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Press Release

Source: Sanofi (EURONEXT: SAN) (NASDAQ: SNY)

New long-term data reinforcing promising safety and efficacy profile of brain-penetrant tolebrutinib presented at ECTRIMS 2021

- One-year results from Phase 2b extension study of brain-penetrant tolebrutinib showed 98 percent of patients remained on treatment
- After 48 weeks, mean MRI lesion activity remained low in patients who started on or switched to tolebrutinib 60mg
- Data from *in vitro* studies in human microglia extended previous observations that BTK-dependent inflammatory signalling can be modulated by tolebrutinib

PARIS – October 13, 2021 - Sanofi's investigational oral Bruton's tyrosine kinase (BTK) inhibitor, tolebrutinib, demonstrated favorable one-year tolerability in a Phase 2b long-term extension study (LTS) in patients with relapsing forms of multiple sclerosis (RMS). The results showed that after 48 weeks of treatment, tolebrutinib reduced multiple sclerosis (MS) disease activity as measured by magnetic resonance imaging (MRI). These data are being presented as ePosters at the 37th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) on October 13 – 15, 2021.

> *"Understanding the ability of a brain-penetrant therapy to slow disability accumulation has the potential to bring new hope to people suffering from difficult-to-treat MS. For nearly two decades, Sanofi has been unwavering in its efforts to accelerate research and treatment options for these patients,"* says Erik Wallström, M.D., Ph.D., Therapeutic Area Head, Neurology Development at Sanofi.

Ninety-eight percent (122/125) of LTS-treated patients remained in the Phase 2b extension study through Week 48. The extension study was designed to evaluate the safety of tolebrutinib and provided the opportunity to evaluate efficacy parameters and report MRI outcomes. The LTS consisted of Part A, a double-blind treatment period where patients continued the same tolebrutinib dose as administered in the dose-finding study (5, 15, 30 or 60mg/day) and Part B, where all participants switched to the 60mg tablet (5/60mg, 15/60mg, 30/60mg, 60/60mg), which is the dose being tested in the Phase 3 trials.

> *"Results showed favorable safety and efficacy for tolebrutinib, and nearly all patients remained enrolled at the one-year mark of the long-term extension study,"* says Anthony Traboulsee, M.D., Professor and Research Chair, MS Society of Canada at University of British Columbia and Phase 2b Extension Study Investigator. *"Evaluating the impact BTK inhibitors can have on preventing*

disability accumulation is critical to addressing the needs of people living with MS. These long-term outcomes of tolebrutinib reinforce its potential as a new treatment option for MS patients."

Safety and Efficacy Outcomes:

- Safety data showed continued favorable tolerability of tolebrutinib and no new safety signals. The most frequent AEs were headache (10%), COVID-19 (9%), upper respiratory tract infection (8%) and nasopharyngitis (7%).
- At baseline, mean Expanded Disability Status Scale (EDSS) scores across treatment groups ranged from 2.18 to 2.65. Over 48 weeks of treatment, mean EDSS scores remained relatively stable in all treatment groups. For the 60/60mg treatment group, mean (SD) score was 2.65 (1.22) at baseline and 2.45 (1.31) at Week 48.
- Patients treated with tolebrutinib 60mg experienced low annualized relapse rate (ARR) of 0.17 (95% CI: 0.10, 0.29) over the 48-week treatment period. The majority of patients (89.5%) were free of relapses during this period. The relapse rate for these patients was 1.23 in the year prior to the Phase 2b study.

MRI Outcomes:

- At Week 48 of the extension study, the mean number of new Gd-enhancing lesions/scan remained low (<0.4) in the 60/60mg arm. Patients who switched to 60mg in Part B (Weeks 15-47) of the LTS experienced a reduction in Gd-enhancing lesions, approaching values observed in the 60/60mg treatment arm.

The company also presented data on the effect of tolebrutinib on human microglia that support its capacity to modulate neuroinflammatory processes directly within the central nervous system (CNS). Results from this study extended upon previous findings in mouse microglial cells to show that BTK-dependent inflammatory signalling in human microglia and tri-cultures can be modulated using tolebrutinib *in vitro*. This research contributes to an improved understanding of BTK signalling in neuroinflammation and how BTK inhibitors target the neuroinflammation believed to contribute to disability progression in people with MS. Tolebrutinib is the only BTK inhibitor in development for MS which has been shown to directly modulate microglia, based on publicly available information.

About tolebrutinib

Tolebrutinib is an investigational brain-penetrant Bruton's tyrosine kinase inhibitor that achieves CSF concentrations needed for targeting B lymphocytes and microglial cells, modulating neuroinflammation. Tolebrutinib is being evaluated in Phase 3 clinical trials for the treatment of relapsing forms of MS (RMS), non-relapsing secondary progressive MS (nrSPMS), and primary progressive MS (PPMS), and its safety and efficacy have not been confirmed by any regulatory authority worldwide. For more information on tolebrutinib clinical trials, please visit www.clinicaltrials.gov.

About Sanofi

Sanofi is dedicated to supporting people through their health challenges. We are a global biopharmaceutical company focused on human health. We prevent illness with vaccines, provide innovative treatments to fight pain and ease suffering. We stand by the few who suffer from rare diseases and the millions with long-term chronic conditions.

With more than 100,000 people in 100 countries, Sanofi is transforming scientific innovation into healthcare solutions around the globe.

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Sanofi Forward-Looking Statements
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December 31, 2020. Other than as required by applicable law, Sanofi does not undertake any obligation to update or revise any forward-looking information or statements.