Safety and Clinical Efficacy Outcomes from the Long-Term Extension Study of Tolebrutinib in Patients with Relapsing Multiple Sclerosis: 2-Year Results

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INTRODUCTION AND PURPOSE

- Tolebrutinib is an oral, brain-penetrant inhibitor of Bruton's tyrosine kinase (BTK) currently under investigation as a potential treatment for MS[1]
- Tolebrutinib-induced BTK inhibition results in B-cell functional modulation rather than depletion[2,3]
  - FcγR activation of myeloid cells, including microglia, is also inhibited by tolebrutinib through durable occupancy of BTK[1]
- In a dose-finding Phase 2b trial (NCT03889639; DRI15928),[4] tolebrutinib 60 mg/day over 12 weeks was well tolerated and reduced formation of new contrast enhancing lesions and new or enlarging T2 magnetic resonance imaging (MRI) lesions by >85% versus placebo in participants with relapsing MS (RMS)
- The 60 mg/day dosage regimen is being assessed in the Phase 3 trials GEMINI 1 (NCT04410978) and GEMINI 2 (NCT04410991) for RMS,[3] and PERSEUS (NCT04458051) and HERCULES (NCT04411641) for progressive MS[5]
- LTS16004 (NCT03996291) is an ongoing long-term extension study of tolebrutinib in participants who completed the Phase 2b trial
- We report tolebrutinib's safety and efficacy at Week 96 (2 years) in the Phase 2b trial's long-term safety (LTS) extension

References:

1. Owens TD, et al. *Clin Transl Sci* 2022;15:442-50. **2.** Sanofi. Data on file. **3.** Reich DS, et al. *Lancet Neurol* 2021;20:729-38. **4.** Reich D et al. EAN 2020, Presentation O4010. **5.** Vermersch P, et al. EAN 2021, Poster EPO-455.

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CONCLUSIONS

- **90.5% of participants with MS who enrolled in the tolebrutinib LTS extension remained on study as of 7 March 2022**
- **ARR in participants on tolebrutinib 60 mg/day was low, and ~81% of participants were free of relapses**
- **Safety data from the LTS extension study continue to show favourable tolerability**
- **Longer follow-up in the ongoing extension, as well as data from the Phase 3 trials, will continue to build on the safety and efficacy profile of tolebrutinib for people with MS**

Through LTS Week 96, tolebrutinib 60 mg/day is associated with a low ARR and stable disability status

Safety

- The most common TEAEs were COVID-19, headache, nasopharyngitis, upper respiratory tract infection, cystitis bacterial, pharyngitis, and arthralgia
- LTS Part A: No dose effects for TEAEs or serious adverse events were observed
- LTS Part B: No new safety signals were observed for participants who switched to the 60 mg dose
- One participant (1%, on 5 mg/day) discontinued Part A due to progressive disease, and 10 discontinued Part B due to AEs (n=3 [2%])†, perceived lack of efficacy (n=3 [2%]),
- progressive disease (n=1 [1%]), emigration (n=2 [2%]), and participant decision (n=1 [1%])

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