EVOBRUTINIB RELAPSING MULTIPLE SCLEROSIS (RMS) UPDATE CALL

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Today's Agenda

1

Significant Unmet Need in MS

Evobrutinib's potential

2

Efficacy & Safety

Updated ~96 weeks data (RMS, Phase II)

3

Modified Phase III Study Design

Data-driven decision making

4

Next Steps

Data expected in-house in late 2023

Significant unmet medical need remains in RMS

Need for new mechanisms to control disease

- **Approx. 50% of patients with RMS continue to have ongoing disease activity** over 2 years even when treated with the most effective agents[1]
- Therapies addressing adaptive and innate pathobiology **peripherally and in the CNS**

Need for higher efficacy oral therapies

- 5 approved therapeutic classes considered "higher efficacy"[2], **only 2 of which are oral**
- No approved oral therapy with **efficacy on progression vs. an active control**

Opportunity to advance on benefit-risk

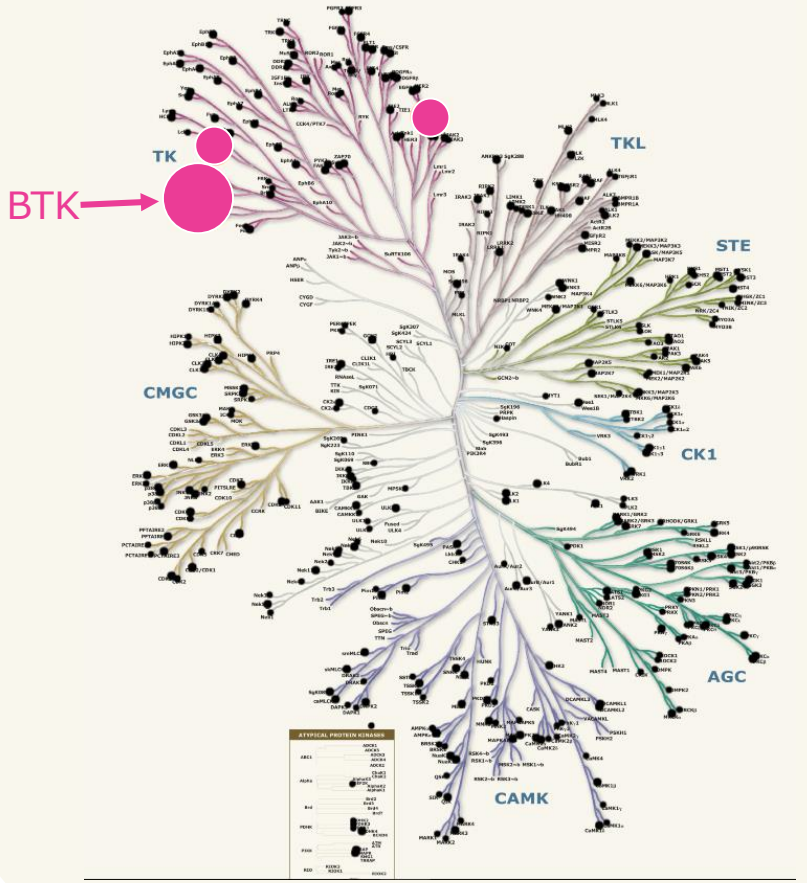
- **Systemic side effects** of therapies limit patient acceptance and compliance
- All approved higher efficacy therapies **associated with elevated risk of infection**

1: Disease activity based on NEDA/No Evidence of Disease Activity; 2: 5 Higher efficacy classes: VLA-4 (Natalizumab, IV), CD52 (Alemtuzumab, IV), CD-20 (Ocrelizumab, IV), S1PR (Fingolimod & Siponimod, Oral), Cd-ATP (Cladribine tablets, Oral); Acronyms: CNS = Central Nervous System, RMS = Relapsing Multiple Sclerosis

Evobrutinib's target benefit-risk profile addresses this unmet need

- Merck KGaA, Darmstadt, Germany **discovered a highly selective BTKi in-house** and **pioneered its usage in RMS**[1]
- Small molecule Evobrutinib **crosses blood-brain barrier**[2] **and demonstrates BTK occupancy in the brain**[3]
- ~96 weeks data from Phase II RMS study[4] confirms Evobrutinib's potential to **demonstrate mAb like efficacy**
- **Optimal Phase III dose selection** informed by MRI and relapse data from a **placebo controlled RCT with ~250 patients**
- Evobrutinib is the only BTKi in MS with **safety characterized in ≥1,200 patients up to 2 years** across RMS, RA and SLE
- Initiated a Phase III program in RMS, fully committed to bringing Evobrutinib **rapidly with high POS** to clinical practice

Evobrutinib[5]

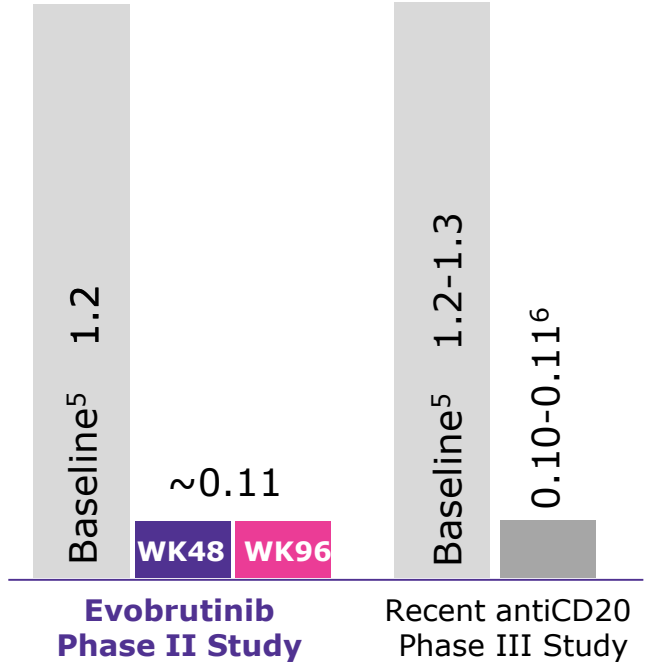


1: Montalban et al., June 2019 NEJM; 2: Experiment in Healthy Mice (Data on file); 3: Boschert U et al. ECTRIMS 2017 [P678]; 4: September 2019 cut-off, ≥ 96 weeks; 5: Haselmeyer et. al. J Immunology 2019; Acronyms: BTKi = Bruton's Tyrosine Kinase inhibitor, mAb = monoclonal Antibody, MRI = Magnetic Resonance Imaging, POS = Probability of Success, RA = Rheumatoid Arthritis, RCT = Randomized Control Trial, SLE = Systemic Lupus Erythematosus

~96 weeks data from Phase II confirms potential for mAb like efficacy with a rapid onset of action

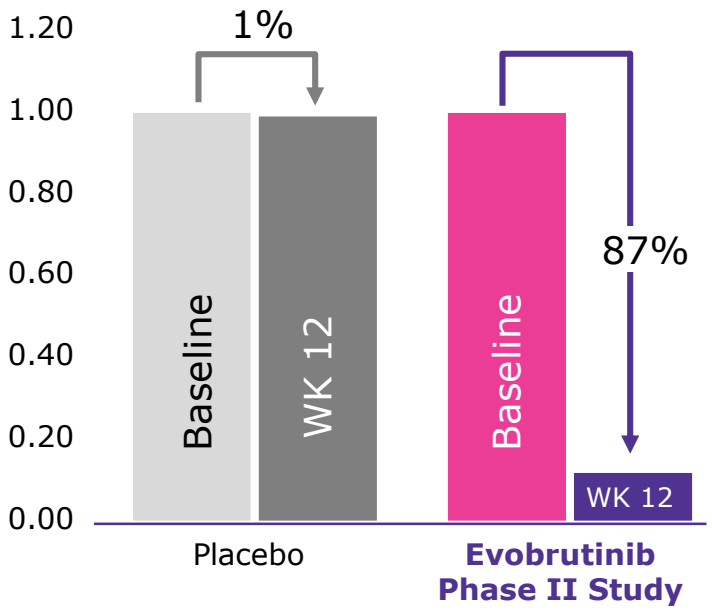
UPDATED DATA

"mAb like" Efficacy[4]



Annualized Relapse Rate

Rapid Onset of Action



Mean Number of T1 Gd+ lesions by visit[2] (Week 12 Indexed vs. Baseline)

Direct CNS and Peripheral Effects

- **Impacts B-Cells and Myeloid Cells**, which play a key role in the pathophysiology of MS
- **Crosses the blood-brain barrier[1]**
- Achieves **Brain BTKi occupancy[3]**
- **Potential to impact CNS** resident innate immunity as well as peripheral immune components

1: Experiment in Healthy Mice (Data on file); 2: Exploratory analysis; 3: Boschert U et al. ECTRIMS 2017 [P678]; 4: Aspirational indirect comparison, no H2H studies performed; 5: Mean number of relapses in last 12 months; 6: Flexible duration, maximum duration for up to 30 months; Acronyms: BTKi = Bruton's Tyrosine Kinase inhibitor, CNS = Central Nervous System, mAb = monoclonal Antibody, Gd+ = Gadolinium Enhancing Lesions, WK = Weeks

Evobrutinib is the only BTKi in MS with safety characterized in ≥1,200 patients up to 2 years

21,200 patient data base

2 years+ in RMS

- **Well Tolerated**, **no new safety signals** identified up to ~96 weeks
- Long term exposure of Evobrutinib did **not result in increase of serious infections nor lymphopenia**, consistent with Evobrutinib's mechanism of action
- Evobrutinib is **not associated with systemic side effects** (e.g. GI disturbances)
- **LFT elevations in a minority of patients restricted to first 6 months** enabling patient management through appropriate monitoring
- **Comprehensive safety characterization** based on exposure to Evobrutinib across RMS, RA and SLE studies

Acronyms: BTKi = Bruton's Tyrosine Kinase inhibitor, GI = Gastrointestinal, LFT = Liver Function Tests, RA = Rheumatoid Arthritis, RMS = Relapsing Multiple Sclerosis, SLE = Systemic Lupus Erythematosus

mAb like efficacy data drives modification of Phase III study design

Initial Design
- Evobrutinib 48 wk data
- No data from H2H studies vs. Aubagio®

CIS + RRMS + aSPMS

Evobrutinib

Avonex®

2 x Ph III

Treatment period 96 Weeks

Modified Design
- Evobrutinib ~96 wk data
- Data from 2 H2H studies vs. Aubagio®

CIS + RRMS + aSPMS

Evobrutinib

Aubagio®

2 x Ph III

Treatment period 96 Weeks

Impact

- Studies vs Avonex® will be replaced by **2 new studies vs Aubagio®**
- **Fundamentally unchanged study design**, POS, and cost
- **Broad network of sites selected** for study vs. Avonex® ready to pivot to modified design
- Goal is to have **Phase III RMS data in-house in Q4 2023, and filing shortly thereafter**

Acronyms: aSPMS = active Secondary Progressive Multiple Sclerosis, CIS = Clinically Isolated Syndrome, H2H = head-to-head, mAb = monoclonal Antibody, wk = weeks, POS = Probability Of Success, RRMS = Relapsing-Remitting Multiple Sclerosis; Avonex® is a registered trademark of Biogen; Aubagio® is a registered trademark of Sanofi

Summary & Next steps

- **Only BTKi in MS with up to 2 years of compelling efficacy & safety data** from placebo controlled RCT[1]
- **Optimal Phase III dose selection based on efficacy data** from a placebo controlled RCT[1]
- RMS Phase III program **designed to ensure rapid and high POS entry to the largest MS segment** (~75% of all MS patients)
- **MS Franchise will remain strong** through to Evobrutinib launch (**blockbuster potential**) given portfolio of Mavenclad® and Rebif®

- Modified Phase III study design to be **shared during AAN 2020**
- **Start of recruitment** in the modified studies
- **Detailed clinical data from 2+ years (RMS)** to be shared at a future scientific conference
- **Clinical data from RA and SLE** Phase IIb expected in 2020

1: Placebo controlled for the first 24 weeks; Acronyms: AAN = American Academy of Neurology (AAN), BTKi = Bruton's Tyrosine Kinase inhibitor, POS = Probability of Success, RA = Rheumatoid Arthritis, RCT = Randomized Control Trial, RMS = Relapsing Multiple Sclerosis, SLE = Systemic Lupus Erythematosus

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BACK-UP

Broad portfolio positions Merck KGaA, Darmstadt, Germany as a growing Multiple Sclerosis player

core portfolio

Rebif®

- **Stable market share:** within declining interferon class
- **Renewed HCP interest:** driven by updated pregnancy & lactation label
- **Continued blockbuster status in 2020**

Launch

MAVENCLAD® (cladribine) tablets 10 mg

- **Growth:** Continued growth within the high efficacy and oral class dyamic share
- **Focused execution:** Driving depth and 2nd year returns
- **Global peak sales: €1 - 1.4 bn**

Development

evobrutinib (BTK-inhibitor)

- **Advancing on benefit-risk in high efficacy oral category**
- **Blockbuster potential**

Acronyms: HCP = Healthcare Professional