

## **Public Comment**

### **Robert Dickey**

My name is Rob Dickey and I am Senior Vice President at Hemispherx Biopharma, Inc. I would like to update you on two items that are relevant to the CFS community. The first is an analysis out of Harvard and the Centers for Disease Control and Prevention (CDC) on the economic cost of CFS and the second is just published data on Hemispherx's Phase III study in CFS with our investigational compound Ampligen.

The US government estimates that as many as 4 million adults in the United States suffer from CFS. This is roughly equivalent to the prevalence of Alzheimer's (5.4 million people) and 10 times larger than that of multiple sclerosis (400,000), a condition with similar functional impairment, also of unknown etiology, but with more than five FDA approved therapies. Presently, there is no approved therapy for CFS.

CFS occurs in all ethnic groups and races, and in countries around the world. It most often occurs in people age 40 - 59 and women are three times more likely than men to develop it. Published data have estimated that 14.3% of CFS sufferers have severe disease. Such patients are house-ridden, bed-ridden and when ambulatory may need to be in a wheelchair. CDC studies have shown that CFS can be as debilitating as multiple sclerosis, lupus, rheumatoid arthritis, heart disease, end-stage renal disease, chronic obstructive pulmonary disease (COPD) and similar chronic conditions. The more severely ill patients die prematurely, often from organ failure, cancer and heart disease or suicide.

Last year, the CDC and Harvard School of Public Health published an analysis based on a group of patients in Georgia where they calculated the economic burden for a CFS sufferer both in terms of additional healthcare expenditures and lost earnings which they estimated at \$11,780 per year per person. If it was assumed that the CFS patient population that was currently under care was 1 million, then the annual cost to society would be \$11.8 billion. The full cost assuming 4 million CFS sufferers would be \$47.1 billion per year.

Ampligen is an experimental therapeutic for CFS that is in advanced clinical development. Ampligen is a synthetic immunomodulatory double-stranded RNA compound that activates innate immunity and is a highly selective toll-like receptor 3 (TLR-3) activator. Ampligen meets the definition of a New Molecular Entity (NME). Ampligen, as an experimental therapeutic, has completed Phase I, Phase II and Phase III clinical studies but is not yet approved for commercial sale. It should be noted that the mechanism of action of Ampligen as a TLR-3 activator is shared in part with a TLR-4 activator, which has been approved as a component of a HPV vaccine (Cervarix) to prevent infection in adolescent populations.

Ampligen, an experimental therapeutic, has been tested in human clinical studies with more than 90,000 injections administered to more than 800 patients. Over 200 patients have received Ampligen for one or two years or longer. There is no indication of a specific adverse event that appears after long term Ampligen administration (i.e., greater than 1-2 years) which would limit a CFS patient's ability to continue treatment. No evidence of a dose-limiting organ toxicity has been observed in well-controlled clinical studies including hematologic, liver, or renal toxicity.

Transitory side effects such as mild flu-like symptoms and malaise, when seen, usually occur during the initial weeks of treatment and tend to subside on repeated administration. In addition to the clinical studies, Hemispherx has been conducting a Treatment Protocol under IND 39,250 since 1997.

Previously, Hemispherx published data showing that patients on Ampligen reduced their use of concomitant medications (Stouch et al. 2010. *J Applied Res* 10(3):80-87). In particular, there was a reduction in medications which prolong the QT interval by those patients. Prolongation of the QT interval is a risk factor for sudden cardiac death and arrhythmias and is associated with certain drugs often used by CFS sufferers which, as a side effect, prolong the QT interval.

In mid-March, Hemispherx announced the publication of a peer-reviewed article providing the results from our AMP-516 Phase III Clinical Trial in the online journal, PLoS ONE (Strayer et al. 2012. *PLoS ONE* 7(3):e31334). This study involved 234 severely debilitated CFS patients at 12 clinical sites in the US with disease greater than 12 months duration. The primary endpoint of the study was exercise tolerance, an endpoint which has been used to approve numerous drugs, including those for chronic congestive heart failure, chronic angina and pulmonary arterial hypertension (PAH). The improvement in exercise tolerance over placebo with those approved drugs on an intra-treatment group basis ranged from 4.1% (Remodulin) to 10.6% (Tracleer), both of which are for PAH. In the Hemispherx study, those patients on Ampligen who completed the 40 week study had an improvement of 14.0% and for the intent to treat population the improvement was 11.8%. On an intra-patient basis, patients on Ampligen improved an average of 21% compared to placebo.

In another analysis, the proportions of patients with exercise improvements of at least 25% and at least 50% were, respectively, 1.7 and 1.9-fold greater for the Ampligen group versus placebo (39% versus 23% ( $p=0.013$ ) and 26% versus 14% ( $p=0.028$ )). Further, an ad hoc continuous responder analysis which looked at response levels from 25% to 50% in 5% increments showed a significantly greater improvement in exercise tolerance for patients receiving Ampligen versus placebo at every 5% increment above 25%.

It is our understanding that the CFS patient community is seeking a stakeholder meeting with the FDA. As the sponsor of the most advanced experimental treatment for CFS, Hemispherx would be willing to participate should such a meeting take place.