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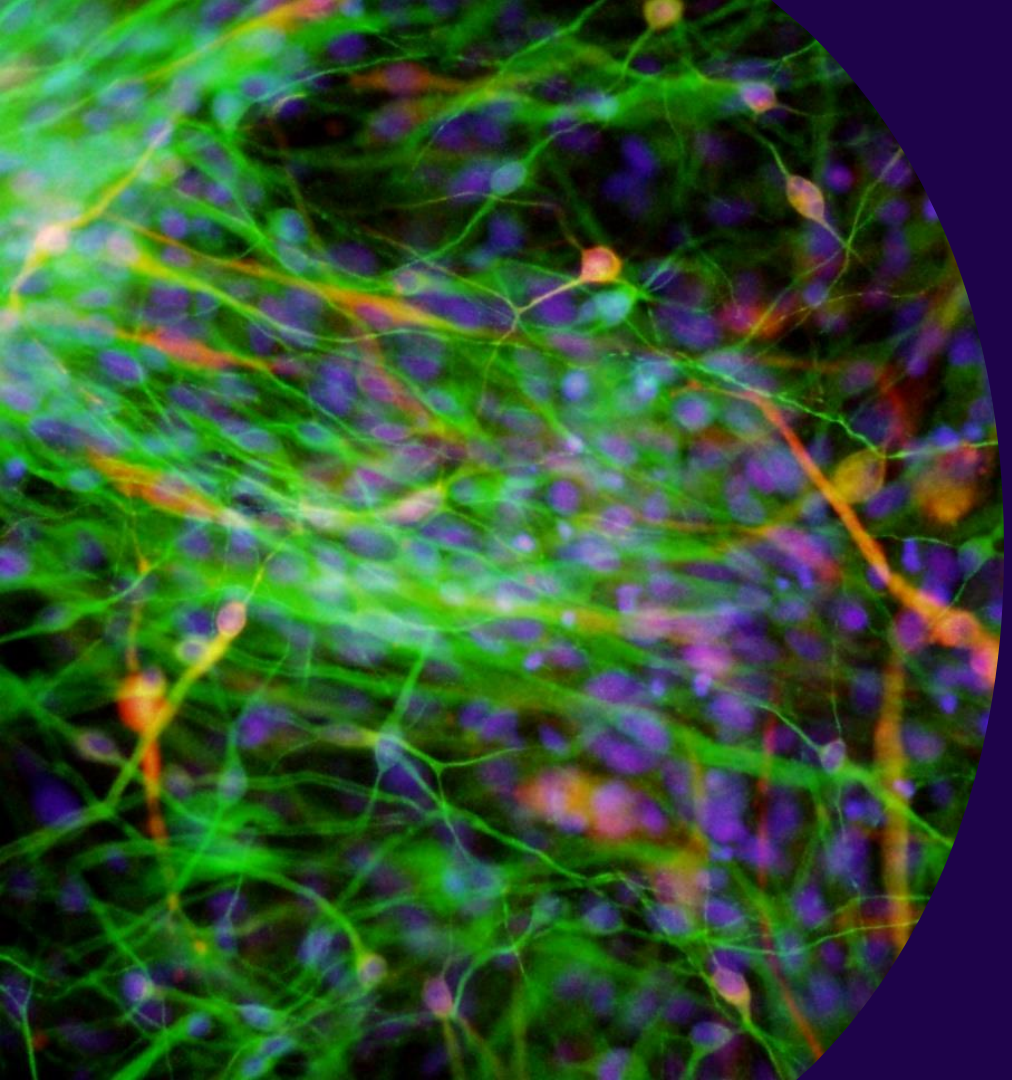

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ECTRIMS 2024

Investor science call

September 20, 2024

Forward-looking statements

This document contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, as amended. Forward-looking statements are statements that are not historical facts. These statements include projections and estimates and their underlying assumptions, statements regarding plans, business transformations, objectives, intentions and expectations with respect to future financial results, events, operations, services, product development and potential, and statements regarding future performance. Forward-looking statements are generally identified by the words "expects", "anticipates", "believes", "intends", "estimates", "plans", "potential", "outlook", "guidance" and similar expressions. Although Sanofi's management believes that the expectations reflected in such forward-looking statements are reasonable, investors are cautioned that forward-looking information and statements are subject to various risks and uncertainties, many of which are difficult to predict and generally beyond the control of Sanofi, that could cause actual results and developments to differ materially from those expressed in, or implied or projected by, the forward-looking information and statements. These risks and uncertainties include among other things, the uncertainties inherent in research and development, future clinical data and analysis, including post marketing, decisions by regulatory authorities, such as the FDA or the EMA, regarding whether and when to approve any drug, device or biological application that may be filed for any such product candidates as well as their decisions regarding labelling and other matters that could affect the availability or commercial potential of such product candidates, the fact that product candidates if approved may not be commercially successful, the future approval and commercial success of therapeutic alternatives, Sanofi's ability to benefit from external growth opportunities, to complete capital markets or other transactions and/or obtain regulatory clearances, risks associated with developing standalone businesses, risks associated with intellectual property and any related pending or future litigation and the ultimate outcome of such litigation, rends in exchange rates and prevailing interest rates, volatile economic and capital market conditions, cost containment initiatives and subsequent changes thereto, and the impact that pandemics, political disruption or armed conflicts or other global crises may have on us, our customers, suppliers, vendors, and other business partners, and the financial condition of any one of them, as well as on our employees and on the global economy as a whole. The risks and uncertainties also include the uncertainties discussed or identified in the public filings with the SEC and the AMF made by Sanofi, including those listed under "Risk Factors" and "Cautionary Statement Regarding Forward-Looking Statements" in Sanofi's annual report on Form 20-F for the year ended December 31, 2023. Other than as required by applicable law, Sanofi does not undertake any obligation to update or revise any forward-looking information or statements.

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Agenda

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Dr Jiwon Oh, MD, PhD, St. Michael's Hospital, University of Toronto, Toronto, Canada

03 **Tolebrutinib phase 3 in nrSPMS**
Dr Robert Fox, MD, Mellen Center for MS, Cleveland Clinic, Cleveland, USA

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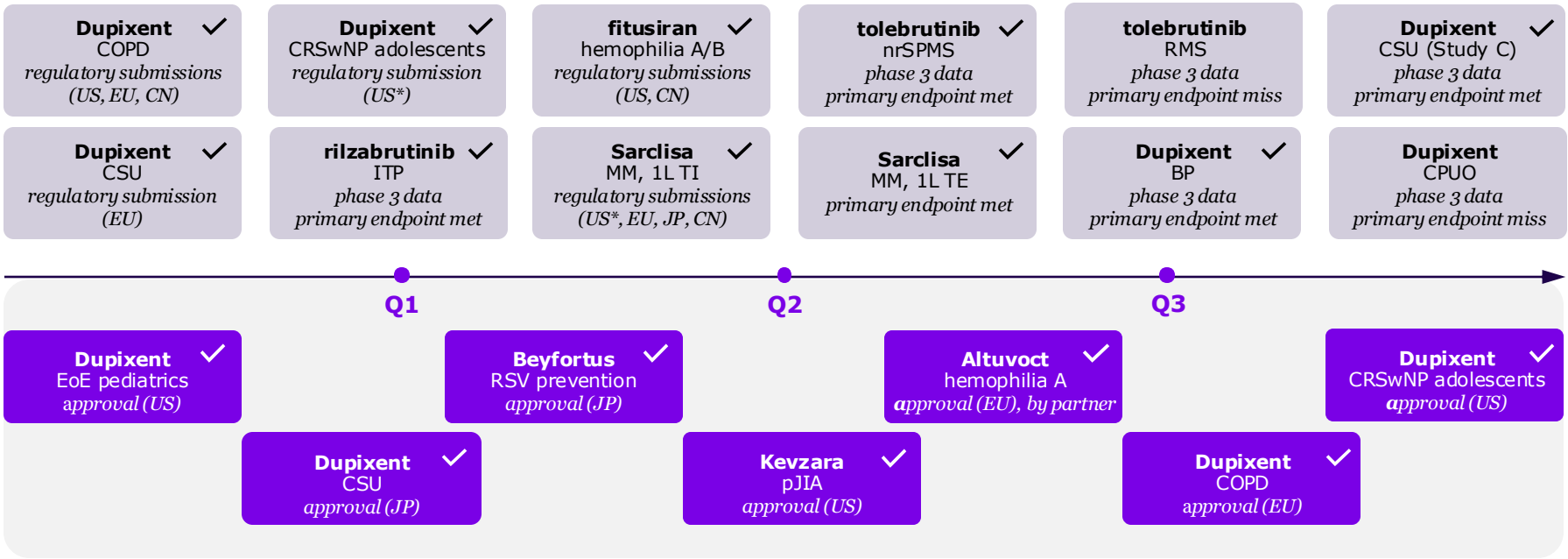
Houman Ashrafian, Executive Vice President, Head of Research and Development

05 **Q&A**
Presenters

YTD pipeline *news flow*: unlocking new patient benefits



Illustrative. *US priority review. For disease and indication abbreviations, please see the Q2 2024 results presentation. Current as of mid September 2024.

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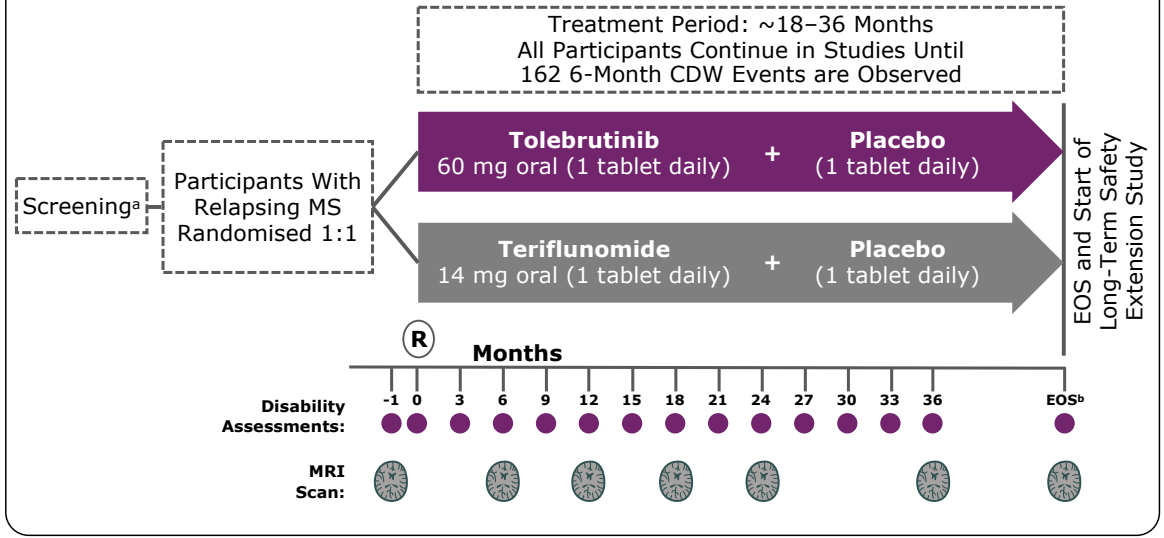
Tolebrutinib phase 3 in RMS

Dr Jiwon Oh, MD, PhD,
St. Michael's Hospital,
University of Toronto, Toronto, Canada

GEMINI 1 and 2: Study Design

Phase 3, Multicentre, Randomised, Double-Blind, Double-Dummy, Active-Controlled, Parallel-Group, Event-Driven Trials



Key Inclusion Criteria

- Age 18–55 years
- Diagnosis of relapsing MS
- EDSS score ≤5.5
- At least 1 of the following:
  - ≥1 relapse within previous year
  - ≥2 relapses within previous 2 years
  - ≥1 gadolinium (Gd)-enhancing T1 brain lesion on MRI within previous year

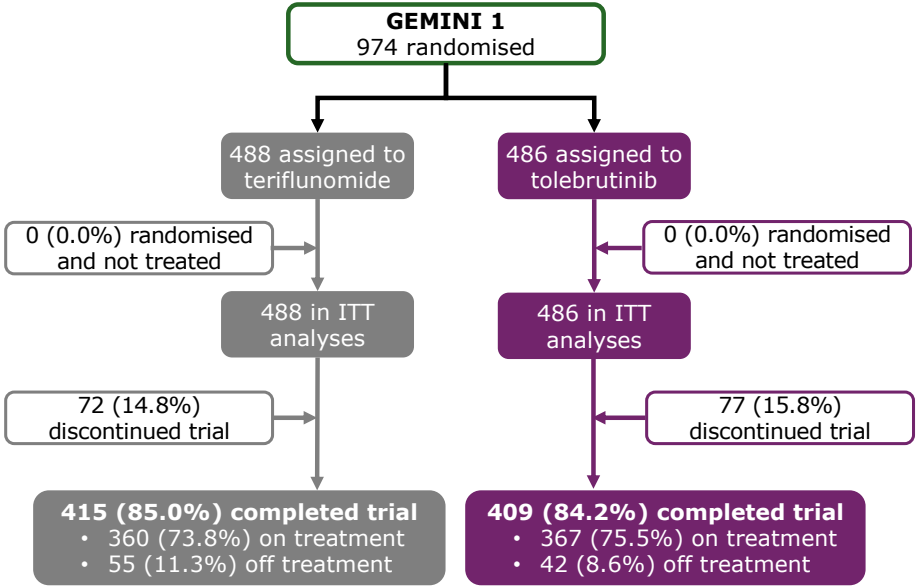
Key Exclusion Criteria

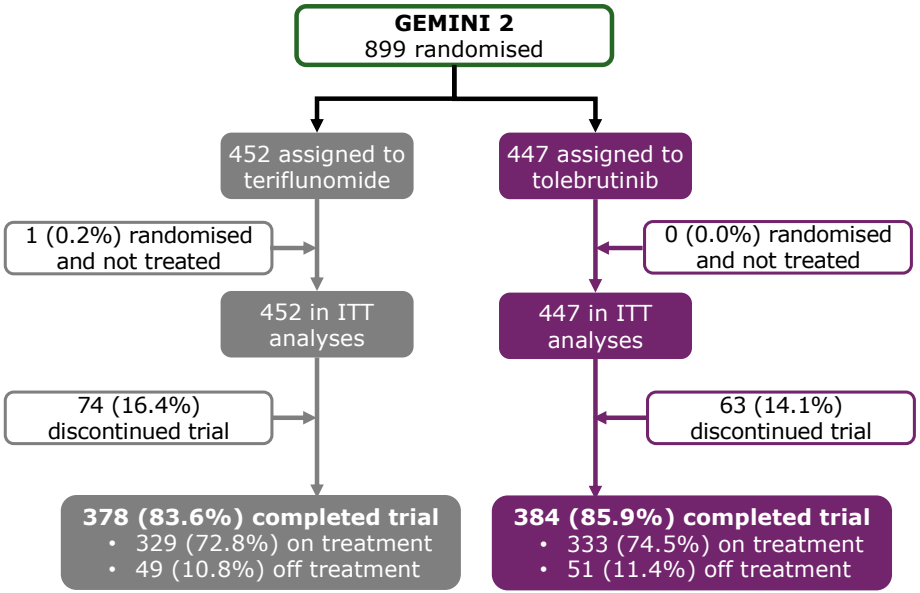
- Prior diagnosis of primary progressive MS or non-relapsing secondary progressive MS

[a]The 28-day screening period was considered Month –1. [b]EOS safety follow-up visit occurred 4 weeks after the last dose of study treatment for participants not entering the long-term safety study.

CDW=confirmed disability worsening; EDSS=Expanded Disability Status Scale; EOS=end of study; MRI=magnetic resonance imaging; R=randomisation.

Participant Disposition





ITT=intent to treat.

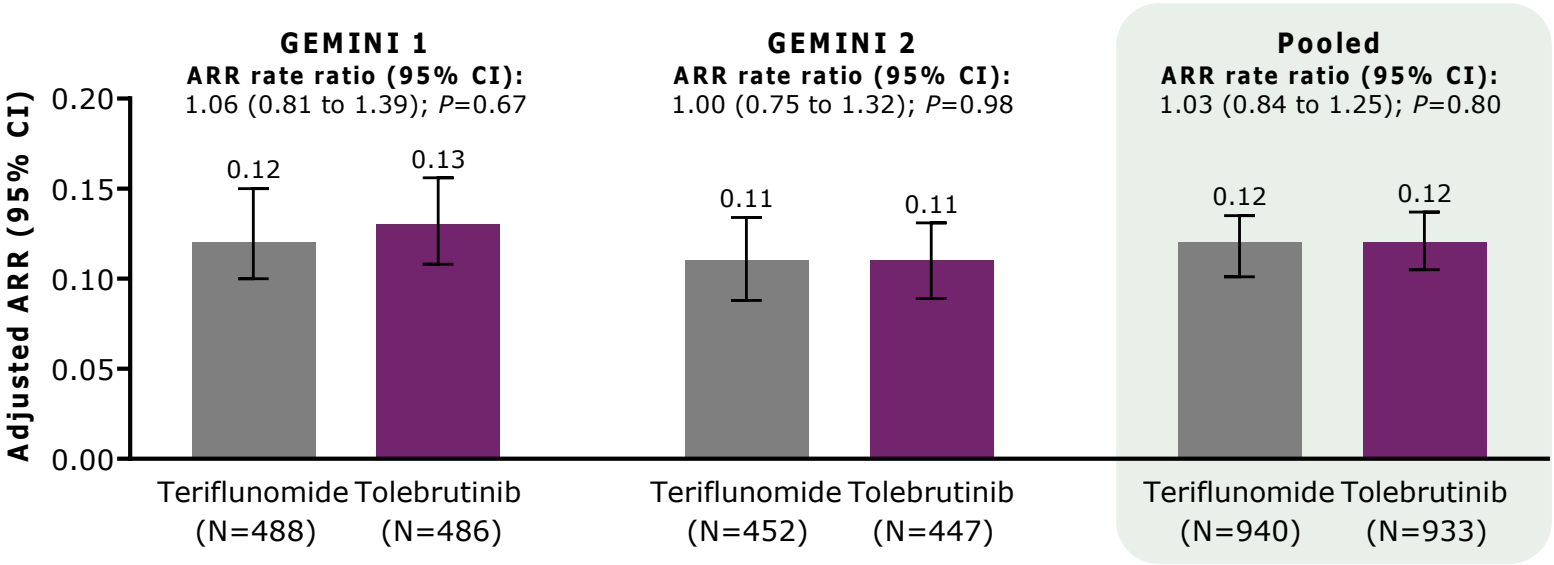
Baseline Characteristics

Characteristic	GEMINI 1		GEMINI 2	
	Teriflunomide (N=488)	Tolebrutinib (N=486)	Teriflunomide (N=452)	Tolebrutinib (N=447)
Age, years	36.6 (9.4)	36.8 (9.0)	36.1 (9.3)	36.6 (9.3)
Female, n (%)	325 (66.6)	334 (68.7)	293 (64.8)	300 (67.1)
MS subtype, n (%)				
Relapsing remitting	483 (99.0)	480 (98.8)	450 (99.6)	444 (99.3)
Secondary progressive	5 (1.0)	6 (1.2)	2 (0.4)	3 (0.7)
EDSS score[a]				
Mean (SD)	2.37 (1.20)	2.42 (1.19)	2.32 (1.19)	2.42 (1.17)
Median (IQR)	2.0 (1.5–3.0)	2.0 (1.5–3.0)	2.0 (1.5–3.0)	2.3 (1.5–3.3)
Time since relapsing MS symptom onset, years	7.1 (7.2)	7.3 (7.3)	5.9 (6.9)	6.2 (6.9)
Number of relapses within previous 1 year	1.2 (0.6)	1.2 (0.6)	1.2 (0.6)	1.1 (0.5)
Participants with ≥1 Gd-enhancing T1 lesion, n (%)	186 (38.4)	168 (34.7)	146 (32.6)	145 (32.4)
Number of Gd-enhancing T1 lesions	1.5 (4.2)	1.3 (3.7)	1.0 (3.2)	1.0 (2.4)
T2 lesion volume, cm^3, median (IQR)	10.7 (4.9–19.4)	11.6 (4.8–19.5)	7.7 (3.5–15.4)	8.3 (3.8–15.5)
Participants who were treatment-naïve, n (%)	291 (59.6)	315 (64.8)	300 (66.4)	301 (67.3)

- Baseline characteristics were well-balanced across both treatment arms and between trials

Values are mean (SD) unless otherwise indicated.
[a]Average of screening and randomisation EDSS scores.
EDSS=Expanded Disability Status Scale; Gd=gadolinium; IQR=interquartile range; SD=standard deviation.

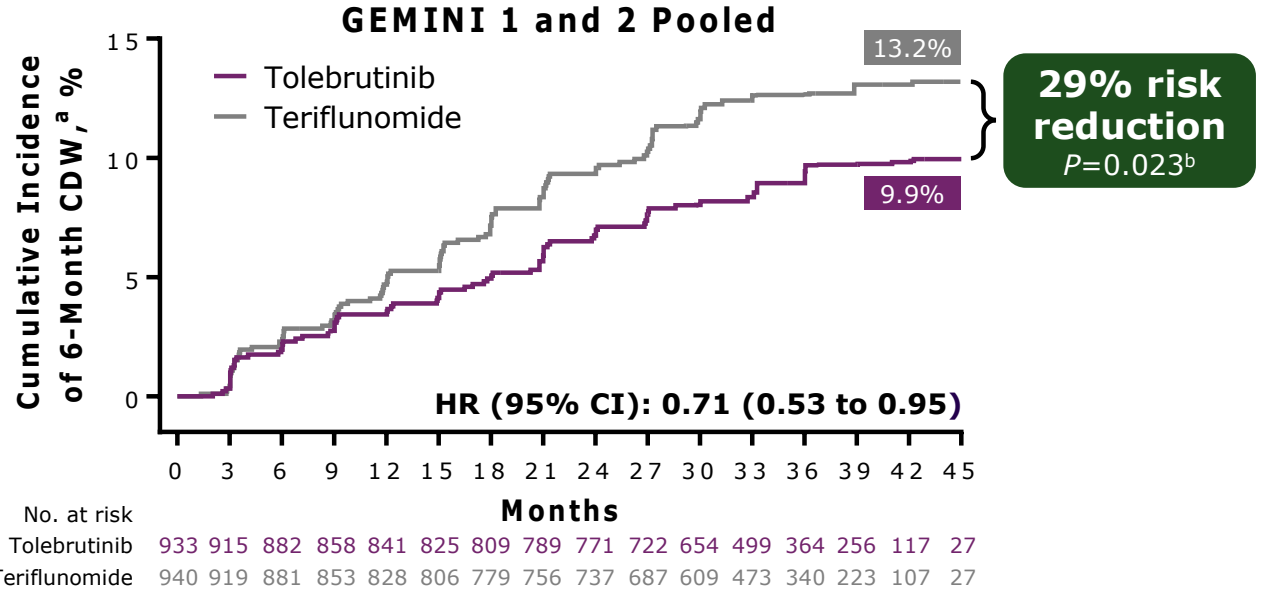
Primary Endpoint: Annualised Relapse Rate



- ARR was low in the teriflunomide arm in both GEMINI 1 and 2 and no difference was observed between tolebrutinib and teriflunomide

ARR=annualised relapse rate; CI=confidence interval.

Key Secondary Endpoint: Time to 6-Month CDW



- For 6-month CDW, tolebrutinib demonstrated clear separation from teriflunomide (29% relative risk reduction) in a population with very low relapse activity

[a]6-month CDW is defined as a sustained increase from baseline in EDSS score of ≥1.5 points when baseline score is 0, ≥1.0 points when baseline score is 0.5 to ≤5.5 or ≥0.5 points when baseline score is >5.5, confirmed over ≥6 months. [b]Nominal p-value (stratified log-rank test).

 CDW=confirmed disability worsening; CI=confidence interval; EDSS=Expanded Disability Status Scale; HR=hazard ratio.

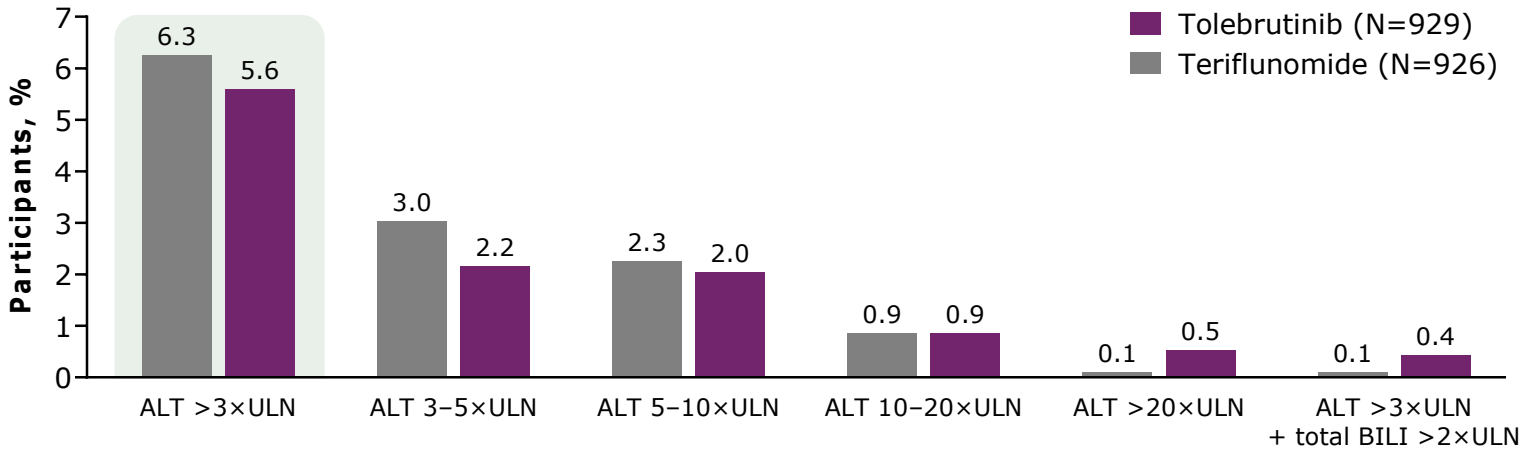
Adverse Events

Event, n (%)	GEMINI 1 and 2	
	Teriflunomide (N=939)	Tolebrutinib (N=933)
Any TEAE	810 (86.3%)	792 (84.9%)
Any serious TEAE	77 (8.2%)	91 (9.8%)
Any TEAE leading to treatment discontinuation	41 (4.4%)	42 (4.5%)
Deaths[a]	2 (0.2%)	1 (0.1%)
Most common TEAEs (≥5% in the tolebrutinib arm)		
COVID-19 infection	252 (26.8%)	225 (24.1%)
Nasopharyngitis	105 (11.2%)	119 (12.8%)
Headache	98 (10.4%)	117 (12.5%)
Upper respiratory tract infection	82 (8.7%)	77 (8.3%)
Alopecia	146 (15.5%)	73 (7.8%)
Urinary tract infection	57 (6.1%)	59 (6.3%)
Back pain	55 (5.9%)	58 (6.2%)
Viral upper respiratory tract infection	59 (6.3%)	50 (5.4%)

- Based on preliminary analysis, adverse events were generally balanced

[a]In the teriflunomide arm, 1 participant completed suicide by firearm and 1 participant died by fatal brain oedema and subarachnoid haemorrhage (both were assessed as unrelated to teriflunomide by the investigator). In the tolebrutinib arm, 1 participant died from homicidal gunshot wound that was assessed as unrelated to tolebrutinib by the investigator.
TEAE=treatment-emergent adverse event.

Liver Safety



- All cases of ALT >3×ULN resolved without sequelae
- A small (0.5%) proportion of participants in the tolebrutinib group experienced peak ALT increases of >20×ULN, all occurring within the first 90 days of treatment

ALT=alanine aminotransferase; BILI=bilirubin; ULN=upper limit of normal.

Conclusions

- There was no significant difference in ARR between tolebrutinib and teriflunomide
- Tolebrutinib demonstrated a 29% risk reduction in 6-month CDW vs. teriflunomide
- The number of new Gd-enhancing T1 lesions was higher in the tolebrutinib vs. teriflunomide arm
- Liver enzyme elevations (>3× ULN) were observed in 5.6% of tolebrutinib participants, a signal reported with other BTK inhibitors in MS
  - All cases resolved without sequelae
  - Frequent liver monitoring in the first 90 days has been implemented

Tolebrutinib showed a clear reduction in disability accumulation despite no differences in relapses vs. teriflunomide

These results are consistent with the hypothesis that acute focal inflammation and smoldering neuroinflammation are two distinct biological processes

ARR=annualised relapse rate; BTK=Bruton's tyrosine kinase; CDW=confirmed disability worsening; Gd=gadolinium; ULN=upper limit of normal.

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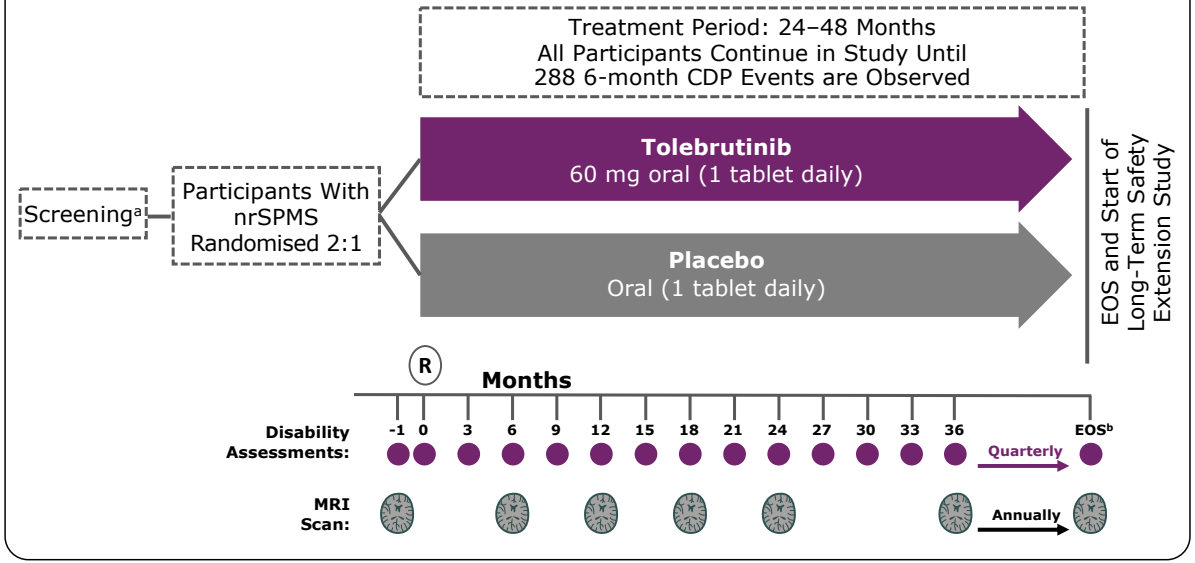
Tolebrutinib phase 3 in nrSPMS

Dr Robert Fox, MD,
Mellen Center for MS,
Cleveland Clinic, Cleveland, USA

HERCULES: Study Design

Phase 3, Multicentre, Randomised, Double-Blind, Placebo-Controlled, Event-Driven, Trial in Participants With nrSPMS

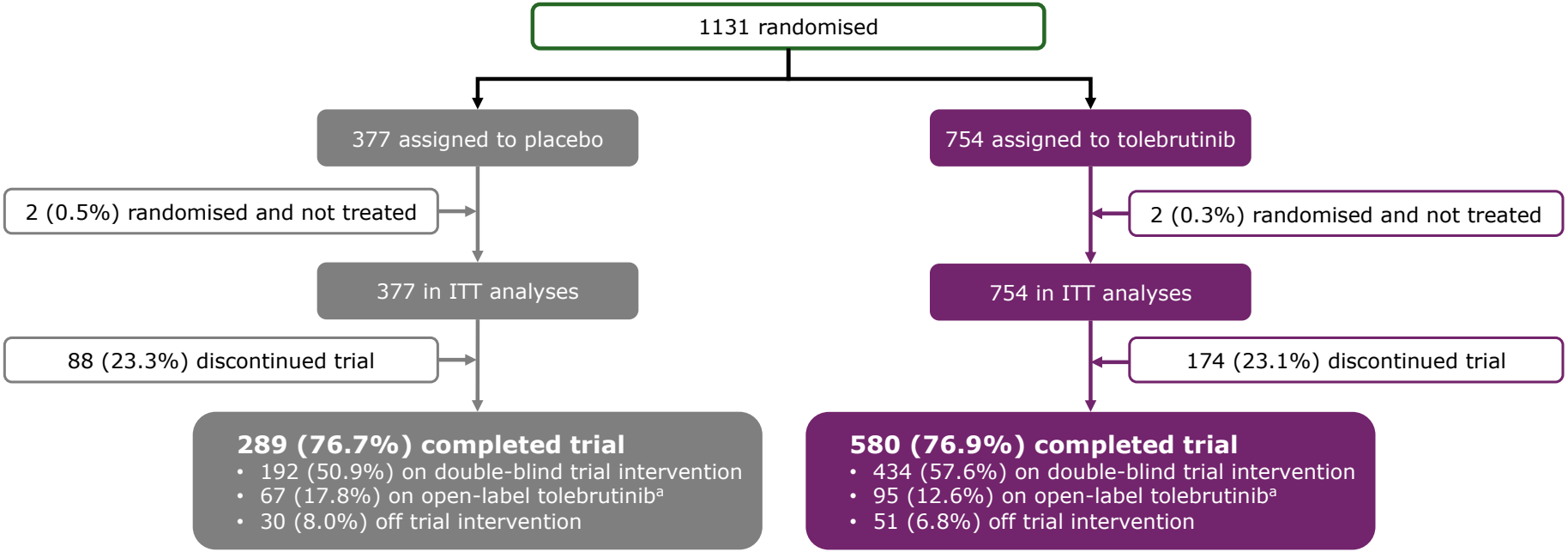


Key Eligibility Criteria

- Age 18–60 years
- Diagnosis of SPMS
- Absence of clinical relapses in the 24 months before screening
- Documented evidence of disability progression in the 12 months before screening
- EDSS score ≥3.0 and ≤6.5 at screening

[a]The 28-day screening period was considered Month –1. [b]EOS safety follow-up visit occurred 4 weeks after the last dose of study treatment for participants not entering the long-term safety study.
CDP=confirmed disability progression; EDSS=Expanded Disability Status Scale; EOS=end of study; MRI=magnetic resonance imaging; nrSPMS=non-relapsing secondary progressive MS; R=randomisation; SPMS=secondary progressive MS.

Participant Disposition



[a]Participants who experienced 6-month CDP were offered rescue treatment with open-label tolebrutinib.
CDP=confirmed disability progression; ITT=intent to treat.

Baseline Characteristics

Characteristic	Placebo (N=377)	Tolebrutinib (N=754)
Age, years	48.9 (8.0)	48.9 (8.0)
Female, n (%)	242 (64.2)	454 (60.2)
EDSS score[a]		
Mean (SD)	5.59 (0.94)	5.49 (0.99)
Median (IQR)	6.0 (5.0–6.3)	6.0 (4.8–6.3)
Time since relapsing remitting MS symptom onset, years	17.6 (8.4)	17.1 (8.3)
Time since most recent relapse, years	7.6 (5.5)	7.4 (5.3)
Participants with ≥1 Gd-enhancing T1 lesions, n (%)	49 (13.1)	93 (12.5)
Number of T2 lesions, median (IQR)	49 (33–75)	50 (35–73)
T2 lesion volume, cm³, median (IQR)	14.9 (7.5–28.3)	15.3 (7.2–25.8)
Participants with ≥1 prior DMTs, n (%)	288 (76.4)	549 (72.8)

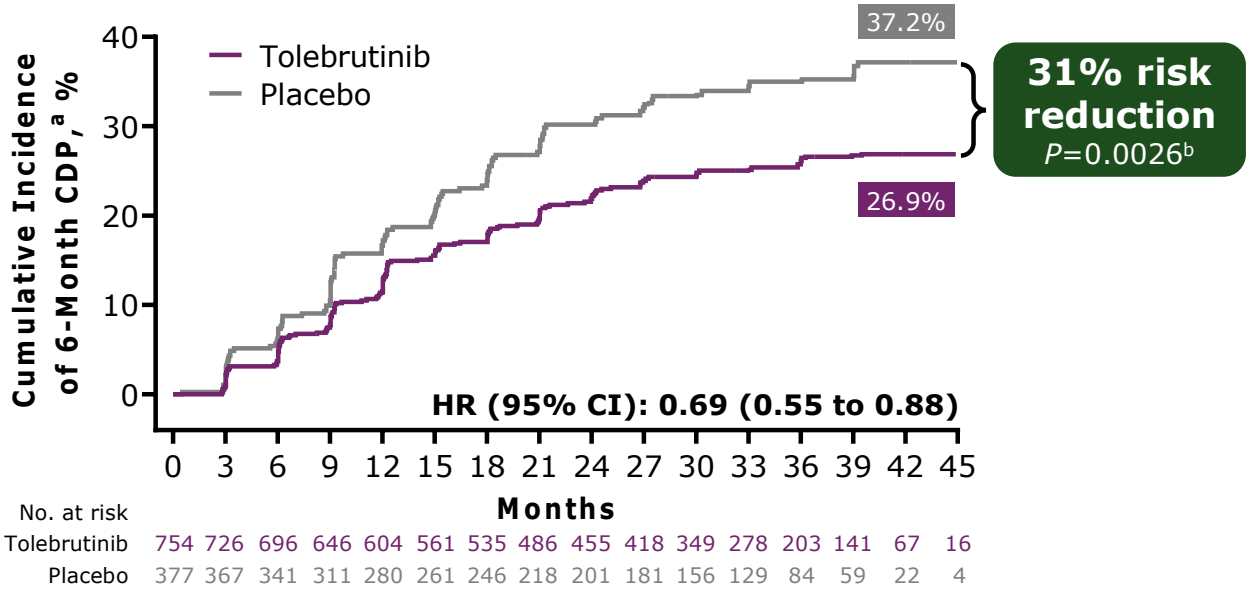
~50% of participants were ≤50 years

40% of participants had EDSS ≤5.5

- Baseline characteristics were well-balanced across both treatment arms

Values are mean (SD) unless otherwise indicated.
[a]Average of screening and randomisation EDSS scores.
[18]DMT=disease-modifying therapy; EDSS=Expanded Disability Status Scale; Gd=gadolinium; IQR=interquartile range; SD=standard deviation.

Primary Endpoint: Time to 6-Month CDP

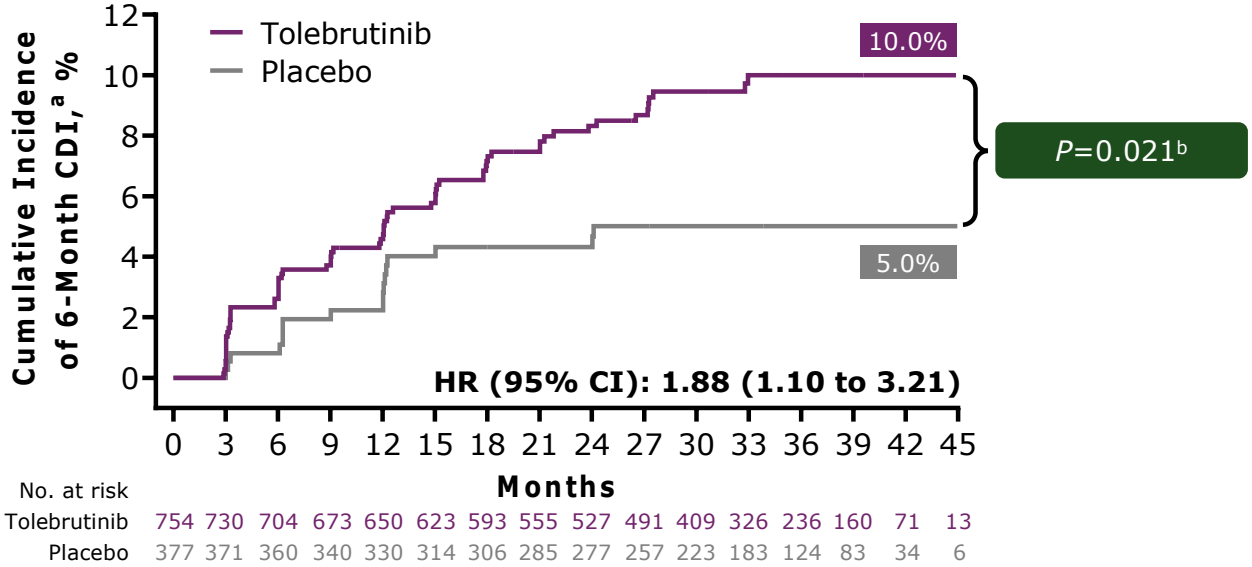


- Tolebrutinib demonstrated a significant effect on disability accumulation in a non-relapsing SPMS population

[a]6-month CDP is defined as an increase of ≥1.0 point from baseline EDSS score when baseline score is ≤5.0 or an increase of ≥0.5 points when baseline score is >5.0, confirmed over ≥6 months. [b]P-value is from Cox proportional hazards model.

 CDP=confirmed disability progression; CI=confidence interval; EDSS=Expanded Disability Status Scale; HR=hazard ratio.

Secondary Endpoint: Time to 6-Month CDI



- Proportionally more participants experienced CDI on tolebrutinib vs. placebo

[a]6-month CDI is defined as a decrease of ≥1.0 point from baseline EDSS score confirmed over ≥6 months. [b]Nominal p-value from Cox proportional hazards model.

[20] CDI=confirmed disability improvement; CI=confidence interval; EDSS=Expanded Disability Status Scale; HR=hazard ratio.

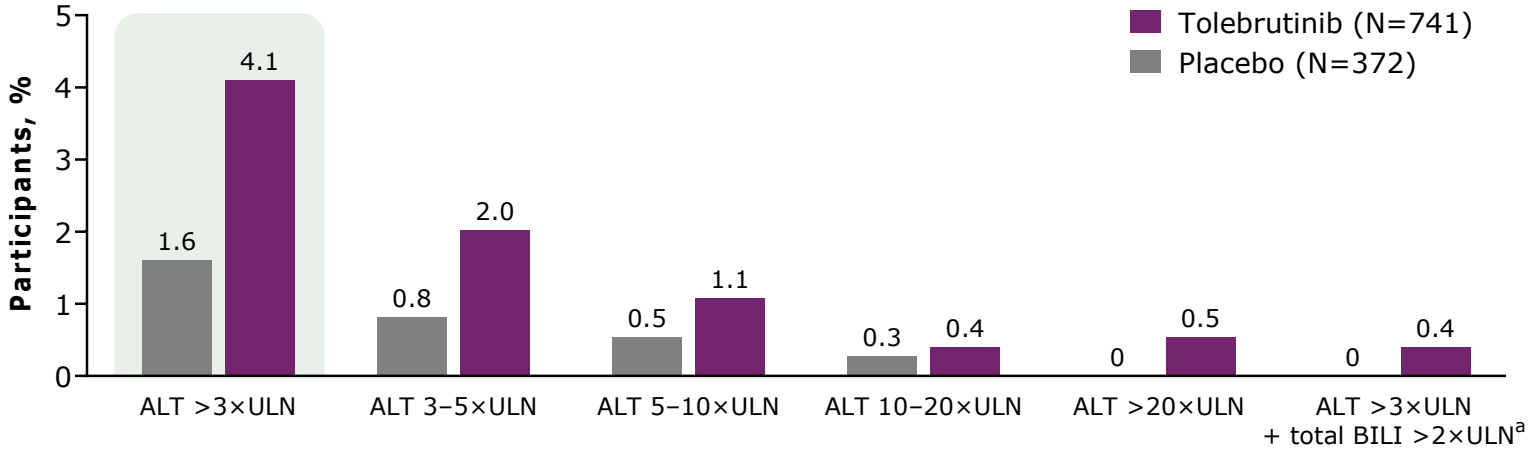
Adverse Events

Event, n (%)	Placebo (N=375)	Tolebrutinib (N=752)
Any TEAE	293 (78.1%)	613 (81.5%)
Any serious TEAE	39 (10.4%)	113 (15.0%)
Any TEAE leading to treatment discontinuation	11 (2.9%)	29 (3.9%)
Deaths[a]	1 (0.3%)	2 (0.3%)
Most common TEAEs (≥5% in the tolebrutinib arm)		
COVID-19 infection	85 (22.7%)	192 (25.5%)
Urinary tract infection	49 (13.1%)	85 (11.3%)
Fall	41 (10.9%)	72 (9.6%)
Nasopharyngitis	26 (6.9%)	70 (9.3%)
Headache	27 (7.2%)	54 (7.2%)
Arthralgia	19 (5.1%)	49 (6.5%)
Back pain	24 (6.4%)	47 (6.3%)
Influenza	13 (3.5%)	42 (5.6%)
Hypertension	11 (2.9%)	38 (5.1%)

- Based on preliminary analysis, there was a slight increase in the tolebrutinib arm in some adverse events, including respiratory infections, compared to placebo

[a]In the placebo arm, 1 participant died from cerebral oedema and haemorrhage due to a fall (assessed as unrelated to the placebo intervention by the investigator). In the tolebrutinib arm, 1 participant died due to post-operative complications of a liver transplant (assessed as related to tolebrutinib) and 1 participant completed assisted suicide (assessed as unrelated to tolebrutinib).
TEAE=treatment-emergent adverse event.

Liver Safety



- A small (0.5%) proportion of participants in the tolebrutinib group experienced peak ALT increases of >20×ULN, all occurring within the first 90 days of treatment and most resolving without sequelae

[a]One participant on tolebrutinib received a liver transplant and died due to post-operative complications. This case occurred prior to the implementation of a revised protocol with more stringent monitoring.

ALT=alanine aminotransferase; BILI=bilirubin; ULN=upper limit of normal.

Conclusions

- Tolebrutinib showed a 31% risk reduction in time to 6-month CDP vs. placebo (*P*=0.0026)
- Tolebrutinib increased the probability of achieving 6-month CDI vs. placebo
- Tolebrutinib significantly lowered the annualised rate of new/enlarging T2 lesions vs. placebo
- Liver enzyme elevations (>3x ULN) were observed in 4.1% of tolebrutinib participants, a signal reported with other BTK inhibitors in MS
  - The vast majority of cases resolved without sequelae
  - Frequent liver monitoring in the first 90 days has been implemented

HERCULES is the first trial to show a significant slowing of disability progression in people with nrSPMS – a population with a large unmet need

The totality of data from HERCULES and GEMINI indicate that tolebrutinib has a consistent impact on disability accumulation that may be largely driven by effects on smoldering neuroinflammation

BTK=Bruton's tyrosine kinase; CDI=confirmed disability improvement; CDP=confirmed disability progression; nrSPMS=non-relapsing secondary progressive MS; ULN=upper limit of normal.

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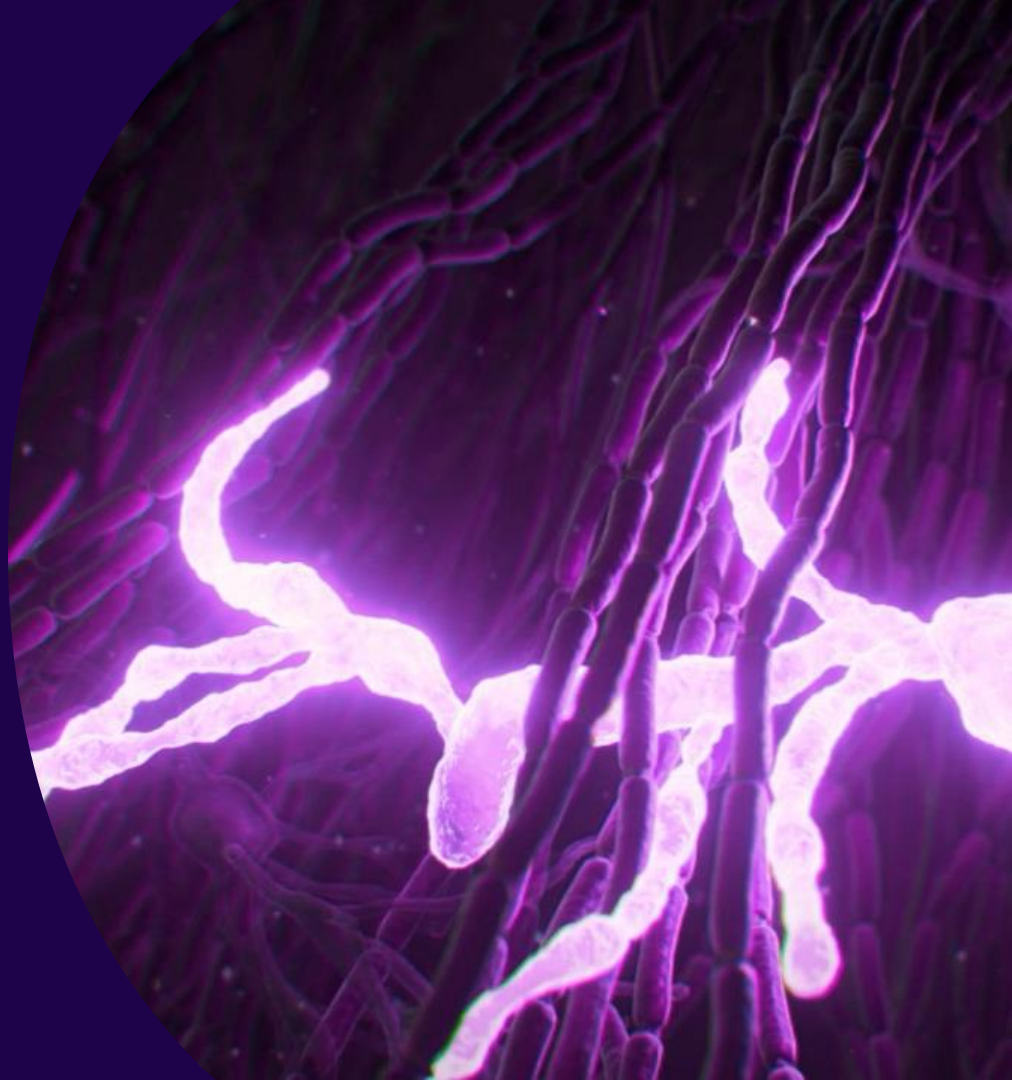
Sanofi in MS

Houman Ashrafian,
Executive Vice President,
Head of Research and Development



Tolebrutinib: potential new medicine for *patients with SPMS*

Summary

- Tolebrutinib is the *first and only* medicine to demonstrate delay in time to onset of confirmed disability progression in nrSPMS
- Patients experiencing *confirmed disability improvement* nearly two-fold higher with tolebrutinib
- Pooled analysis of the key secondary endpoint in RMS showed a *considerable delay* in time to onset of 6-month confirmed disability worsening, which supports the CDP data in nrSPMS
- Potential for *a new standard of care* in the treatment of SPMS

Next steps

Future discussions with global regulatory authorities

Regulatory submissions
- US H2 2024
- EU H1 2025

PPMS phase 3 data
- H2 2025

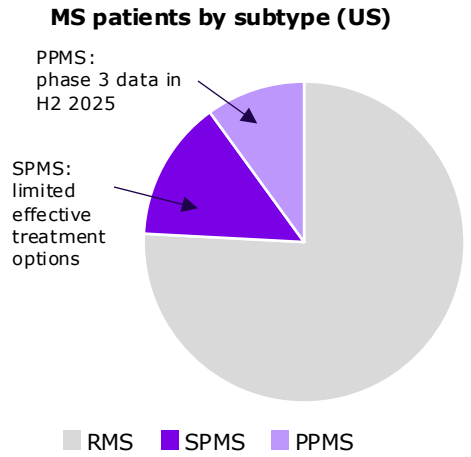
Tolebrutinib is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

Tolebrutinib: unmet medical need in *SPMS*

Facts

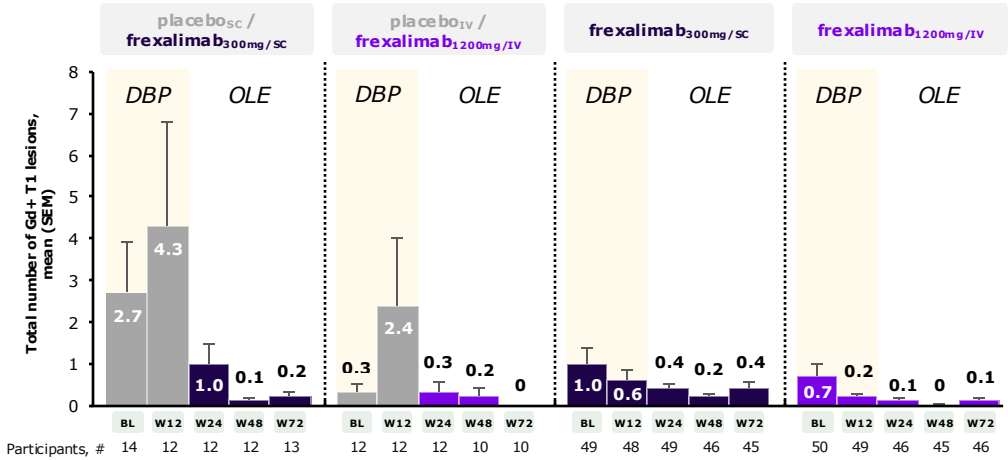
- SPMS is a disease stage that can develop after RMS and is characterized by accumulation of disabilities progressively over time, *regardless of relapse activity*
- Progressive forms of MS like SPMS have proven *harder to treat* than RMS
- *172,000* patients diagnosed, of which 65,000 are treated by disease-modifying therapies (US, EU5)
- Underdiagnosed and undertreated, due to *lack of effective treatments* in this setting

Initial focus on SPMS



Source: Sanofi epidemiology analysis, December 2023. EU5 includes Germany, France, Italy, Spain, and United Kingdom.
Tolebrutinib is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

Frexalimab: continued *encouraging* open-label phase 2 extension



Numbers of Gd+ T1 lesions were reduced at week 72 in patients who switched from placebo to frexalimab at week 12

Data summary at 72 weeks

- Gd+ T1 lesions and new or enlarging T2 lesions remained *low*
- ARR in the frexalimab$_{1200mg/IV}$ arm was *low* (0.07 [95% CI, 0.03–0.20]), *94%* participants were relapse-free
- EDSS score remained *stable* from baseline
- Frexalimab remained well tolerated with no emergence of new safety signals
- Lymphocyte counts were *stable*
- *86%* of randomized participants *completed* and continue their frexalimab treatment

Phase 3 studies in RMS and nrSPMS ongoing
Data readouts anticipated from 2027

BL: baseline. DBP: Double-blind period. Gd+: gadolinium-enhancing. OLE: open-label extension. SEM: standard error of the mean.
Frexalimab is currently under clinical investigation, and its safety and efficacy have not been evaluated by any regulatory authority.

Sanofi: increased commitment to patients with *multiple sclerosis*

From a *legacy* in multiple sclerosis

Once-daily AUBAGIO® (teriflunomide) 14mg tablets

- Reliable combination of efficacy, safety, and once-daily oral dosing

LEMTRADA® alemtuzumab 12mg IV

- Long-term disease control in the absence of continuous dosing
- >24,000 patients currently controlled[1]

To a *future of new options* for patients

tolebrutinib
BTK inhibitor

- Brain-penetrant BTKi with initial focus on SPMS
- PPMS phase 3 readout in H2 2025

frexalimab
CD40L mAb

- Safe and well-tolerated novel mode of action with adaptive and innate immune effects
- RMS, nrSPMS phase 3 data readout from 2027

oditrasertib
RIPK1 inhibitor

- Oral, brain-penetrant RIPK1 inhibitor regulating inflammatory signaling and activation of cell death pathways
- Phase 2 in RMS, SPMS, and PPMS

1. Patients previously dosed with Lemtrada and did not require additional Lemtrada doses in 2021, potential discontinuations not included. Source: Sanofi analysis. Oditrasertib is also known as SAR4443820/DNL78, in partnership with Denali Therapeutics. Tolebrutinib, frexalimab, and oditrasertib are currently under clinical investigation, and their safety and efficacy have not been evaluated by any regulatory authority.

Q&A session

To ask a question

By zoom 

Click on the **Raise hand** icon

Check your audio device is well connected

By phone 

Raise and lower your hand: dial *9

Unmute and mute your microphone: dial *6

Any problems? 

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