Glatiramer Acetate Depot (Extended-Release) Phase IIa Study in Patients with Primary Progressive Multiple Sclerosis: Safety and Efficacy Snapshot Interim Analysis

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Background

PPMS is characterized by worsening neurologic function from the onset of symptoms, without early relapses or remissions. Glatiramer Acetate (GA) Depot consists of extended-release microspheres containing GA, administered intramuscularly (IM) once every 28 days at a 40 mg and a 25 mg dose. Results from a large placebo-controlled phase III trial show that GA Depot effectively reduced clinical and radiological activity compared to placebo in patients with relapsing forms of MS (RMS), with significantly less frequent injections than subcutaneous GA. It is hypothesized that the IM administration route together with the slow-release formulation may result in an effect on primary progressive MS (PPMS) patients as well.

Objective

To assess the safety and efficacy of GA Depot in 30 PPMS patients, 20 in the 40 mg dose, 10 in the 25 mg dose, over a period of up to three years.

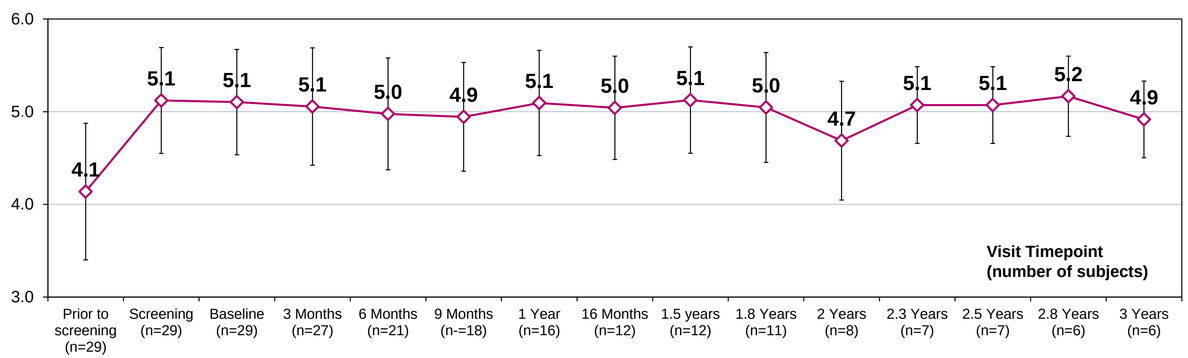
Design/Methods

Key eligibility criteria included: age 18-65, PPMS diagnosis with disease progression at a rate of ≥1 point EDSS score increase/year in the year prior to screening and a baseline EDSS score of 2.0 - 6.5. Safety was monitored through adverse events (AEs) and laboratory tests. Efficacy was assessed using EDSS, 9-Hole Peg Test (9HPT), Timed 25-Foot Walk (T25FW) and MRI volumetric analysis. The analysis also evaluated the proportion of patients with No Evidence of Progression (NEP), defined as the absence of worsening in EDSS (12-week Confirmed Disability Progression (CDP)), T25FW and 9HPT.

Results

This interim analysis provides data based on varying patient treatment duration. Mean EDSS score remained stable, with values of 5.1 at baseline and 4.9 at three years (Figure 1), and only one case of 12-week CDP. Additionally, 89.7% of patients maintained stability in the 9HPT, while 79.3% did so in the T25FW test (Table 1). Notably, 69.0% of patients exhibited NEP (Table 1). MRI volumetric analysis summarized in Table 2. Overall, 83% of the recorded AEs were mild. A trend of lower incidence and rates of AEs and injection site reactions (ISRs) was seen with the 25 mg dose vs. the 40 mg dose, with rates of 0.20 vs. 0.49 and 0.01 vs. 0.15, respectively. No unexpected AEs were reported. Three SAEs were recorded in the 40 mg dose: two were unrelated to study drug, one was possibly related. No SAEs were recorded in the 25 mg dose

Figure 1: Mean EDSS Score By Visit – All Subjects



Mean EDSS score is presented prior to study start, baseline and every 3 months thereafter. Data presented as mean ± SE.

Table 2: MRI Volumetric Analysis

Percent of whole brain volume change from baseline	GA Depot 40 mg (n)	GA Depot 25 mg (n)	All subjects (n)
V16 week 52	-0.90 (11)	-0.54 (6)	-0.77 (17)
Visit 28 week 100	-1.39 (6)	-1.85 (1)	-1.46 (7)
EOT visit 40 week 148	-2.14 (5)	0	-2.14 (5)
Percent of Neocortical volume change from baseline			
V16 week 52	-2.57 (11)	-0.66 (5)	-1.97 (16)
Visit 28 week 100	-3.03 (6)	3.54 (1)	-2.09 (7)
EOT visit 40 week 148	-3.30 (5)	0	-3.30 (5)

Table 1: No Evidence of Progression (NEP)

	GA Depot 40 mg n (%)	GA Depot 25 mg n (%)	All Subjects n (%)
No 12 weeks CDP	19/19 (100%)	9/10 (90%)	28/29 (96.6%)
No 12 weeks confirmed progression in T25FW of ≥20%	14/19 (73.7%)	9/10 (90%)	23/29 (79.3%)
No 12 weeks confirmed progression in 9HPT of ≥20%	17/19 (89.5%)	9/10 (90%)	26/29 (89.7%)
No Evidence of Progression (NEP)	**13/19 (68.4%)**	**7/10 (70%)**	**20/29 (69%)**

Conclusions

This Phase II Study interim analysis suggests that GA Depot is a safe and effective treatment for PPMS patients, showing a low rate of AEs and stable disability outcomes supporting a global Phase III study. Additionally, the data also suggests a favorable trend in safety and tolerability for the 25 mg dose of GA Depot compared to the 40 mg dose while maintaining similar efficacy.

Disclosures: Dr. Ron Milo, Dr. Anda Eilam, Prof. Adi Vaknin-Dambinsky, Dr. Mark Hellmann and Dr. Alla Shifrin, served as site Principal Investigators .Prof. Arnon Karni held a dual role as the study Coordinating PI and site PI.. Dr. Hadar Kolb is an external consultant to Mapi Pharma. Dr. Laura Popper, Dr. Nadav Bleich Kimelman, Dr. Shai Rubnov (co-inventor of GA Depot) and Uri Danon are employed by Mapi Pharma. Ehud Marom, co-inventor of GA Depot, is the founder and CEO of Mapi Pharma.

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