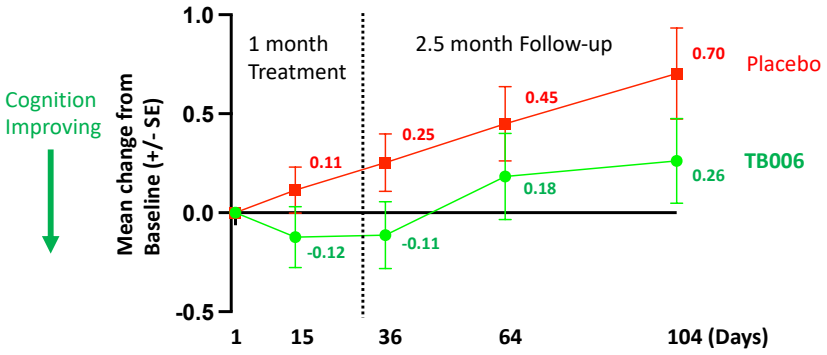
TrueBinding Announces Results of TB006 Phase 1b/2 Placebo Controlled Proof-of-Concept Trial Showing Improvement on the Primary Cognition and Function Endpoint in Patients with Mild to Severe Alzheimer's Disease

- Top line data from a one-month TB006 treatment regimen shows improvements in Clinical Dementia Rating-Sum of Boxes (CDR-SB) in patients, indicating the potential of slowing or reducing clinical decline
- Key secondary endpoints were consistent with the primary findings that TB006 improved cognition and function in patients
- Those cognition improvements were accompanied by reductions of amyloid beta (Aβ) 42 plasma levels
- TB006 treatment was well-tolerated with only minor adverse events (AEs), no treatment related serious adverse events (SAEs), and no imaging-related abnormalities

FOSTER CITY, CA, Nov. 18, 2022 -- TrueBinding Inc. a clinical-stage biotherapeutics company focused on pioneering the development of innovative monoclonal antibodies for the treatment of some of the most challenging neurodegenerative diseases and other serious diseases, today announced top line results from its Phase 1b/2 proof-of-concept trial of TB006, an investigational monoclonal antibody against Galectin-3 for the treatment of mild to severe Alzheimer's disease (AD) with baseline Mini Mental State Examination (MMSE) scores of 2-24). The primary endpoint (CDR-SB*, a patient and caregiver combined assessment) showed improvement that trended toward significance (p=0.08), a startling finding given the one-month treatment duration. Key secondary endpoints also showed improvements that reached or trended toward statistically significant results.

TB006 vs placebo greatly reduces CDR-SB through D104 (p=0.08)



	TB006	n= 67	65	66	63	63
	Placebo	n= 72	70	69	69	69

Responders (%) at D36 (≥ 1 point reduction from baseline)	TB006	n=	17 (25.4%)*
	Placebo	n=	7 (9.7%)
			*p=0.016

Following a short regimen of five doses given weekly using a placebo control, TB006 showed a reduction on the primary endpoint of a change from baseline through day 104 on the global cognitive and functional scale, CDR-SB, compared to placebo (through 75 days after the last dose). The data showed a treatment difference of 63 percent versus placebo, which represents a score change of -0.44 points (p=0.08); indicating a trend toward improvement in clinical function of patients in the analysis of the Intent-to-treat (ITT) population. At two and five weeks after initiation of treatment, TB006 and placebo reached -0.12 and 0.11, and -0.11 and 0.25, respectively, change from baseline score, indicating improvement in the TB006 group on the CDR-SB. Additionally, TB006 treatment demonstrated improvement on the secondary endpoint, the MMSE** with statistical significance (p=0.02) at Day 36. TB006 also significantly reduced Aβ 42 plasma levels, further evidence of an impact on the underlying disease.

“These are exciting data from our proof-of-concept trial in patients with Alzheimer’s disease, demonstrating that our novel monoclonal antibody, TB006, showed improvements in cognition and function after just one month of treatment,” said Dongxu Sun, Ph.D., Chief Executive Officer of TrueBinding. “TB006 inhibits Galactin-3, which has a role in the formation of toxic protein oligomers that compromise normal neuronal function in the brain and lead to disease progression. We look forward to studying TB006 for a longer duration to investigate its potential to further improve cognition and functioning and perhaps reverse the course of AD.”

“After running numerous Alzheimer's disease trials for over a decade, I can say that this particular project has made a very positive impact on my staff and me,” said Pilar F Trueba, MD, Medical Director, Future Care Solution, LLC. “We've been able to see the improvement of Alzheimer's Disease symptoms of participants and have received great comments on behalf of the caregivers. When former participants were informed about the possibility of the open- label extension they were really excited to be able to continue receiving TB006 and were eager to enroll.”

“We've seen positive responses from patients and their caregivers and are encouraged that the results of the TB006 trial were promising enough for TrueBinding to pursue an open-label extension trial,” said Marshall L Nash, MD, CPI, FAPCR, FAHA, Accel Research Site Network-NeuroStudies, Medical Director-Chief Principal Investigator, Member Global Alzheimer Platform. “Patients with Alzheimer’s disease are in desperate need of therapies that do more than just slow disease progression and instead demonstrate improvements in cognition and function. We at Accel Research have capabilities in conducting early-stage trials and look forward to partnering with TrueBinding to further study TB006 as a potential novel treatment for patients with Alzheimer’s disease.”

TB006 was safe and well tolerated through the observation period of 3.5 months. The most common AE was infusion reaction. There were no safety signals detected with clinical laboratory evaluations, imaging, or ECGs. There were also no treatment-related serious adverse events.

The trial was a seamless Phase 1b/2 double-blinded, placebo controlled, multicenter study conducted at 15 active sites in the U.S. to assess the safety and short-term efficacy of TB006 in 157 patients with mild to severe AD. Patients who met clinical diagnostic criteria for AD and had a screening MMSE <24 with no confounding neurologic or psychiatric disease were eligible. Amyloid positivity was not required for study participation. In the Phase 1b portion, three groups (140 mg, 420 mg, 1,000 mg) of eight patients

received either weekly TB006 or placebo infusions in sequential ascending fashion for one month. In the Phase 2 portion, participants were randomized (1:1) to receive either TB006 (1,000 mg) or placebo weekly for one month. Other endpoints were the MMSE, neuropsychiatric inventory (NPI), CDR battery and plasma and imaging (MRI/PET) biomarkers. Cognition testing was performed at baseline and on days 15, 36, 64 and 104. Safety assessments were conducted at each visit.

TrueBinding will present the TB006 study results on December 2, 2022, at the Clinical Trials on Alzheimer's Congress (CTAD).

* **CDR-SB** is a numeric scale used to quantify the various severity of symptoms of dementia. Based on interviews of people living with AD and family/caregivers, qualified healthcare professionals assess cognitive and functional performance in six areas: memory, orientation, judgment and problem solving, community affairs, home and hobbies, and personal care. The total score of the six areas is the score of CDR-SB, and CDR-SB is also used as an appropriate item for evaluating the effectiveness of therapeutic drugs targeting the early stages of AD.

****The Mini Mental State Examination (MMSE)** is a tool that can be used to systematically and thoroughly assess mental status. It is an 11-question measure that tests five areas of cognitive function: orientation, registration, attention and calculation, recall, and language.

About Alzheimer's Disease

Alzheimer's disease (AD) is a chronic progressive neurodegenerative brain disorder. AD is the leading cause of dementia among older adults, affecting as many as 55 million patients worldwide[1] with an incidence expected to increase as the global population ages. AD is a type of dementia that begins with mild memory loss but eventually symptoms can become severe enough to affect other cognitive abilities that are required for daily living.

Major pathological hallmarks of AD include the formation of toxic oligomers in the brain involving the major proteins: amyloid beta (Aβ) peptides and phospho-tau, alpha synuclein, and ApoE4. Galactin-3 (Gal-3), an endogenous protein that is found at abnormally high levels in the brains of AD patients, has been shown to play a key role in AD pathology.[2] Gal-3 is involved in the sustained release of proinflammatory molecules, such as cytokines and chemokines which contribute to the toxic environment in the brain that drives the progression of AD[2]. Gal-3 binds to Aβ peptides, p-Tau and other amyloid proteins, and acts as a glue, causing these proteins, which normally exist as monomers, to bind and form toxic oligomers. These oligomers cause plaque deposits in the brain, inflammation, and direct toxicity to intact neurons; thereby resulting in cognition defect symptoms in AD patients. While there is currently no known cure for AD, Gal-3 inhibition may provide a multi-pronged approach to the treatment of AD.

About TB006

TB006 is a humanized monoclonal antibody that, based on preclinical data and early clinical studies, has the potential to improve cognition and functioning of patients with Alzheimer's disease (AD). In pre-clinical evaluations, Galectin-3 was shown to intrinsically promote the aggregation of Aβ and pTau proteins. In AD in vivo model studies, TB006 showed promising capabilities in significant reduction of the aggregation of Aβ/Tau proteins and neuroinflammation, and significant improvement of cognitive performance, which show potential therapeutic effect of TB006 in addressing underlying pathology and ameliorating the course of AD. Human safety of TB006 was established in a single, escalating dose safety

and tolerability study, where doses of up to 5000 mg were safe and well tolerated. In a Phase 1b/2 proof-of-concept trial in mild to severe AD patients, TB006 demonstrated statistically significant improvements in cognition and functioning. TB006 is currently being evaluated in a Phase 2 open-label extension trial in patients with AD and in a Phase 2 trial in patients with acute ischemic stroke.

About TrueBinding, Inc.
TrueBinding Inc. is a clinical-stage biotherapeutics company focused on pioneering the development of innovative monoclonal antibodies for the treatment of some of the most challenging neurodegenerative diseases, including Alzheimer's disease (AD), as well as stroke, oncology and other serious diseases. The company is focused on rapidly advancing its lead drug candidate, TB006, a humanized monoclonal antibody targeting Galectin-3, that is being evaluated in a Phase 2 open-label extension trial in patients with AD and in a Phase 2 trial in patients with acute ischemic stroke. For more information, visit www.truebinding.com.

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