UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MYLAN PHARMACEUTICALS INC.,
Petitioner,

v.

BIOGEN MA INC.,
Patent Owner.

Case IPR2018-01403
Patent 8,399,514 B2

DECLARATION OF EVA KUBALA HAVRDOVA, M.D., PH.D.

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I, Eva Kubala Havrdova, have personal knowledge of the facts stated herein and provide the following testimony:

I. Personal Background and Introduction

1. I am a Professor of Neurology at the First Faculty of Medicine, General University Hospital, Charles University in Prague, Czech Republic. I obtained my medical degree from the same university. My clinical specialization is in the area of neurology, including the treatment of diseases like multiple sclerosis (MS). I am a member of the MSIF International Medical and Scientific Board and the Czech Neurological Society Committee. Over the course of my career as a practicing neurologist, I have been involved in several clinical trials involving pharmaceuticals for the treatment of neurological conditions.

2. I understand that the U.S. Patent and Trademark Office has instituted an *Inter Partes* Review, IPR2018-01403, involving Biogen's U.S. Patent No. 8,399,514 ("the '514 patent").

3. I also understand that Mylan has submitted the following exhibits in the that proceeding:

- **Ex. 1007:** L. Kappos et al., *Efficacy of a Novel Oral Single-Agent Fumarate, BG0012, in Patients with Relapsing-Remitting Multiple Sclerosis: Results of a Phase 2 Study*, 253 (Supp. 2) J. Neurol. II27, O108 (2006)

- **Ex. 1046:** L. Kappos et al., *Efficacy of a Novel Oral Single-Agent Fumarate, BG0012, in Patients with Relapsing-Remitting*

Multiple Sclerosis: Results of a Phase II Study, 253 (16th Meeting of the European Neurological Society, May 20, 2006)

- **Ex. 1016:** NewsRoom document, *Oral Compound BG-12 Achieves Primary Endpoint in Phase II Study of Relapsing-Remitting Multiple Sclerosis; Treatment with BG-12 Led to Statistically Significant Reductions in MRI Measures* (May 30, 2006)

4. I provide this declaration based on my personal knowledge and my role in the Phase II trial of BG-12 for the treatment of MS.

II. My Role in the Phase II Trial

5. I was a member of the Scientific Advisory Committee, and the Czech Republic's Principal Clinical Investigator, for Biogen's Phase II trial of BG-12 for the treatment of MS. The information I received as a member of the Scientific Advisory Committee and investigator in Biogen's Phase II trial was confidential and non-public. This is standard practice for clinical trials.

6. Dr. Gilmore O'Neill was my primary contact for Biogen's BG-12 program. He was Biogen's Medical Director for the BG-12 MS program and the leader of the Phase II trial. Throughout the study, Dr. O'Neill and Biogen held several meetings of the Scientific Advisory Committee, either in-person or via phone, to discuss issues with the study as they came up. All of us on the Scientific Advisory Committee, as well as the numerous other people whose work went into

carrying out the clinical trial, worked under the direction and supervision of Dr. O'Neill and Biogen.

7. By the time I became involved in the Phase II study, around 2004, Biogen had already finalized the clinical trial protocol, including the selection of the three doses that would be tested: 120mg, 360mg, and 720mg. I was not involved in selecting those doses.

8. Dr. O'Neill and Biogen provided information and training for the Clinical Investigators, MRI technicians, and others involved in carrying out the clinical trial protocol. In September 2004, prior to the beginning of the study, Dr. O'Neill convened a meeting of the Clinical Investigators in Versailles, France that I attended. At that meeting, Dr. O'Neill and Biogen formally introduced us to the study plan and procedures and provided training to support the execution of the trial. The neurologists (including myself) were trained and certified on the Expanded Disability Status Scale (EDSS) by Dr. Kappos, whom Biogen had designated as "Coordinating Investigator." *See* Ex. 2089. MRI technicians were trained by Dr. David Miller's group. Dr. Miller was another member of the Scientific Advisory Committee. *See id.*

9. Throughout the Phase II trial, my job, like that of the other Clinical Investigators, was to oversee administration of the drug, monitor adverse events, and ensure compliance with all aspects of the protocol and applicable policies and

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