FAU SCHMIDT COLLEGE OF MEDICINE
Florida Atlantic University

**Project summary for the NIH grant**

Dr James Galvin was recently awarded a $7.7 Million multiple-PI grant from the National Institute on Aging to study the efficacy of the gonadotropin-releasing hormone (GnRH) analogue Lupron for use in Alzheimer's Disease (AD). The three sites are NYU Langone Medical Center (Dr Tracy Butler), the University of Wisconsin (Dr Craig Atwood) and FAU (Dr Galvin). Lupron is currently FDA-approved for prostate cancer, endometriosis and uterine fibroids in adults and for central precocious puberty in children. We propose to confirm and extend results from a prior phase II study that demonstrated that Lupron halted cognitive and functional decline in a subgroup of women with mild-moderate AD who were also taking an acetylcholinesterase inhibitor (AChEI). Our objectives are to demonstrate the clinical EFFICACY of Lupron and elucidate Lupron's likely multiple mechanisms of action in AD using MRI, amyloid PET scans and plasma BIOMARKERS. These mechanisms include decreasing levels of Luteinizing Hormone (LH) based on extensive preclinical evidence that decreasing LH preserves cognition and decreases amyloid deposition and tau phosphorylation in animal models of AD, as well as new evidence that GnRH analogues may have important anti-inflammatory effects. We will **(1)** Conduct a three site, double-blind, randomized trial of Lupron (22.5 mg/12 weeks) compared with placebo to evaluate the changes over 48 weeks in cognition and function in women with mild-moderate AD who are also taking a stable dose of AChEI. We hypothesize that patients taking Lupron + AChEI will show a smaller pre- to post-treatment decline in cognition and function when compared to patients taking placebo + AChEI. **(2)** We will assess Lupron’s effect on structural and functional (ASL-MRI) neuroimaging biomarkers of AD. We hypothesize that patients who receive Lupron + AChEI will demonstrate less atrophy in AD-related brain regions and preserved hippocampal perfusion as compared to those who receive placebo + AChEI. **(3)** We will assess changes in plasma markers of inflammation. We hypothesize that patients taking Lupron + AChEI, as compared to those taking placebo + AChEI, will show decreased plasma pro-inflammatory cytokines. If this second phase II trial of Lupron + AChEI for AD is positive we will proceed to a phase III trial with the goal of gaining FDA approval for this novel combination therapy for AD. By re-purposing an existing medication, in combination with a current AD treatment, we will be able to build upon extensive previous research and development efforts, reducing the time frame and costs of making this promising therapy available to patients with AD. Results from this project have the potential for significant, near term clinical impact in patients currently suffering from or at risk of AD.