27 December 2016

To Whom It May Concern:

I am writing to wholeheartedly endorse Dr. Marilyn Carter. I can state with certainty that Dr. Carter established herself at the forefront of vitally needed research on neurological diseases such as Alzheimer's Disease (AD) and Huntington's Disease (HD); furthermore, her groundbreaking research into the causal nature of the APO3 amino group in AD symptomology and pathology has led to clinical trials in treatment of AD currently underway at the University of Michigan's Alzheimer's Disease Center, blazing a trail in the amelioration of symptoms-and potentially the cure-of AD.

To introduce myself, and to indicate my qualifications to recommend Dr. Carter, I was her PhD advisor at the Department of Neurosciences at Case Western Reserve University, Cleveland, Ohio. I hold a BA in chemistry and biochemistry and a PhD in neurosciences from the University of Michigan, Ann Arbor and have served as a postdoctoral fellow at Harvard University School of Medicine. As a neuroscientist, as editor of the *Journal of Neuroimmune Pharmacology,* and a senior member of the Professional Advisory Board of the Alzheimer's Association, I have followed Dr. Carter's work regarding the genetic causal factors of AD with both interest and excitement.

Doctor Carter holds a BS in zoology and MS in neuroscience from Taiwan University, Taipei, and a PhD in Neuroscience at Case Western Reserve University, serving as postdoctoral research fellow in neuroscience at the Center for Neurobehavioral Genetics, University of California (UCLA), Los Angeles. She has been published eleven times in peer reviewed journals, notably in the *Journal of Neural Transmitters*, *Journal of Neuroscience,* and *Neuron.* She has been cited by her peers in their scholarly works 1008 times to date.

During her graduate work, Dr. Carter conducted extensive research into the specific roles of ApoE in the formation of Aβ peptides, the key protein in formation of plaque, in the brains of AD patients. Aβ deposition and accumulation leads to diminution of synaptic function and to neuron loss which typifies the disease. Prior to her research, there was little understanding of the causal factors of AD and certainly no prospect of a cure. The only treatment available has been to mitigate some of the worst symptoms of AD in the short term.

Dr. Carter's study addressed the manifold and complex genetic causes of AD, revealing that heredity alone is not a determinant factor. Several patients were determined to have no AD gene, yet showed symptomology. Carter's studies confirmed that increasing ApoE levels, particularly since ApoE4 proliferation has been linked to as many as 50% of AD cases. Carter determined that ApoE-corresponding lipidation in the brain helps to reduce Aβ peptides, eventually retarding-and potentially curing-Alzheimer's Disease.

Dr. Carter's clinical studies with mouse models isolated BXR as a key factor in the formation of Aβ peptides. It was determined that treatment with Bexarotene reduced the proliferation of the BXR receptor, thus decreasing Aβ levels in mice, and therefore plague-related pathology. Mouse models treated with Bexarotene, an FDA approved drug for the treatment of subcutaneous T-cell lymphoma, showed a marked amelioration of Alzheimer's related deficits in overall memory, cognition, and social behaviors.

The fact that the treatment is currently undergoing Phase II clinical trials speaks eloquently of the vital import of her work and its potential impact on American health. Dr. Carter's most recent research into treatment of AD has already been reported in *Wall Street Journal*, which has published a detailed discussion of her research into AD. Dr. Carter's article in *Science* ("ApoE-directed therapeutics improve symptoms in AD mouse models", 2012) has been extensively cited, notably by Agapios et al. in the journal *Neuron* in 2015.

Alzheimer's Disease affects 40% of patients over age 85, an estimated 5.4 million people in the United States. Prior to Dr. Carter's work, there has been no prospect for treatment that would significantly reduce or delay symptoms of AD and/or effectively address a cure. By 2050, it is estimated that as many as 11 to 16 million Americans will be diagnosed with AD. Equally appalling is the cost: Treatment of Alzheimer's patients reached a staggering $183 billion in 2011. Worse, the cost is projected to increase to $ 1.1 trillion in 2050.

Again, before Dr. Carter's breakthroughs, there has been no realistic prospect for any comprehensive treatment to effectively ameliorate symptoms and/or delay the progression of AD and/or affect a cure. Dr. Carter has plowed new ground that has isolated the complex causality of AD at the genetic and molecular levels, and points to a realistic and clinically viable treatment, if not a complete cure to a disease which has baffled scientist since its discovery 100 years ago. Dr. Carter has achieved a feat unequalled by any other researcher. The impact this will have on the American health and in addressing the massive cost of patient care for AD cannot be overstated.

It is my great privilege to bring Dr. Carter's record of excellence and her numerous accomplishments to your attention. Without her leadership in the field, the medical and neurological research communities of the United States would be at a grave disadvantage in addressing one of the most dreaded and costly diseases to affect the United States, especially as our senior population continues to grow,

Thank you for your attention. Please consider me to be at your service to answer any additional questions you may have in regard to Dr. Carter's work and my own credentials.

Respectfully yours,