Pfizer Announces New Phase 1 Data From Two Novel Compounds For Alzheimer’s Disease At ICAD Annual Meeting

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Data Suggest Pfizer’s Humanized Anti-Amyloid Monoclonal Antibody was Well-Tolerated in Patients with Mild to Moderate Alzheimer’s Disease Safety Results from Dimebon in Combination with Donepezil Showed that Combination was Well-Tolerated

(BUSINESS WIRE)--Pfizer Inc announced today results from two Phase 1 safety studies, one of PF-04360365, a humanized anti-amyloid monoclonal antibody (mAb), and another of dimebon (latrepirdine*) in combination with donepezil HCl tablets, in patients with Alzheimer’s disease.1,2 Based on the Phase 1 study results, PF-04360365 has advanced into Phase 2.3 Dimebon (latrepirdine), being co-developed by Pfizer and Medivation Inc., is in Phase 3 development.4 These data were presented this week at the Alzheimer’s Association 2009 International Conference on Alzheimer’s Disease (ICAD) in Vienna, Austria.

A Phase 1, single-dose, dose escalation study (0.1 to 10 mg/kg) showed that the investigational compound PF-04360365 was well-tolerated in all patients, with no clinical or imaging evidence of vasogenic edema, and no new microhemorrhage or encephalitis reported to date in the ongoing follow-up period.1 In the Phase 1 dimebon (latrepirdine) study, results from a four-week, placebo-controlled trial of 24 patients on a stable dose of donepezil for at least 60 days showed that dimebon (latrepirdine) was well-tolerated when used in combination with donepezil.2 Alzheimer’s disease, a progressive and degenerative brain disease, is the most common type of dementia.5 Worldwide societal

costs associated with dementia were estimated to be $315.4 billion in 2005.6

“Alzheimer’s disease is a destructive illness and Pfizer is committed to lifting the burden of the disease on patients and those who care for them,” said Steven J. Romano, MD, vice president, Medical Affairs Head for Pfizer’s Primary Care Business Unit. “We are continuing to work with the global Alzheimer’s community to advance research in Alzheimer’s disease and currently have an investigational compound, dimebon (latrepirdine), in Phase 3 and two other compounds in Phase 2.”

Pfizer’s mAb PF-04360365 Well-Tolerated in Phase 1

Pfizer’s PF-04360365 is a highly selective and potent monoclonal antibody that targets the C-terminal end of the beta amyloid 1-40 peptide. It does not bind to the Amyloid Precursor Protein (APP), from which beta amyloid is derived, and which the body needs to function normally. This may contribute to a favorable risk/benefit profile, which will be further examined in long-term pivotal trials. This mAb has been designed to remove the toxic beta amyloid from the brain and potentially slow or halt Alzheimer’s disease progression.

In the Phase 1 double-blind, placebo controlled trial, patients with mild-to-moderate Alzheimer’s disease (n=37) were randomized to one of five study groups to receive PF-04360365 as a single two-hour intravenous infusion ranging from 0.1-10 mg/kg (n=26) or placebo (n=11).1 These patients were monitored for one-year, and to date, four of the five study groups have completed the one year observation period. Results showed PF-04360365 was well-tolerated over this dose range. Routine safety lab values were unremarkable and there were no safety signals from brain Magnetic Resonance Imaging (MRIs), electrocardiograms (ECGs), cognitive scales or physical/neurological examinations.1 While the one-year observation period is still ongoing, the most common adverse events observed to date were upper respiratory tract infection (n=10), headache (n=9), back pain (n=6) and diarrhea (n=5), and all were mild to moderate in severity.1

“We are encouraged by these preliminary safety results and look forward to studying the safety, as well as the efficacy, of PF-04360365 in Phase 2 multiple dose trials,” said Martin M. Bednar, MD, PhD, senior director and Pfizer clinical lead for the PF-04360365 program. “As we explore multiple compounds and mechanisms to treat Alzheimer’s disease, safety is of paramount importance given the vulnerability of the elderly population afflicted.”

Dimebon (latrepirdine) Shown to be Well-Tolerated in a Four-Week Combination Study

In another study presented earlier in the week, Medivation and Pfizer announced that the investigational drug dimebon (latrepirdine) was well-tolerated when used in combination with donepezil HCl tablets. In this Phase 1, four-week, placebo-controlled safety study, 24 patients with Alzheimer’s disease on a stable dose of donepezil for at least 60 days were randomized to receive dimebon (latrepirdine) or placebo for two to four weeks.2

The first group of patients enrolled (dimebon, n=9, placebo, n=5) underwent gradual dose-titration in one-week intervals ranging from 2.5 mg three times daily (TID) up to 20 mg TID, over one month. The second group of patients (dimebon, n=6, placebo, n=4) titrated from 10 mg TID for one week to 20 mg TID for one week. No serious adverse events were reported in the study.2 The most commonly reported adverse events compared to placebo were fatigue (dimebon, n=3/15, placebo, n=0), abdominal distension (dimebon, n=2/15, placebo, n=0), fall (dimebon, n=2/15, placebo, n=0), hyperkalemia (dimebon, n=2/15, placebo, n=1/9) and nightmare (dimebon, n=2/15, placebo, n=0). These events were mild to moderate in severity and resolved with continued treatment.2

In addition to PF-04360365 and dimebon (latrepirdine), Pfizer is investigating several other compounds targeting different pathways for the treatment of Alzheimer’s disease.

About Dimebon (latrepirdine)

Dimebon (latrepirdine) is an investigational compound for the treatment of Alzheimer's disease. Three Phase 3 trials are underway and two additional Phase 3 trials are scheduled to start later this year. CONCERT is a 12-month clinical trial examining the safety and efficacy of dimebon (latrepirdine) when added to donepezil in patients with mild to moderate Alzheimer’s disease, which recently began enrollment. CONCERT is designed to complement previous and ongoing studies evaluating the potential for dimebon (latrepirdine) to be used as monotherapy, as well as in combination with donepezil.

Based on preclinical studies completed thus far, dimebon (latrepirdine) is thought to potentially stabilize or improve mitochondrial function in a way that prevents neurons from damage and dysfunction. The mechanism of action of dimebon (latrepirdine) is thought to be distinct from currently available Alzheimer’s medications.

* Latrepirdine is the proposed generic (nonproprietary) name for dimebon.

About Pfizer’s Commitment to Alzheimer’s Disease

Alzheimer’s disease touches everyone. As the world population over age 65 grows rapidly, more people are at risk for this degenerative brain disease. Pfizer researchers are working diligently to find a way to help those affected by the disease. Building on a foundation of more than two decades of research, education and support for the global Alzheimer’s community, the company is investing heavily to advance understanding of the disease. Pfizer forms partnerships to develop novel therapies, supports policy initiatives that help ensure availability and access to treatments, and works collaboratively with academia and government on biomarker and diagnostic research initiatives to enable earlier Alzheimer’s diagnosis.

Pfizer is studying different compounds targeting various central nervous system pathways that may be able to better treat Alzheimer’s disease symptoms and/or modify its underlying causes. Four novel compounds in clinical trials include: dimebon (latrepirdine), an investigational compound believed to impact mitochondrial function currently in Phase 3 trials; an antagonist of the Receptor for Advanced Glycation End-products (RAGE) in Phase 2 trials in partnership with the Alzheimer’s Disease Cooperative Study (ADCS) group; a highly selective humanized anti-amyloid monoclonal antibody in Phase 2 trials; and a phosphodiesterase-9A (PDE9A) inhibitor, moving into Phase 2 trials. Pfizer is co-developing dimebon (latrepirdine) with Medivation, and the RAGE development program is a Pfizer-TransTech collaboration.

The Pfizer team is working with the global Alzheimer’s community to make a better future in Alzheimer’s disease a reality.

For more information on Pfizer’s Alzheimer’s disease studies currently enrolling, please call 1-800-718-1021.

DISCLOSURE NOTICE: The information contained in this release is as of July 15, 2009. Pfizer assumes no obligation to update any forward-looking statements contained in this release as the result of new information or future events or developments.

Dimebon and PF-04360365 are in the clinical development stages and not approved for the treatment of Alzheimer’s disease.

This release contains forward-looking information about dimebon, PF-04360365, and certain other compounds in clinical trials for Alzheimer’s disease, including their potential benefits and prospects for advancement within the Company’s research and

development pipeline, that involves substantial risks and uncertainties. Such risks and uncertainties include, among other things, the uncertainties inherent in research and development; decisions by regulatory authorities regarding whether and when to approve any new drug applications that may be filed for any such compounds as well as their decisions regarding labeling and other matters that could affect the availability or commercial potential of such compounds; and competitive developments.

A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2008 and in its reports on Form 10-Q and Form 8-K.

_____ 1 ICAD Submitted Abstract #O4-04-03. Safety and pharmacokinetics of the anti-amyloid monoclonal PF-04360365 following a single infusion in patients with mild-to-moderate Alzheimer's disease: Preliminary results. Oral presentation. July 15, 2009: 3:30-3:45 p.m. M. Bednar – Presenter. 2009 International Conference on Alzheimer's Disease (ICAD), Vienna, Austria. July 11-16, 2009. 2 ICAD Submitted Abstract #P1-254. A safety, tolerability and pharmacokinetic study of dimebon in patients with Alzheimer's disease already receiving donepezil. Poster Session. July 12, 2009: 12:30-3:00 p.m. P Tariot – Presenter. 2009 International Conference on Alzheimer's Disease (ICAD), Vienna, Austria. July 11-16, 2009.
3 ClinicalTrials.gov. Multiple IV Dose Study of PF-04360365 In Patients With Mild To Moderate Alzheimer's Disease. Available at: http://www.clinicaltrials.gov/ct2/show/NCT00722046. Accessed June 17, 2009.

4 ClinicalTrials.gov. Safety and Efficacy Study Evaluating Dimebon in Patients With Mild to Moderate Alzheimer's Disease on Donepezil (CONCERT). Available at: http://www.clinicaltrials.gov/ct2/show/NCT00829374. Accessed June 17, 2009.

5 Alzheimer's Association. What is Alzheimer's? Accessed at: http://alz.org/alzheimers_disease_what_is_alzheimers.asp? Accessed June 9, 2009.

6 Wimo A, Winblad B, and Jonsson L. An estimate of the total worldwide societal costs of dementia in 2005. Alzheimer's Dement. 2007;3:81-91.

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