# Relationship between serum neurofilament-light chain and disease activity in relapsing MS: Observations from a phase 2 trial of IMU-838

## 37th Congress of the European Committee for Treatment and Research in Multiple Sclerosis


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### IMU-838
(Vidofludimus Calcium)

**Next-generation, small-molecular DHODH inhibitor for RRMS[1]**
- Optimized for human dihydroorotate dehydrogenase (DHODH) inhibition
- Lack of off-target effect on kinases
- Safety profile available from exposure to more than 800 humans

**Convenient pharmacokinetic profile[2]**
- Once daily oral application
- Serum half life in humans: ~ 30 hours
- Steady state trough level reached in 6-8 days
- Elimination from blood in most patients within 10 days without need for accelerated elimination procedure

### Study population

- Male or female, age ≥18 to 55 years
- RRMS diagnosis (revised McDonald criteria 2017)
- Evidence of disease activity based on relapse (1 relapse in last 12 months or 2 relapses in last 24 months) and MRI criteria (at least 1 Gd+ lesion in last 6 months before study)
- Baseline EDSS between 0 and 4.0

### Double-Blind, Placebo-Controlled, Randomized, Parallel-Group Trial

- To assess the effect of IMU-838 on disease activity, as measured by magnetic resonance imaging (MRI), as well as safety and tolerability
- Blinded main treatment period of 24 weeks
- Extended treatment period of up to 9.5 years to observe long-term safety
- MRI every six weeks (BL, W6, W12, W18, W24)

### Objective

To report the effect of IMU-838 on serum neurofilament-light chain (sNfL) and the relationship of sNfL to MRI measures of tissue injury.

### Methods

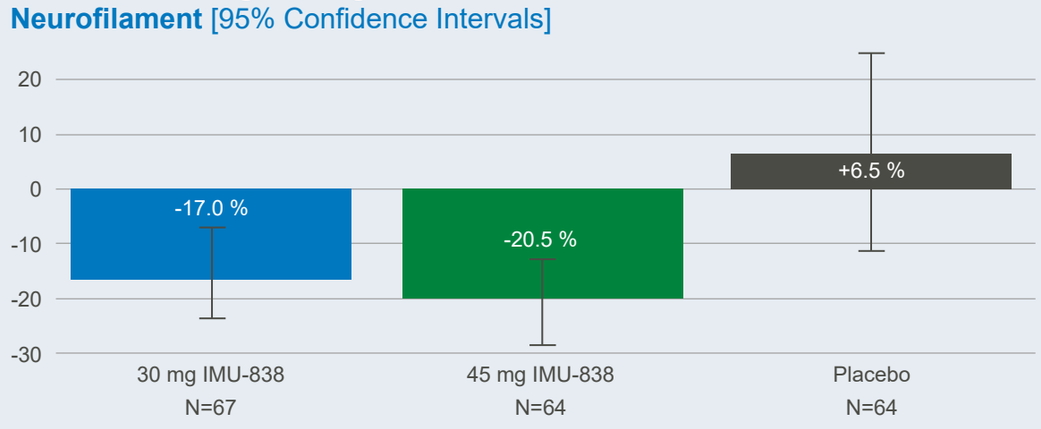
sNfL was measured using an electrochemiluminescent immunoassay (ECLIA, Meso Scale Discovery®) at baseline, Week 6, and Week 24. The assessments were done on the analysis set, including the following number of subjects in 30mg IMU-838, 45mg IMU-838 and placebo arms: $N_{30}$ = 71, $N_{45}$ = 69, $N_{PBO}$ = 69.

MRI scans were performed at Baseline and then every 6 weeks up to Week 24. MRI with field strength of ≥1.5 Tesla was used. Combined unique active (CUA) lesions are sum of the number of all new Gd-enhanced (Gd+) lesions on T1 weighted MRI and all new or enlarged lesions on T2-weighted MRI, without double counting.

## Results

Median percentage change from Baseline to Week 24 in sNfL indicated decrease in IMU-838 arms and slight increase in the placebo arm.

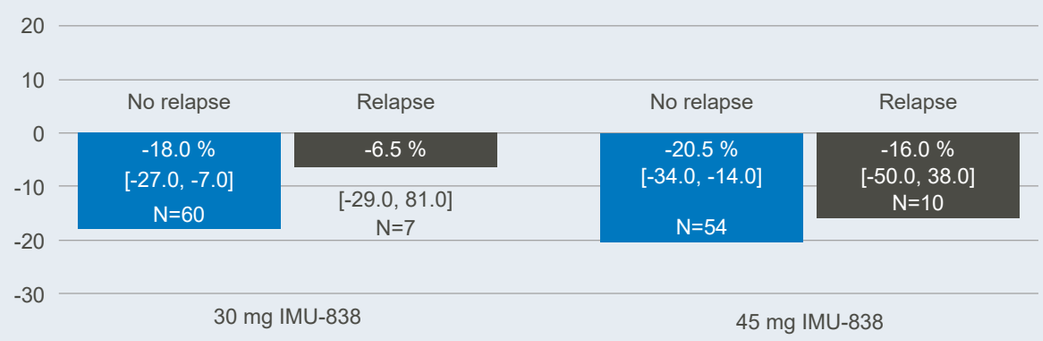
**Median Percentage Change from Baseline to Week 24 in Serum Neurofilament** [95% Confidence Intervals]




| | Median of differences between percentage change of serum neurofilament (Hodges-Lehmann estimation) | Lower 95% Hodges-Lehmann confidence bound | Upper 95% Hodges-Lehmann confidence bound |
|---|---|---|---|
| **45 mg IMU-838 vs. placebo** | -26.0 | -41.0 | -12.0 |
| **30 mg IMU-838 vs. placebo** | -18.0 | -33.0 | -3.0 |

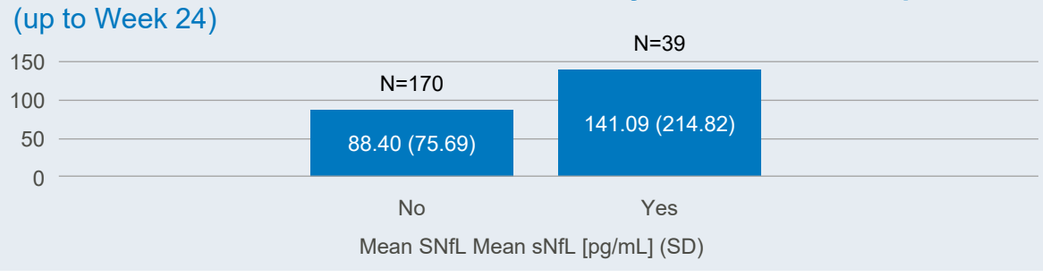
Decrease in serum NfL levels in IMU-838 arms were more prominent in those patients without relapse as compared to those with at least one relapse up to week 24.

**Median Percentage Change from Baseline to Week 24 in serum neurofilament by occurrence of relapses during main treatment period** [95% Confidence Intervals]



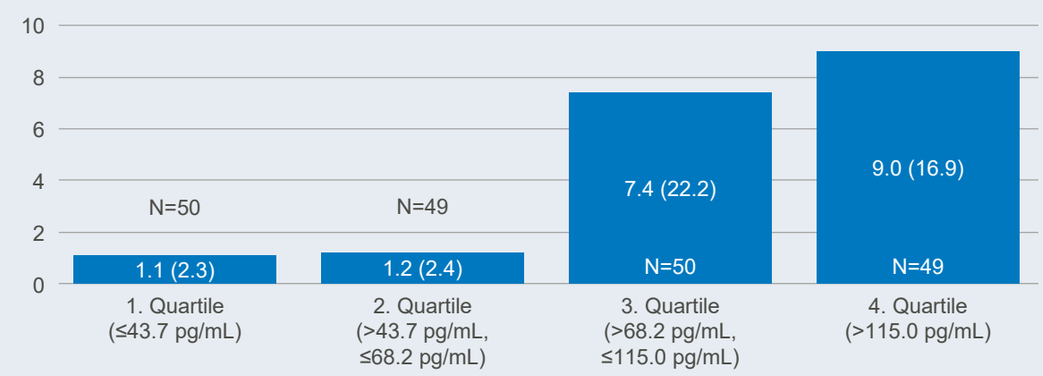

In all treatment groups combined, patients who experienced at least one relapse during the study had almost double mean sNfL at Baseline than patients with no relapse during the study.

**Mean sNfL at Baseline in all treatment arms by occurrence of relapses** (up to Week 24)




In all treatment groups combined, the lowest two quartiles of baseline sNfL had a lower mean incidence of cumulative CUA lesions at Week 24, than the highest two quartiles of baseline sNfL.

**Cumulative number of new CUA lesions from Baseline up to Week 24 by baseline serum neurofilament quartiles** (mean number of CUA lesions (SD))




## Conclusion

Treatment with IMU-838 was associated with reduction of NFL. Baseline levels and on-study changes and on-study changes in sNfL were associated with clinical and MRI measures of disease activity.

These results support NfL as a prognostic and treatment response biomarker that will be included in future clinical studies studies of IMU-838.


1 Muehler et al. Mult Scler Relat Disord. 2020;43:102129. doi:10.1016/j.msard.2020.102129
2 Muehler et al. Eur J Drug Metab Pharmacokinet (2020). https://doi.org/10.1007/s13318-020-00623-7