IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Confirmation No.: 5197
LUKASHEV, Matvey E.	Art Unit: 1649
Appl. No. 12/526,296	Examiner: Ulm, John D.
§ 371(c) Date: January 13, 2011	Atty. Docket: 2159.3210001/JMC/M-R/U-S
For: **Treatment for Multiple Sclerosis** ***(As Amended)***	

Declaration of Katherine T. Dawson, M.D. Under 37 C.F.R. § 1.132

US Patent and Trademark Office
PO Box 1450
Alexandria, Virginia 22313-1450

Dear Sir:

I, the undersigned, Katherine T. Dawson, M.D. residing at 561 Canton Street, Westwood, MA 02090 declare and state as follows:

I. My Background

1. I am a Senior Director of Medical Research at Biogen Idec MA Inc. ("Biogen Idec"), the assignee of the currently pending application. I have seven years of experience in the clinical development of MS drug products. I was involved in the development of Tysabri® and was the medical director of the Avonex® program. Tysabri® and Avonex®, both parenteral therapies, are among the few currently-approved treatment options for MS patients. I am currently responsible for developing BG-12, a new oral MS therapy. A copy of my *curriculum vitae* accompanies this declaration as Exhibit A.

2. I have personal knowledge of the matters in this declaration – knowledge which is either first-hand, or derived from my experience in this field and from interacting with others on the BG-12 development team at Biogen Idec.

II. Long Felt Need for Oral Treatment of Multiple Sclerosis

3. Multiple sclerosis ("MS") is an autoimmune disease characterized by inflammation, myelin destruction, axonal damage and neuronal loss in the central nervous system and affects about 2.5 million people worldwide.

4. Patients with MS are typically treated with injectable medications. Despite the recent approval of one oral MS therapy, a substantial challenge remains to develop efficacious yet safe oral therapies to treat MS patients. As such, there is a high, unmet, long-felt need for oral therapies that are effective in treating MS.

5. In an attempt to address this high, unmet, long-felt need, Biogen Idec has completed Phase 2 and Phase 3 clinical trials to investigate BG-12 as an oral treatment for MS. The only active ingredient of BG-12 is dimethyl fumarate ("DMF").

III. The 480 mg DMF Per Day Dose is Unexpectedly Efficacious

A. Phase 2 Clinical Trial

6. In 2004, Biogen Idec initiated a Phase 2 six-month placebo controlled clinical trial of BG-12 in 10 countries and enrolled 257 patients with relapsing remitting MS (RRMS). The clinical trial included an additional six-month safety extension. Overall, ninety-one percent of the patients completed the placebo-controlled part of the Phase 2 clinical trial.

a. Men and women 18 to 55 years of age were eligible for the study if they had a diagnosis of RRMS and an Expanded Disability Status Scale ("EDSS") score (a well-known measure of the disabilities suffered by MS patients) between 0.0 and 5.0. Additionally, the patients had to have had at least 1 relapse within 12 months prior to randomization or gadolinium-enhancing (Gd+) lesions (Gd+ lesions in the brain are a well-known marker of MS) on brain MRI within six weeks of randomization.

b. The patients were randomly assigned to one of four treatment groups for 24 weeks: (a) 120 mg BG-12 once daily (120 mg/day); (b) 120 mg BG-12 three times daily (360 mg/day); (c) 240 mg BG-12 three times daily (720 mg/day); and (d) placebo.

c. The primary end point of the Phase 2 clinical trial was the sum of all new Gd+ lesions from four brain MRI scans obtained at Weeks 12, 16, 20, and 24. The number of Gd+ lesions is considered a surrogate end point for clinical efficacy and as such is accepted as a primary end point for a proof of concept study.

d. The secondary end points of the Phase 2 clinical trial included the cumulative number of new Gd+ lesions on scans from Weeks 4 and 24, the number of new or newly enlargingT2-hyperintense lesions at Week 24, and the number of new T1 hypointense lesions at week 24.

e. Additional end points included annualized relapse rate ("ARR") and disability progression as measured by EDSS.

7. The results of the Phase 2 clinical trial are reported in the peer-reviewed publication of Kappos, L., *et al.*, "Efficacy and safety of oral fumarate in patients with relapsing-remitting multiple sclerosis: a multicentre, randomised, double-blind, placebo-controlled phase IIb study,"

Lancet 372:1463-72 (2008) (Exhibit B); as well as in Kappos, L., *et al.*, "Efficacy of a novel oral single-agent fumarate, BG00012, in patients with relapsing-remitting multiple sclerosis: results of a phase 2 study," 16th Meeting of the European Neurological Society (presentation given on May 30, 2006) (Exhibit C); Kappos, L., *et al.*, "Efficacy of a novel oral single-agent Fumarate, BG00012, in patients with relapsing-remitting multiple sclerosis: results of a phase II study," 16th Meeting of the European Neurological Society (abstract to presentation given on May 30, 2006) (Exhibit D); and "Oral Compound BG-12 Achieves Primary Endpoint in Phase II Study of Relapsing-Remitting MS with BG-12 Led to Statistically Significant Reductions in MRI Measures," Biogen Idec News Release (May 30, 2006) (Exhibit E).

a. Only the patients who were administered 720 mg/day DMF exhibited a statistically significant effect on the primary endpoint vs. placebo. Patients in this dose group showed a 69% decrease ($P<0.001$) in the mean number of new Gd+ lesions over MRI scans Weeks 12 to 24 as shown in Figure 1 below.

17. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the present patent application or any patent issued thereon.

Respectfully submitted,

Katherine T. Dawson

Date: Oct 13, 2011

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