how amyloid-targeted therapies can be optimized to treat Alzheimer's disease," said Dr. Jeffrey Cummings. "We now understand much more about the underlying pathogenesis of the disease, as well as the role of toxic amyloid oligomers in the cascade of Alzheimer's, and the patient populations most likely to respond to amyloid-targeted therapies. By overlaying this new understanding of amyloid's role in Alzheimer's, we can revitalize our efforts to develop targeted therapies that are on the near-term horizon for bringing desperately needed treatment options to patients with this disease."

The oral presentation reviews the central role of toxic beta amyloid (Aβ) oligomers in the development and progression of AD, highlighting Alzheon's discovery of the novel mechanism of action of tramiprosate, the active agent in optimized prodrug ALZ-801 that blocks formation of Aβ oligomers.[1] The presentation also features recent analyses that translate this molecular mechanism of action of tramiprosate to clinical effects in AD patients, specifically genetically-defined high risk patients with two APOE4 alleles (APOE4/4 homozygotes) at the Mild stage of AD.[2,3,4]

- APOE4/4 AD patients have a substantially higher brain concentration of Aβ oligomers compared to APOE4 non-carriers.
- Soluble toxic Aβ oligomers play a key role early in the Alzheimer's disease process.
- ALZ-801 inhibits the formation of Aβ oligomers at clinically relevant concentrations achieved in brains of AD patients.

"While the Alzheimer's field has recognized for over 100 years that amyloid plaques are the hallmark of Alzheimer's disease, only the new insights into the role of toxic amyloid oligomers has finally shed light on how we can therapeutically target the amyloid pathway. Based on the recent series of new scientific and clinical data from Alzheon, we have established ALZ-801 as a pioneering small molecule anti-amyloid therapy, which directly inhibits the formation of toxic oligomers that are the pathogenic driver of the development and progression of Alzheimer's," said Martin Tolar, MD, PhD, Founder, President and CEO of Alzheon. "Bolstered by these new data, we are confident in our path ahead with the pivotal program with ALZ-801 for Alzheimer's patients likely to be most responsive to amyloid-targeted, disease-modifying treatment."

Alzheon is also presenting two posters at CTAD that further support the Phase 3 development of ALZ-801 as a Precision Medicine approach to treat Alzheimer's patients with APOE4 genotype, with future expansion to additional Alzheimer's populations.

- In the poster presentation *Sustained Clinical Effects of Tramiprosate in APOE4/4 Homozygous Patients with Alzheimer's Disease Over 130 Weeks: Results of Phase 3 Extension Study,* Alzheon shows clinical data that analyzed efficacy and safety of tramiprosate, the active agent in ALZ-801, in AD patients with two APOE4 alleles (APOE4/4 homozygotes), who after completion of the North American Phase 3 trial continued into a 1-year Extension Study. Patients who received tramiprosate showed persistent and superior efficacy, compared to subjects who had a delayed start on active drug, i.e., initial placebo-treated subjects. These clinical benefits in APOE4/4 AD patients are consistent with the crucial role Aβ oligomers play in AD pathogenesis, as well as the recently discovered molecular mechanism of tramiprosate, where tramiprosate inhibits Aβ monomer aggregation and formation of toxic Aβ oligomers at clinically relevant doses.[1] These clinical data support the company's Precision Medicine approach with ALZ-801 in the upcoming Phase 3.
- In a poster presentation *Beta Amyloid Anti-Oligomer Action of ALZ-801 and Clinical Dose Translation Analyses Support Confirmatory Phase 3 Program in Alzheimer's Disease*, Alzheon describes results from clinical studies with ALZ-801, an optimized prodrug of tramiprosate. These clinical studies demonstrated the substantially improved tolerability and pharmacokinetics of ALZ-801 in comparison to oral tramiprosate, and established a dose that achieves equivalent target drug exposure. The completed ALZ-801 Phase 1 bridging program supports the pivotal Phase 3 clinical program for development of ALZ-801 as an oral, anti-oligomer inhibitor for targeting Aβ pathology in the treatment of Alzheimer's disease.[4] The poster presentation highlights findings from a newly published scientific article on ALZ-801 (https://link.springer.com/article/10.1007%2Fs40262-017-0608-3).

About ALZ-801

ALZ-801 is a novel, oral anti-amyloid drug candidate that is an optimized prodrug of tramiprosate, which has shown promising results in analyses of clinical data and therapeutic mechanism of action. This includes the discovery of its novel molecular mechanism of action blocking the

formation of toxic amyloid oligomers[1] associated with the development and progression of AD. The clinical data for ALZ-801 and its active agent, tramiprosate, suggest long-term clinical efficacy in AD patients with the APOE4 genotype, along with a favorable safety profile.[2,3] The initial Phase 3 program for ALZ-801 will focus on patients with the homozygous APOE4/4 genotype at the Mild stage of AD, with the potential for future expansion to additional Alzheimer's populations. ALZ-801 received Fast Track designation by the U.S. Food and Drug Administration (FDA) in October 2017.

About Apolipoprotein E

Apolipoprotein E, or APOE, is a gene that provides a predictive window into an individual's Alzheimer's disease prognosis. In the brain, apolipoprotein E helps shuttle cholesterol to neurons to support their normal function. There are three forms, or alleles, of the APOE gene, called ε2, ε3 and ε4. The ε4 allele has been found to correlate with high risk and earlier onset of Alzheimer's disease. It is estimated that up to 65% of all AD patients in the U.S. are carriers of at least one APOE4 allele, and that 10-15% of the AD population, or approximately 560,000 individuals in the U.S., are APOE4/4 homozygotes. APOE4 carriers – and more considerably APOE4/4 homozygotes – show faster rates of cognitive decline, at pre-symptomatic, early and dementia stages of the disease. In addition, APOE4 carriers, in comparison to non-carriers, show a higher and faster accumulation of amyloid pathology, including soluble amyloid oligomers.

About Alzheon

Alzheon, Inc. is committed to developing innovative medicines by directly addressing the underlying pathology of devastating neurodegenerative disorders. Our lead Alzheimer's clinical candidate, ALZ-801, is a Phase 3-ready, first-in-class, small molecule oral inhibitor of amyloid aggregation and neurotoxicity – hallmarks of Alzheimer's disease. ALZ-801 is a novel prodrug that builds on the safety and efficacy profile of the active compound tramiprosate, which has been evaluated in clinical trials involving over 2,000 Alzheimer's patients. Our clinical expertise and technology platform is focused on developing drug candidates using a Precision Medicine approach based on individual genetic and biological information to advance therapies with the greatest impact for patients.

The details for the presentations are as follows:

Oral Presentation (OC6)

Title: *Amyloid Beta Oligomers in Alzheimer's Disease: A Missing Piece of the Alzheimer's Puzzle*
Date: Thursday, November 2, 2017
Time: 9:45 am ET
Presenter: Jeffrey Cummings, MD, Director, Cleveland Clinic Lou Ruvo Center for Brain Health in Las Vegas and Professor of Neurology at Cleveland Clinic
Other Authors: Sandrine Andrieu, MD, MPH, University of Toulouse, France; Philip Scheltens MD, PhD, VU University Medical Center, Amsterdam, Netherlands; Kaj Blennow, MD, PhD, The Sahlgrenska Academy at University of Gothenburg, Molndal, Sweden; Petr Kocis PhD, Alzheon, Inc.; John A. Hey PhD, Alzheon, Inc.; Aidan Power, MD, Alzheon, Inc.; Martin Tolar, MD, PhD, Alzheon, Inc.; Susan Abushakra, MD, Alzheon, Inc.

Poster Presentation (P29)
Title: *Sustained Clinical Effects of Tramiprosate in APOE4/4 Homozygous Patients with Alzheimer's Disease Over 130 Weeks: Results of Phase 3 Extension Study*
Poster Session: Clinical Trials: Results
Date: Wednesday, November 1 and Thursday, November 2
Presenter: Susan Abushakra, MD, Chief Medical Officer, Alzheon, Inc.
Other Authors: Anton Porsteinsson, MD, University of Rochester; Carl Sadowsky, MD, Palm Beach Neurology, Florida; Bruno Vellas, MD, University of Toulouse, France; Serge Gauthier, MD, McGill University, Montreal, Canada; Aidan Power, MD, Alzheon, Inc.; Larry Shen, PhD, Pharmapace, Inc., San Diego; Peter Wang, PhD, Pharmapace, Inc., San Diego; John Hey, PhD, Alzheon, Inc.; Martin Tolar, MD, PhD, Alzheon, Inc.

Poster Presentation (P65)
Title: *Beta Amyloid Anti-Oligomer Action of ALZ-801 and Clinical Dose Translation Analyses Support Confirmatory Phase 3 Program in Alzheimer's Disease*
Poster Session: Clinical Trials: Biomarkers
Date: Friday, November 3 and Saturday, November 4
Presenter: John A. Hey, PhD, Chief Scientific Officer, Alzheon, Inc.
Other Authors: Petr Kocis, PhD, Alzheon, Inc.; Susan Abushakra, MD, Alzheon, Inc.; Jeremy Yu, MD, PhD, Alzheon, Inc.; Aidan Power, MD, Alzheon, Inc.; Kaj Blennow, MD, University of Gothenburg, Molndal, Sweden; Martin Tolar, MD, PhD, Alzheon, Inc.

Alzheon Publications:
[1] Kocis et al. *CNS Drugs*, 2017
[2] Abushakra et al. *Journal of Prevention of Alzheimer's Disease*, 2016
[3] Abushakra et al. *Journal of Prevention of Alzheimer's Disease*, 2017
[4] Hey et al. *Clinical Pharmacokinetics*, 2017

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