Phase III SUNBEAM and RADIANCE PART B trials for Ozanimod in relapsing multiple sclerosis demonstrate superiority versus interferon- β -1a (Avonex[®]) in reducing annualized relapse rates and MRI brain lesions

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“Celgene is committed to delivering life-changing solutions for patients suffering from severe diseases with significant unmet medical need, with MS being a key focus of Celgene’s research and development efforts.”

Biography: Volker Koscielny, MD, is the Vice President, Global Medical Affairs, for Inflammation and Immunology at Celgene. Volker trained as a doctor in his native Germany and worked for several pharmaceutical companies prior to joining Celgene in January 2015.

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Please could you introduce yourself, & tell us about your role at Celgene?

I am Volker Koscielny, MD, Vice President, Global Medical Affairs, for Inflammation and Immunology at Celgene. In this role, I am responsible for medical activities around and after the marketing authorization.

Two Phase III trials were presented at theECTRIMS–ACTRIMS conference in October 2017; the SUNBEAM[™] trial [1] & the RADIANCE[™] Part B trial [2]; could you briefly summarize the goals & end points of these trials?

Celgene has completed two Phase III studies of ozanimod in relapsing forms of MS (RMS). SUNBEAM is a pivotal, Phase III, multicenter, randomized, double-blind, double-dummy, active-controlled trial evaluating the efficacy, safety and tolerability of two doses of oral ozanimod (1 mg and 0.5 mg) against weekly intramuscular IF β -1a (Avonex[®]) after all patients completed a 12-month treatment period.

The primary end point of the SUNBEAM study [1] was annualized relapse rate (ARR) during the treatment period. The secondary MRI endpoints were number of new or enlarging hyperintense T2-weighted brain MRI lesions over 12 months, number of gadolinium-enhanced brain MRI lesions at month 12 and percent change from baseline in brain volume at month 12.

RADIANCE Part B [2] is a pivotal, Phase III, multicenter, randomized, double-blind, double-dummy, active-controlled trial evaluating the efficacy, safety and tolerability of two doses of oral ozanimod (1 and 0.5 mg) against IF β -1a (Avonex) over a 24-month treatment period.

The primary endpoint of RADIANCE Part B was ARR over 24 months. The secondary MRI endpoints were number of new or enlarging hyperintense T2-weighted brain MRI lesions over 24 months, number of gadolinium-enhanced brain MRI lesions at month 24 and percent change from baseline in brain volume at month 24.

What were the main results, in terms of ARR & imaging findings?

In SUNBEAM and RADIANCE Part B, ozanimod demonstrated statistically significant reductions in ARR, statistically significant reductions in new or enlarging T2 lesions, statistically significant reductions in gadolinium-

enhanced MRI lesions and a nominally significant reduction in brain volume loss compared with IFβ-1a (Avonex) [1,2].

In the SUNBEAM trial, a significant reduction in ARR was demonstrated for ozanimod 1 mg (ARR = 0.18; $p < 0.0001$) and for ozanimod 0.5 mg (ARR = 0.24; $p = 0.0013$) compared with IFβ-1a (Avonex) (ARR = 0.35) over an average of 13.6 months of treatment [1].

Ozanimod demonstrated a significant reduction in new or enlarging T2 lesions over one year for 1 mg (48%; $p < 0.0001$) and 0.5 mg (25%; $p = 0.0032$) compared with IFβ-1a (Avonex). A significant reduction in gadolinium-enhanced MRI lesions at one year was also demonstrated for ozanimod 1 mg (63%; $p < 0.0001$) and ozanimod 0.5 mg (34%; $p = 0.0182$) compared with IFβ-1a (Avonex) [1].

In the RADIANCE Part B trial, a significant reduction in ARR was demonstrated for ozanimod 1 mg (ARR = 0.17; $p < 0.0001$) and for ozanimod 0.5 mg (ARR = 0.22; $p = 0.0167$) compared with IFβ-1a (Avonex) (ARR = 0.28) over 2 years of treatment [2].

A significant reduction in new or enlarging T2 lesions was demonstrated for ozanimod 1 mg (42%; $p < 0.0001$) and 0.5 mg (34%; $p = 0.0001$) compared with IFβ-1a (Avonex). A significant reduction in gadolinium-enhanced MRI lesions was also demonstrated for ozanimod 1 mg (53%; $p = 0.0006$) and ozanimod 0.5 mg (47%; $p = 0.0030$) compared with IFβ-1a (Avonex).

How did the safety profile of ozanimod compare with that found in prior trials?

The overall safety and tolerability profile demonstrated in SUNBEAM was consistent with results from the previously reported Phase II RADIANCE Part A study in RMS. RADIANCE Part B demonstrated an overall safety and tolerability profile that was consistent with results from the previously reported Phase II RADIANCE Part A and Phase III SUNBEAM studies in RMS [1,3].

How is this new data significant for MS patients?

There is an arguably increased need for additional effective therapeutic options which have an acceptable safety profile, for use earlier in the treatment of RMS. Based on the Phase III results from SUNBEAM and RADIANCE Part B, we at Celgene believe that ozanimod has the potential to provide RMS patients and their physicians an additional oral option for treating this debilitating illness.

Looking forward, can you elaborate on Celgene's main areas of research focus in this area?

Celgene is committed to delivering life-changing solutions for patients suffering from severe diseases with significant unmet medical need, with MS being a key focus of Celgene's research and development efforts. Additional studies in MS are currently ongoing or under evaluation.

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