ADDITIONAL DISCLOSURE DATA FOR SWITZERLAND

Name of Sponsor/Company: Actelion Pharmaceuticals Ltd (a Janssen Pharmaceutical Company of Johnson & Johnson)

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Date: 20 Jan 2022

Swiss marketing authorisation data

Swiss Marketing Authorisation number: 68114

Swiss Marketing Authorisation date: 16 November 2021

Name of the preparation: Ponvory – 2+3+4+5+6+7+8+9+10+20 mg – filmcoated tablets.

Name of active pharmaceutical ingredient: Ponesimod (JNJ-67896153 / ACT-128800)

Clinical trial data

1. **Clinical trial identification**

Protocol No.: AC-058B201

Title of Study: A Multicenter, Randomized, Double-blind, Placebo-controlled, Parallel-group, Dose Finding Study to Evaluate the Efficacy, Safety, and Tolerability of Three Doses of Ponesimod (ACT-128800), an Oral Sphingosine 1-phosphate 1 (S1P1) Receptor Agonist, Administered for Twenty-Four Weeks in Patients with Relapsing-Remitting Multiple Sclerosis

Study Name: None

EudraCT Number: 2008-006786-92

NCT No.: NCT01208090

2. **Protocol change history**

Protocol and Amendments:

Original Protocol, 11 February 2009

Amendment-1, 26 October 2009– substantial

Amendment-2, 09 March 2010– substantial

3. Clinical trial investigators and study centres

Principal Investigator*:* Tomas Olsson, MD, PhD

Study Centres: 94 centers in 23 countries

4. Medication used

Test Product, Dose and Mode of Administration, Batch No.:

Ponesimod 10, 20 or 40 milligrams (mg) ACT-128800 free base as hard gelatin capsules was administered orally once daily for a period of 24 weeks. Ponesimod Batch Numbers: PD07071 and PD08129 for 10 mg; PD07072 and PD08130 for 20 mg; PD07073 and PD08131 for 40 mg.

Reference Therapy, Dose and Mode of Administration, Batch No:

Matching placebo capsules administered orally once daily for a period of 24 weeks. Batch Numbers: PD07069 and PD08127 for Placebo.

5. Study population

Number of participants – planned: 400

Number of participants – analysed: 464

6. Summary and conclusion

- The primary objective of demonstrating the efficacy of at least one of the three doses of ponesimod in patients with relapsing-remitting multiple sclerosis (RRMS) was met with a statistically significant decrease in the cumulative number of new T1 gadolinium-enhancing (Gd+) lesions on MRI at Weeks 12–24 for each ponesimod dose compared to placebo. There was clear dose-dependent relationship for the effect on the primary endpoint with a plateau of efficacy achieved with the 20 mg dose.
- The two-step study drug dose up-titration scheme was successful in minimizing the first dose effect of ponesimod on heart rhythm and conduction. The peripheral lymphocyte count reduction (mean % decrease of 46%–70%) was not associated with the occurrence of severe or serious infections during the treatment period. Treatment with Ponesimod was associated with dose-dependent decreases from baseline in Pulmonary function tests (PFTs), which were reversible upon treatment discontinuation. The magnitude of this decrease was highest in the 40 mg dose group and was associated with reduced tolerability due to dyspnea leading to treatment discontinuation in several patients. Based on the comprehensive analysis of efficacy, safety, and tolerability results of this Phase 2b study, further supported by modeling of dose/concentration-response relationships, a maintenance dose of 20 mg appears the most appropriate ponesimod dose for treatment of multiple sclerosis patients.

7. Results reporting

Date of Clinical Trial Report: 31 January 2013

Prepared by: Actelion Pharmaceuticals Ltd (a Janssen Pharmaceutical Company of Johnson & Johnson)

Publication(s) Reference(s):

- Olsson T, Boster A, Fernández Ó, Freedman MS, Pozzilli C, Bach D, Berkani O, Mueller MS, Sidorenko T, Radue EW, Melanson M. Oral ponesimod in relapsing-remitting multiple sclerosis: a randomised phase II trial. J Neurol Neurosurg Psychiatry. 2014 Nov;85(11):1198-208.

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