March 25, 2019

For Immediate Release

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Otsuka's Subsidiary Avanir Pharmaceuticals Reports Phase 3 Data Evaluating Investigational AVP-786 for the Treatment of Moderate-to-Severe Agitation in Patients with Alzheimer's Dementia

Otsuka Pharmceutical Co., Ltd. (Otsuka) announces that its U.S. -based, indirect subsidiary Avanir Pharmaceuticals, Inc. (Avanir) reports results from the first study of its phase 3 clinical development program investigating the efficacy, safety and tolerability of AVP-786 (deudextromethorphan hydrobromide [d6-DM]/quinidine sulfate [Q]) for the treatment of moderate-to-severe agitation in patients with Alzheimer's dementia.

This study, which used the Sequential Parallel Comparison Design (SPCD), demonstrated a significant improvement on the primary endpoint on the Cohen-Mansfield Agitation Inventory for one of the two doses being evaluated; the other dose demonstrated numerical but not significant improvement on the SPCD analysis. Similar improvements were also observed on the key secondary endpoint. The most common adverse events in patients receiving AVP-786 versus placebo (greater than 5% incidence in either of the two doses of AVP-786) were falls, urinary tract infection, headache and diarrhea. Overall mortality during the study was low and none of the deaths were considered related to treatment.

"These initial data from the first phase 3 study are encouraging and we look forward to continuing to evaluate AVP-786 for the treatment of moderate-to-severe agitation in patients with Alzheimer's dementia as the clinical program progresses," said Sanjay Dubé, MD, vice president, Research & Development, head of Clinical Development & Scientific Strategy at Avanir. "Currently there is no FDA-approved treatment for agitation in patients with Alzheimer's dementia. Any advancement in the treatment and management of agitation in patients with Alzheimer's dementia would help to bridge the treatment gap in these patients. It is important to note that there are two additional phase 3 studies ongoing in the clinical development program, which use a conventional parallel-arm design, rather than the Sequential Parallel Comparison Design used in this first study. We will continue to analyze the full set of data from this first study and plan to communicate more about the results at the time of publication in a peer-reviewed journal," said Dr. Dubé.

An estimated 5.8 million people in the U.S. have Alzheimer's dementia. Over the course of the disease, many patients with Alzheimer's dementia will likely experience agitation, which is characterized by excessive motor activity, verbal aggression and physical aggression, that causes emotional distress to these patients. Symptoms of agitation place a serious burden on the people afflicted with the disease and their caregivers, significantly affecting their health-related quality of life for all concerned. Agitation has also been associated with increased risk of institutionalization and earlier progression to severe dementia.

About AVP-786 (deudextromethorphan hydrobromide [d6-DM]/quinidine sulfate [Q])

AVP-786 is a combination of deudextromethorphan hydrobromide (d6-DM) and quinidine sulfate (Q), a CYP2D6 inhibitor. Deuteration was observed to significantly reduce susceptibility to cytochrome P450 (CYP2D6) enzyme metabolism thereby increasing the bioavailability. AVP-786 is being studied in a phase 3 clinical development program as

a candidate for moderate-to-severe agitation in patients with Alzheimer's dementia. AVP-786 is also being investigated in patients with negative symptoms of schizophrenia and neurobehavioral disinhibition in traumatic brain injury.

About the Phase 3 Clinical Development Program

This initial 12-week, phase 3, multicenter, randomized, double-blind, placebo-controlled study employed the Sequential Parallel Comparison Design (SPCD). This study (15-AVP-786-301) enrolled 410 U.S. patients aged 50 to 90 with moderate-to-severe agitation and probable Alzheimer's dementia. Patients living in either community or institutional care settings were included in the study. Patients were randomized to one of two doses of drug or placebo in stage 1 of the treatment period (6 weeks); those randomized to drug in stage 1 continued their assigned drug treatment in stage 2 (6 weeks). Patients receiving placebo in stage 1 were re-randomized to either dose of drug or placebo in stage 2 in a 1:1:1 ratio; however, only placebo non-responders (identified by a priori criteria) were used in the SPCD analysis. An algorithm utilizing data weighted from both stages of the treatment periods was used to analyze the primary endpoint on the CMAI. The SPCD design is being utilized in clinical studies for neuroscience indications to mitigate against placebo response. There are two additional ongoing phase 3 studies (15-AVP-786-302 and 17-AVP-786-305) that use a conventional, parallel-group, placebo-controlled design.

About Avanir Pharmaceuticals, Inc.

Avanir is a pharmaceutical company committed to delivering innovative central nervous system (CNS) solutions to improve the lives of patients and their care communities. As part of our commitment, we have invested extensively in our pipeline and are dedicated to advancing CNS treatments in areas of high unmet medical need. For more information about Avanir, please visit http://www.avanir.com.