TrueBinding Highlights the Potential of TB006's Unique Mechanism of Action as a Novel Approach for the Treatment of Alzheimer's Disease at the 15th Clinical Trials on Alzheimer's Disease (CTAD) Conference

- Novel antibody, TB006, demonstrated improvements in cognition and function and was well tolerated in a one-month Phase 1b/2 trial in mild to severe Alzheimer's disease (AD) patients
- TB006 also demonstrated improvements in PET and MR imaging, consistent with dissolution of toxic amyloid plaque shown in preclinical studies
- Ongoing open-label extension study with more than 100 participants is generating long-term safety and efficacy data

FOSTER CITY, CA, Dec. 06, 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, highlighted the unique method of action (MOA) of TB006, an investigational monoclonal antibody against Galactin-3 (Gal-3) for the treatment of mild to severe AD, at the recent 15th Clinical Trials on Alzheimer's Disease (CTAD) Conference.

Aβ, p-Tau and other pathogenic factors are not considered toxic when they exist as monomers; however, when they are aggregated and become oligomers, they become very toxic, which leads to neuronal death and neuroinflammation. Gal-3 has been shown to play a detrimental role in AD pathology by promoting the aggregation of Aβ, p-Tau, Apo-E4 and other pathogenic factors. In preclinical studies, TB006, a humanized monoclonal antibody, was shown to block Gal-3 and dissolve the toxic aggregates, which reversed disease progress in animal models of AD.

"Our monoclonal antibody, TB006, targets Gal-3, which acts as a glue and has a role in the formation of toxic protein oligomers that compromise normal neuronal function in the brain and leads to disease progression," said Dongxu Sun, Ph.D., chief executive officer of TrueBinding. "Unlike other antibodies in development that target the components of the aggregates, TB006 is unique in that it targets what may be the key nucleating factor for the aggregates to inhibit its activity. We are encouraged by the early clinical data and look forward to advancing our understanding of TB006 and its potential to improve cognition and functioning with an ambitious goal of potentially reversing the course of AD."

Dr. Sun continued, "Our Phase 1b/2 proof-of-concept trial demonstrated the potential of TB006 to improve cognition and function in patients with Alzheimer's disease with a short one-month weekly treatment regimen. Improvements in patient cognition and function were seen as early as 15 days after the first treatment, and continued through day 36, only diminishing once we stopped treatment with TB006. Notably, this efficacy was observed across the patient population, whose disease severity ranged from mild to severe. Beyond the quantitative clinical measures we track, we've also received an overwhelming number of touching personal stories from participating physicians and caregivers about the dramatic improvement in symptoms of trial participants and the hope they have for a safe and effective treatment for this debilitating disease."

"There is an immense need for disease modifying treatments that can help the more than 6.5 million patients diagnosed with Alzheimer's disease in the U.S," said Malisa Agard, MD, principal investigator, Conquest Research. "Unfortunately, our existing treatment options are quite limited, so I was excited to

review the data from the TB006 trial. Despite it being early-stage data, it gives me a great deal of hope in the potential of TB006 to help the millions of patients who are suffering now and, additionally, the millions more who are likely to develop this disease in the future."

Data from the Phase 1b/2 trial presented at CTAD and more information on the promising mechanism of action of novel antibody TB006 can be found on the TrueBinding website at www.truebinding.com.

In the Phase 1b/2 trial, administration of TB006 versus placebo reduced the Clinical Dementia Rating-Sum of Boxes (CDR-SB*) score, a patient and caregiver combined assessment, after just one month treatment. Through day 104, 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. Of note, at Day 36 TB006 versus placebo significantly improved not only Mini Mental State Examination (MMSE**) scores by 1.02 points (p=0.02), but also the percentage of responders (one or more points reduction of CDR-SB from the baseline, p=0.016). In addition, treatment with TB006 resulted in patient improvements across a range of disease severity, including within the difficult-to-treat moderate and severe patient population. In addition, TB006 significantly reduced Aβ 42 plasma levels and reduced amyloid plaques, further evidence of an impact on the underlying disease.

TB006 was safe and well tolerated through the observation period of 3.5 months. There were no treatment-related serious adverse events and no imaging-related abnormalities (ARIA). The most common adverse event (AE) was infusion reaction.

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.

An ongoing open-label extension study assessing monthly injections of TB006 at 4,000 mg in over 100 participants is generating long-term safety and efficacy data, with initial, interim data expected in the first quarter of 2023. A longer-term, 12-month, randomized, placebo-controlled Phase 2b trial is planned.

* **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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