News Release

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3 September 2020

Merck KGaA, Darmstadt, Germany to Showcase New Data at ACTRIMS-ECTRIMS MSVirtual2020 Meeting, Furthering Innovation in Multiple Sclerosis

- **Company to present 54 abstracts across its MS portfolio - MAVENCLAD® (cladribine) tablets, Rebif® (interferon beta-1a) and investigational evobrutinib**
- **New data and real-world evidence further characterize the efficacy and safety profiles of MAVENCLAD®**
- **New MAVENCLAD® and Rebif® safety data to be shared regarding risk of respiratory viral infections**

Darmstadt, Germany, 3 September 2020 – Merck KGaA, Darmstadt, Germany, a leading science and technology company, today announced it will present data on its approved and investigational multiple sclerosis (MS) treatments at MSVirtual2020: 8th Joint ACTRIMS-ECTRIMS Meeting. The Company will present 54 abstracts at the meeting, taking place virtually from 11-13 September 2020, including new efficacy and real-world safety data on MAVENCLAD® (cladribine) tablets and new safety data for Rebif® (interferon beta-1a).

In addition, data will be presented on the efficacy profile of evobrutinib, an investigational, oral, highly selective Bruton's Tyrosine Kinase inhibitor (BTKi), through 108 weeks of treatment in the Phase II open-label extension (OLE) in adult patients with relapsing multiple sclerosis (RMS). Preclinical data will also be presented providing insights into evobrutinib's potential impact on progression in MS.

"The broad range of research revealed through these data demonstrate our strategic approach to advancing the MS treatment landscape through new medicines and patient-focused research initiatives," said Luciano Rossetti, Head of Global Research

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& Development for the biopharma business of Merck KGaA, Darmstadt, Germany. "Much of our data provide insights on how MAVENCLAD® and Rebif® affect the risk of respiratory viral infections and COVID-19 outcomes in MS patients. These insights will help support clinicians as they make treatment decisions for their patients living with MS."

Key MAVENCLAD® (cladribine) tablets data include:

- Efficacy results from the Phase IV MAGNIFY-MS study and its impact on a reduction in mean combined unique active (CUA) lesion count in the first six months of MAVENCLAD® treatment for highly active RMS
- New data evaluating cumulative relapse incidence over five years in patients enrolled in the MAVENCLAD® CLARITY and CLARITY Extension trials
- Late-breaking interim data from the CLASSIC-MS study on the long-term efficacy and real-world treatment patterns for patients receiving MAVENCLAD®, with eight to 14 years of follow up, will be available as part of the late-breaker sessions from 25 September 2020
- Results from a *post hoc* analysis from the CLARITY Extension and the impact of MAVENCLAD® on the prevalence of disability improvement over five years, as measured by the Expanded Disability Status Scale (EDSS)
- Results from the MAGNIFY and CLARIFY studies regarding clinical outcomes in patients with COVID-19 infection during these Phase IV studies of MAVENCLAD® for the treatment of MS will be available as part of the late-breaker sessions from 25 September 2020
- Updated post-approval safety data of MAVENCLAD® in the treatment of MS, including respiratory viral infections and findings that the safety profile was consistent with that from the clinical development program

Key Rebif® (interferon beta-1a) data include:

- Post-approval results on the safety of Rebif® in the treatment of MS, showing no new safety signals

Key evobrutinib data include:

- Efficacy results of the Phase II OLE in patients treated with evobrutinib 75 mg BID (twice a day), as measured by annualized relapse rate from Week 48 to Week 108

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- Safety results from the ≥60 week Phase II OLE
- Preclinical data demonstrating evobrutinib's potential to reduce CNS compartmentalized inflammation thought to drive the progression of disability seen in MS

Additional Merck KGaA, Darmstadt, Germany activities at MSVirtual2020:

- Live presentation "Exploring the role of real-world data in multiple sclerosis" chaired by Prof. Gavin Giovannoni, Chair of Neurology, Barts and The London School of Medicine and Dentistry (12 September 2020, 14:30–15:30 EDT; recording available after the event)
- Two product theatres on demand throughout the congress starting from 11 September 2020, 11:45 EDT
    - "Multiple sclerosis patient management: update from the UK" by Dr. Wallace Brownlee, MS Specialist Neurologist, National Hospital for Neurology and Neurosurgery, and MS researcher at Queen Square MS Centre, University College London Institute of Neurology
    - "Real-world multiple sclerosis management: what can we learn from MSBase?" by Dr. Suzanne Hodgkinson, Associate Professor, University of New South Wales, and a senior consultant neurologist at Liverpool Hospital, New South Wales, Australia

Following the conclusion of MSVirtual2020, Merck KGaA, Darmstadt, Germany will be hosting "Mastering the Neuroscience of Unconscious Bias," the inaugural virtual event for the company`s I'M IN initiative, a diversity, equity and inclusion effort started in February 2019. I'M IN is a US-based initiative started by the Neurology & Immunology franchise, which aims to explore solutions together with healthcare providers to improve equity within the healthcare ecosystem.

Below is the full list of Merck KGaA, Darmstadt, Germany abstracts accepted for presentation at ACTRIMS-ECTRIMS 2020:

MAVENCLAD® (cladribine) tablets Presentations			
Title	**Authors**	**Presentation ID**	**Presentation Details**

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Reduced Grey Matter Atrophy in Patients With Relapsing Multiple Sclerosis Treated With Cladribine Tablets	Battaglini M, Sormani M P, Luchetti L, Gentile G, Cortese R, Alexandri N, De Stefano N	P0231	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT on 11 September 2020 **Presenter:** Marco Battaglini
Reduction in CUA MRI Lesions in the First 6 Months of Cladribine Tablets Treatment for Highly Active Relapsing Multiple Sclerosis: MAGNIFY-MS Study	De Stefano N, Barkhof F, Montalban X, Achiron A, Derfuss T, Chan A, Hodgkinson S, Prat A, Leocani L. Schmierer K, Sellebjerg F, Vermersch P, Wiendl H, Keller B, Roy S	P0382	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT on 11 September 2020 **Presenter:** Nicola De Stefano
Durable Efficacy of Cladribine Tablets: Cumulative Relapse Incidence Over 5 years in CLARITY and CLARITY Extension	Giovannoni G, Rammohan K, Leist T, Coyle P K, Keller B, Jack D, Alexandri N	P0202	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT on 11 September 2020 **Presenter:** Gavin Giovannoni
Disability Improvement in Relapsing-remitting Multiple Sclerosis Patients Receiving Cladribine Tablets, Evaluated by Expanded Disability Status Scale	Sormani M P, Signori A Giovannoni G, Alexandri N	P0201	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT on 11 September 2020 **Presenter:** Maria Pia Sormani
Updated Post-Approval Safety of Cladribine Tablets in the Treatment of Multiple Sclerosis, With Particular Reference to Respiratory Viral Infections	Giovannoni G, Berger J, Leist T, Jack D, Galazka A, Nolting A, Damian D	P0415	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT on 11 September 2020 **Presenter:** Gavin Giovannoni

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Clinical Outcomes in Patients With COVID-19 Infection During Phase IV Studies of Cladribine Tablets for Treatment of Multiple Sclerosis	Karan R, Roy S, Alexandri N	LB1151	**Session:** Latebreaker ePoster **Date:** 25-26 September 2020 **Time:** Available from 9am EDT on 25 September 2020 **Presenter:** Radmila Karan
Treatment Satisfaction in Patients With Highly-active Relapsing Multiple Sclerosis Treated With Cladribine Tablets: CLARIFY-MS Study Interim Analysis	Brochet B, Hupperts R, Langdon D, Solari A, Piehl F, Lechner-Scott J, Montalban X, Selmaj K, Valis M, Rejdak K, Havrdova EK, Patti F, Alexandri N, Nolting A, Keller B	P1066	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT on 11 September 2020 **Presenter:** Bruno Brochet
Initial Findings From a Dynamic Cohort Study of Patients With Multiple Sclerosis: A Proactive Approach for Safety and Comparative Effectiveness	Sabidó, M, Batech M, Foch C, Boutmy E, Verpillat P	P0470	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT on 11 September 2020 **Presenter:** Meritxell Sabidó
Characteristics of Relapsing Multiple Sclerosis Patients Treated With Cladribine Tablets in Five European Countries: Multi-year Chart Review	Zeng F, Harty G, Wong SL, Maslova E, Schade R, Row B	P0846	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT on 11 September 2020 **Presenter:** Feng Zeng
Characterization of Relapsing Multiple Sclerosis Patients Treated With Cladribine Tablets in Germany Since Marketing Authorization	Zeng F, Harty G, Wong SL, Uebler S, Maslova E, Schade R, Row B, Ellenberger D, Stahmann A	P0847	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT on 11 September 2020 **Presenter:** Feng Zeng
CLASSIC-MS: Long-term Efficacy and Real-World Treatment Patterns for Patients	Giovannoni G, Leist T, Aydemir A, Verdun Di Cantogno	LB1229	**Session:** Latebreaker ePoster

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Receiving Cladribine Tablets - Interim Data with 8–14 Years Follow-up	E, on behalf of the CLASSIC-MS Steering Committee		**Date:** 25-26 September 2020 **Time:** Available from 9am EDT 25 September 2020 **Presenter:** Thomas Leist
Age-related Efficacy of Cladribine Tablets in Patients With Relapsing-remitting MS in the CLARITY Extension Study	Freedman M, Pardo G, De Stefano N, Aldridge J, Hyvert Y, Galazka A, Lemieux C	P0284	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT on 11 September 2020 **Presenter:** Mark Freedman
Cladribine Tablets in Patients with RRMS and Active SPMS After Suboptimal Response to Prior DMD (MASTER-2 and CLICK-MS): Initial Baseline Demographics	Miravelle A, Katz J, Robertson D, Hayward B, Walsh JS, Harlow DE, Lebson LA, Sloane JA, Bass AD, Fox EJ	P0310	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT on 11 September 2020 **Presenter:** Augusto Miravelle
Treatment-emergent Adverse Events Occurring Early in the Treatment Course of Cladribine Tablets in two Phase 3 Trials in Multiple Sclerosis	Oh J, Walker B, Giovannoni G, Jack D, Dangond F, Nolting A, Aldridge J, Lebson L, Leist TP	P0411	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT on 11 September 2020 **Presenter:** Jiwon Oh
Identification and Characterization of Adherence Trajectory Subgroups in Patients With MS Initiating Once- or Twice-daily Oral Disease-modifying Drugs	Cisternas MG, Rajagopalan D, Leszko M, Andrade K, Phillips AL	P0967	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT on 11 September 2020 **Presenter:** Amy Phillips
Real-world Patient-level Costs of Administering Infusion Disease-modifying Drugs: A US Retrospective Claims Database Analysis	Kozma CM, Roberts NL, Phillips AL	P1052	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT on 11 September 2020

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			Presenter: Chris Kozma
Value-added Benefits of a Nurse/Pharmacy-led Service for Patients With Multiple Sclerosis Treated Over 2 Years With Cladribine Tablets in the UK	Morgan K, Vernon K, Ayer M	P1069	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT on 11 September 2020 **Presenter:** Kate Morgan
Demonstrating the Value of a Patient Support Program for Multiple Sclerosis Patients Prescribed Cladribine Tablets in Ireland at the end of Year 1	Morgan K, Joseph B, Williams V, Kelly M	P1015	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT on 11 September 2020 **Presenter:** Kate Morgan
Low Discontinuation Rate and Side-effect Burden After Switching to Cladribine Tablets: Canadian Experience from the adveva® Patient Support Program	Oh J, Giacomini P, Devonshire V, Clift F, Lemieux C, Sabido M, Allignol A, Freedman M	P0880	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT on 11 September 2020 **Presenter:** Jiwon Oh
Cladribine Tablets Versus Other Disease-modifying Therapies in Achieving Disability Improvement in Relapsing-remitting Multiple Sclerosis Patients – Network Meta-analysis	Piasecka-Stryczyńska K, Rolka M, Kaczyński Ł, Górecka M, Wójcik R, Adamek I, Kaczor MP, Rejdak K	P0040	**Session:** ePoster **Date:** 11-13 Sept 2020 **Time:** Available from 9am EDT on 11 September 2020 **Presenter:** K. Piasecka-Stryczynska
MS Disease-modifying Therapy Sequencing – Natalizumab to Cladribine Tablets – Experience in 46 Patients	Ziemssen T, Penner IK, Wagner T, Huebschen M, Mueller B, Buescher T, Richter J, Posevitz-Fejfar A	566	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT on 11 September 2020 **Presenter:** Tjalf Ziemssen
Switching disease modifying treatment in relapsing multiple sclerosis: Delphi	Saiz A, Aguera E, Moral E, Brieva L, Rodriguez-Antiguedad A,	P0401	**Session:** ePoster **Date:** 11-13 September 2020

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consensus of the Demyelinating Group of the Spanish Society of Neurology	Casanova-Estruch B, Jordi R, Meca-Lallana V, Garcia-Merino JA, Costa-Frossard L, Arnal-Garice C, Landete L, Meca-Lallana J, Blanco Y, Matías-Guiu J, Ares A, Martínez-Ginés ML, Ara JR, Llaneza M, Castillo-Trivino T, Romero L, Perez-Sempere A, González-Platas M, Mendibe-Bilbao M		**Time:** Available from 9am EDT on 11 September 2020 **Presenter:** Luis Brieva
CLADQoL (CLADribine Tablets – evaluation of Quality of Life) Study: Evaluating QoL 12 Months After Treatment Initiation with Cladribine Tablets	Penner IK, Pul R, Kallmann BA, Raji A, Richter J, Wagner T, Mueller B, Buescher T, Posevitz-Fejfar A	P0849	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT on 11 September 2020 **Presenter:** Iris-Katharina Penner
Effects of Cladribine on Proliferation, Survival and Cytokine Release of Human Astrocytes	Eixarch H, Calvo-Barreiro L, Fissolo N, Boschert U, Comabella M, Montalban X, Espejo C	P0330	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT on 11 September 2020 **Presenter:** Herena Eixarch
Real-world Experience With Cladribine in the MSBase Registry	Butzkueven H, Spelman T, Verdun di Cantogno E, Fabris J, Zeng F, G Harty	P0907	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT on 11 September 2020 **Presenter:** Helmut Butzkueven
2-Chlorodeoxyadenosine (Cladribine) Preferentially Inhibits the Biological Activity of Microglia Cells	Aybar F, Marcora S, Eugenia Samman M, Perez MJ, Pasquini JM, Correale J	P0270	**Session:** ePoster **Date:** 11-13 September 2020

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			Time: Available from 9am EDT on 11 September 2020 **Presenter:** Jorge Correale
Cladribine to Halt Deterioration in People With Advanced Multiple Sclerosis (ChariotMS)	Lieberman D, Mangat H, Allen-Philby K, Baker D, Barkhof F, Chandran S, Chapman C, Chataway J, Ford H, Giovannoni G, Hobart J, Hooper R, Hussain T, Walker N, Macmanus D, Mihaylova B, Pavitt S	P0196	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT on 11 September 2020 **Presenter:** David Lieberman
Predicting Long-term Sustained Disability Progression in Multiple Sclerosis: Application in the CLARITY Trial	Sharmin S, Bovis F, Sormani MP, Butzkueven H, Kalincik T and the MSBase study group	P0131	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT on 11 September 2020 **Presenter:** S Sharmin
A Clinical Data Summary for Cladribine Patients Treated at least 12 Months - A Swedish Nationwide Study of the Long-Term Effectiveness and Safety of Cladribine (IMSE 10)	Forsberg L, Kågström S, Hillert J, Nilsson P, Dahle C, Svenningsson A, Lycke J, Landtblom AM, Burman J, Martin C, Sundström P, Gunnarsson M, Piehl F, Olsson T	P0276	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT on 11 September 2020 **Presenter:** L Forsberg
Impact of Cladribine Tablets on Brain Volume Protection in Highly Active MS	Raji A, Winkler G	P0586	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT on 11 September 2020 **Presenter:** A Raji

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Early Real-World Safety, Tolerability, and Efficacy of Cladribine Tablets: A Single Center Experience	Bain J, Jones A, Overholt S, Guenette M, Selchen D, Jiwon Oh	P0319	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT on 11 September 2020 **Presenter:** J Bain
Switching From Ocrelizumab to Cladribine: Real-world Data	O'Neill DTD, Sharma M, Gonzales B, Vandenheuvel M, Tse B, Hodgkinson SJ	P0399	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT on 11 September 2020 **Presenter:** D O'Neill
The Effect of Cladribine Upon Naïve and Activated $CD4^+$ T Regulatory Cells in MS Patients	Verma ND, Al-Atiyah R, O'Neill D, Sharma M, Tran CT, Hall BM, Hodgkinson SJ	P0406	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT on 11 September 2020 **Presenter:** Suzanne Hodgkinson
Rebif® (interferon beta-1a) Presentations			
A Systematic Review and Meta-analyses of Pregnancy and Fetal Outcomes in Women with Multiple Sclerosis. IMI2 ConcePTION	Lopez-Leon S, Geissbuehler Y, Sabidó M, Turkson, M, Wahlich C, Morris J	P0278	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT on 11 September 2020 **Presenter:** Meritxell Sabidó
Post-approval Safety of Subcutaneous Interferon β-1a in the Treatment of Multiple Sclerosis, With Particular Reference to Respiratory Viral Infections	Freedman M S, Guehring H, Murgasova Z, Jack D	P0370	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT on 11 September 2020 **Presenter:** Mark Freedman
Effect of Neutralizing Antibodies on Pharmacodynamic Biomarkers of Subcutaneous Interferon β-1a in REFLEX and REFLEXION	Freedman MS, Holmberg KH, Fluck M, Hyvert H, Stinchi S, D'Urso V, Dangond F	P0323	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT on 11 September 2020

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			Presenter: Mark Freedman
Baseline Serum Neurofilament Light Chain Levels Predict Conversion to McDonald 2005 MS Within 2 yrs of a First Clinical Demyelinating Event in REFLEX	Kuhle J, Leppert D, Comi G, De Stefano N, Kappos L, Freedman MS, Issard D, Roy S	P0032	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT on 11 September 2020 **Presenter:** Sanjeev Roy
Effect of age on Effectiveness and Discontinuation of Subcutaneous Interferon beta-1a, and Healthcare Utilization, in Patients With Multiple Sclerosis	Sabidó M, Allignol A Marhardt K, Vermersch P, Boutmy EF	P0320	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT on 11 September 2020 **Presenter:** Patrick Vermersch
Comparing Infection-related Outcomes in Patients with Multiple Sclerosis and Matched Controls Using Administrative Claims Data	Bove R, Kozma C, Phillips AL, Harlow DE, Lobo C	P0451	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT on 11 September 2020 **Presenter:** Riley Bove
Assessment of the Effectiveness of a Cognitive Behavioral Program for Fatigue (FACETS +) in 110 French Patients with Relapsing Remitting Multiple Sclerosis (RR MS): A randomized, controlled trial (RCT)	Hemelin F, Marie Claire G, Olivier H, Marie B, Frederic B	P1095	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT on 11 September 2020 **Presenter:** Fanny Hamelin
Impact of Interferon-beta Exposure During Early Pregnancy on Relapse Rate	Tokic M, Thiel S, Litvin N, Ciplea A, Gold R, Hellwig K	P1126	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT on 11 September 2020 **Presenter:** M Tokic
Evobrutinib Presentations			
Clinical Relapse Rates in Relapsing MS Patients Treated with the BTK Inhibitor Evobrutinib:	Montalban X, Arnold D L, Weber MS, Staikov I, Piasecka-	P0197	**Session:** ePoster **Date:** 11-13 September 2020

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Results of an Open-Label Extension to Phase II Study	Stryczynska K, Martin E C, Mandel M, Ona V, Dangond F, Wolinsky JS		**Time:** Available from 9am EDT on 11 September 2020 **Presenter:** Fernando Dengond
Safety of the Bruton's Tyrosine Kinase Inhibitor Evobrutinib in Relapsing Multiple Sclerosis During an Open-label Extension to a Phase II Study	Montalban, X Arnold D L, Weber M S, Staikov I, Piasecka-Stryczynska K, Martin E C, Mandel M, Ona V, Zima Y, Dengond F, Tomic D, Wolinsky JS	P0235	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT on 11 September 2020 **Presenter:** Fernando Dengond
Effect Of Evobrutinib, a BTK Inhibitor, on Immune Cell and Immunoglobulin Levels in Relapsing MS: An Open-Label Extension to a Phase II Study	Montalban X, Shaw J, Dangond F, Martin EC, Grenningloh R, Ying Li, Weber MS	P0070	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT on 11 September 2020 **Presenter:** Jamie Shaw
Evobrutinib, a Highly Selective BTK Inhibitor, Prevents Antigen-activation of B Cells and Ameliorates B Cell–mediated Experimental Autoimmune Encephalomyelitis	Torke S, Pretzsch R, Häusler D, Grenningloh R, Boschert U, Brück W, Weber MS	P0334	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT on 11 September 2020 **Presenter:** Sebastian Torke
Expression of Bruton's Tyrosine Kinase in B Cell-rich Meningeal Infiltrates in two Models of Progressive MS	Kebir H, Ceja G, Miller MC, Li C, May MJ, Vite CH, Church ME, Grenningloh R, Boschert U, Alvarez JI	P0962	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT 11 September 2020 **Presenter:** Kebir Hania
T-bet+ B-cell Development in MS: Association with Bruton's Tyrosine Kinase Activity and Targeting by Evobrutinib	Rijvers L, Melief MJ, van Langelaar J, Wierenga-Wolf AF, Marieke van Ham S, Boschert U, Grenningloh R, Smolders J, van Luijn MM	P0403	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EdT 11 September 2020 **Presenter:** Liza Rijvers

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The Bruton's Tyrosine Kinase Inhibitor Evobrutinib Ameliorates Meningeal Inflammation in Experimental Autoimmune Encephalomyelitis	Kim S, Boschert U Grenningloh R, Bhargava P	P0404	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT on 11 September 2020 **Presenter:** Pavan Bhargava
The Validity and Applicability of the PROMIS SF v2.1 - Physical Function (MS) 15a: A new PROMIS® Short Form for Assessing Physical Function in Relapsing and Progressive Multiple Sclerosis Types	Kamudoni P, Amtmann D, Johns J, Cook K, Salem R, Salek S, Raab J, Middleton R, Repovic P, Alschuler KN, von Geldern G, Wundes A, Henke C	P1062	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT on 11 September 2020 **Presenter:** Paul Kamudoni
The Interpretation and Clinical Application of the PROMIS® SF v1.0 - Fatigue (MS) 8b: A PROMIS Short Form for Assessing Fatigue in Relapsing and Progressive Multiple Sclerosis	Kamudoni P, Johns J, Cook K, Salem R, Henke C, Salek S, Raab J, Middleton R, Repovic P, Alschuler KN, von Geldern G,Wundes A, Amtmann D	P1061	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT on 11 September 2020 **Presenter:** Paul Kamudoni
General MS Franchise			
Identifying Gaps in Knowledge, Skills and Confidence Among MS Specialists to Facilitate Improved MS Care	Schmierer K, Peniuta M, Oh J, Leist T, Lazure P, Péloquin S	P1100	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT on 11 September 2020 **Presenter:** Klaus Schmierer
An Investigation Into the Role and Impact That Carers Play in Consultations Between Healthcare Professionals and People With MS	Langdon D, Sumelahti M L, Potra S, Alroughani R, on behalf of the MS in the 21st Century initiative, Verdun Di Cantogno E	P1006	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT on 11 September 2020 **Presenter:** Dawn Langdon
Characterization of Age-related Changes in Circulating T cells in Multiple Sclerosis and	Zuroff LR, Li R, Shinoda K, Rezk A, Bar-Or A	P0952	**Session:** ePoster **Date:** 11-13 September 2020

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Normal Controls: A Pilot Study			**Time:** Available from 9am EDT on 11 September 2020 **Presenter:** LR Zuroff
Treatment and Care Management, Clinical Outcomes and Mobility Impairment in People With or Without MS Aged ≥50 Years: Observational 6-year Analysis	Freeman L, Lucas A, Zhou J, Hayward B, Livingston T	P0176	**Session:** ePoster **Date:** 11-13 September 2020 **Time:** Available from 9am EDT on 11 September 2020 **Presenter:** Terrie Livingston

About MAVENCLAD®
MAVENCLAD, approved by the U.S. Food and Drug Administration (FDA) on March 29, 2019, is the first and only short-course oral therapy for the treatment of adults with relapsing-remitting disease (RRMS) and active secondary progressive disease (SPMS). Because of its safety profile, use of MAVENCLAD is generally recommended for patients who have had an inadequate response to, or are unable to tolerate, an alternate drug indicated for the treatment of multiple sclerosis (MS), and MAVENCLAD is not recommended for use in patients with clinically isolated syndrome (CIS). Patients should follow healthcare provider instructions including cancer screening, contraception and blood tests. The approved dose of MAVENCLAD is 3.5 mg per kg body weight over two years, administered as one treatment course of 1.75 mg per kg per year, each consisting of two treatment weeks. The mechanism by which cladribine exerts its therapeutic effects in patients with multiple sclerosis has not been fully elucidated but is thought to involve cytotoxic effects on B and T lymphocytes through impairment of DNA synthesis, resulting in depletion of lymphocytes. MAVENCLAD causes a dose-dependent reduction in lymphocyte counts followed by recovery.

Because cladribine is cytotoxic, special handling and disposal instructions should be followed.

MAVENCLAD has been approved in 79 countries, including the European Union (EU), Canada, Australia and Switzerland, for various relapsing MS indications. Visit www.MAVENCLAD.com for more information.

IMPORTANT SAFETY INFORMATION

BOXED WARNING: MALIGNANCIES and RISK OF TERATOGENICITY

- **Treatment with MAVENCLAD may increase the risk of malignancy. MAVENCLAD is contraindicated in patients with current malignancy; evaluate the benefits and risks of the use of MAVENCLAD on an individual patient basis for patients with prior or increased risk of malignancy.**
- **MAVENCLAD is contraindicated for use in pregnant women and in women and men of reproductive potential who do not plan to use effective contraception because of the potential for fetal harm.**

CONTRAINDICATIONS

- Current malignancy.
- Pregnancy, and women and men of reproductive potential who do not plan to use effective contraception during MAVENCLAD dosing and for 6 m after the last dose in each treatment course.
- Human immunodeficiency virus (HIV).
- Active chronic infections (e.g., hepatitis or tuberculosis).
- History of hypersensitivity to cladribine.
- Breastfeeding while taking MAVENCLAD and for 10 days after the last dose.

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DOSING CONSIDERATIONS: After the completion of 2 treatment courses, do not administer additional MAVENCLAD during the next 2 years. The risk of malignancy with reinitiating MAVENCLAD more than 2 years after completion of 2 treatment courses has not been studied.

ADDITIONAL WARNINGS AND PRECAUTIONS

- **Lymphopenia:** In clinical studies, 87% of MAVENCLAD-treated patients experienced lymphopenia. Concomitant use of MAVENCLAD with hematotoxic drugs may increase the risk of adverse reactions because of the additive hematological effects. Monitor lymphocyte counts before and during treatment, periodically thereafter, and when clinically indicated.
- **Infections:** Infections occurred in 49% of MAVENCLAD-treated patients compared to 44% of patients treated with placebo in clinical studies. The most frequent serious infections included herpes zoster and pyelonephritis. Single fatal cases of tuberculosis and fulminant hepatitis B were reported in the clinical program. Administer live-attenuated or live vaccines at least 4 to 6 weeks prior to starting MAVENCLAD. Screen patients for latent infections; consider delaying treatment until infection is fully controlled. Vaccinate patients antibody-negative to varicella zoster virus prior to treatment. Monitor for infections. Administer anti-herpes prophylaxis in patients with lymphocyte counts less than 200 cells per microliter. In patients treated with parenteral cladribine for oncologic indications, cases of progressive multifocal leukoencephalopathy (PML) have been reported. No case of PML has been reported in clinical studies of cladribine in patients with MS.
- **Hematologic Toxicity**: Mild to moderate decreases in neutrophil counts, hemoglobin levels, and platelet counts were observed. Severe decreases in neutrophil counts were observed in 3.6% of MAVENCLAD-treated patients, compared to 2.8% of placebo patients. Obtain complete blood count (CBC) with differential including lymphocyte count before and during treatment, periodically thereafter, and when clinically indicated.
- **Risk of Graft-versus-Host Disease With Blood Transfusions**: Irradiation of cellular blood components is recommended.
- **Liver Injury**: Obtain liver function tests prior to treatment. Discontinue MAVENCLAD if significant injury is suspected.
- **Hypersensitivity**: In clinical studies, 11% of MAVENCLAD-treated patients had hypersensitivity reactions, compared to 7% of placebo patients. Serious hypersensitivity reactions occurred in 0.5% of MAVENCLAD-treated patients, compared to 0.1% of placebo patients. If a hypersensitivity reaction is suspected, discontinue treatment. Do not use MAVENCLAD in patients with a history of hypersensitivity to cladribine.
- **Cardiac Failure**: In clinical studies, one MAVENCLAD-treated patient experienced life-threatening acute cardiac failure with myocarditis, which improved after approximately one week. Cases of cardiac failure have also been reported with parenteral cladribine used for treatment indications other than multiple sclerosis.

Adverse Reactions: The most common adverse reactions with an incidence of >20% for MAVENCLAD are upper respiratory tract infection, headache, and lymphopenia.

Drug Interactions/Concomitant Medication: Concomitant use of MAVENCLAD with immunosuppressive or myelosuppressive drugs and some immunomodulatory drugs (e.g., interferon beta) is not recommended and may increase the risk of adverse reactions. Avoid concomitant use of certain antiviral and antiretroviral drugs. Avoid concomitant use of BCRP or ENT/CNT inhibitors as they may alter bioavailability of MAVENCLAD.

Please see the full **Prescribing Information,** including **boxed WARNING** for additional information.

About Rebif® (interferon beta-1a)
Rebif (interferon beta-1a) is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults. It is used to decrease the frequency of relapses and delay the occurrence of some of the physical disability that is common in people with MS.

IMPORTANT SAFETY INFORMATION:
Rebif is contraindicated in patients with a history of hypersensitivity to natural or recombinant interferon beta, human albumin, or any other component of the formulation.

News Release

Rebif should be used with caution in patients with depression, a condition that is common in people with multiple sclerosis. Depression, suicidal ideation, and suicide attempts have been reported to occur with increased frequency in patients receiving interferon compounds, including Rebif.

Severe liver injury, including some cases of hepatic failure requiring liver transplantation, has been reported rarely in patients taking Rebif. The potential for liver injury should be considered when used in combination with other products associated with liver injury. Monitor liver function tests and patients for signs and symptoms of hepatic injury. Consider discontinuing Rebif if hepatic injury occurs.

Anaphylaxis and other allergic reactions (some severe) have been reported as a rare complication of Rebif. Discontinue Rebif if anaphylaxis occurs.

In controlled clinical trials, injection site reactions occurred more frequently in Rebif-treated patients than in placebo-treated and Avonex-treated patients. Injection site reactions including injection site pain, erythema, edema, cellulitis, abscess, and necrosis have been reported in the postmarketing setting. Do not administer Rebif into affected area until fully healed; if multiple lesions occur, discontinue Rebif until skin lesions are healed.

Decreased peripheral blood counts in all cell lines, including pancytopenia, have been reported in Rebif-treated patients. In controlled clinical trials, leukopenia occurred at a higher frequency in Rebif-treated patients than in placebo and Avonex-treated patients. Thrombocytopenia and anemia occurred more frequently in 44 mcg Rebif-treated patients than in placebo-treated patients. Patients should be monitored for symptoms or signs of decreased blood counts. Monitoring of complete blood and differential white blood cell counts is also recommended.

Cases of thrombotic microangiopathy (TMA), some fatal, have been reported with interferon beta products, including Rebif, up to several weeks or years after starting therapy. Discontinue Rebif if clinical symptoms and laboratory findings consistent with TMA occur, and manage as clinically indicated.

Caution should be exercised when administering Rebif to patients with pre-existing seizure disorders. Seizures have been temporally associated with the use of beta interferons, including Rebif, in clinical trials and in postmarketing reports.

The most common side effects with Rebif are injection-site disorders, headaches, influenza-like symptoms, abdominal pain, depression, elevated liver enzymes, and hematologic abnormalities.

Epidemiological data do not suggest a clear relationship between interferon beta use and major congenital malformations, but interferon beta may cause fetal harm based on animal studies. Data from a large human population-based cohort study, as well as other published studies over several decades, have not identified a drug-associated risk of major birth defects with interferon beta products during early pregnancy. Findings regarding a potential risk for low birth weight or miscarriage with the use of interferon beta products in pregnancy have been inconsistent.

Please see the full Prescribing Information for additional information: https://www.emdserono.com/us-en/pi/rebif-pi.pdf

About Evobrutinib
Evobrutinib (M2951) is in clinical development to investigate its potential as a treatment for multiple sclerosis (MS). It is an oral, highly selective inhibitor of Bruton's tyrosine kinase (BTK) which is important in the development and functioning of various immune cells including B lymphocytes and macrophages. Evobrutinib is designed to inhibit primary B cell responses such as proliferation and antibody and cytokine release, without directly affecting T cells. BTK inhibition is thought to suppress autoantibody-producing cells, which preclinical research suggests may be therapeutically useful in certain autoimmune diseases. Evobrutinib is currently under clinical investigation and not approved for any use anywhere in the world.

About Multiple Sclerosis
Multiple sclerosis (MS) is a chronic, inflammatory condition of the central nervous system and is the most common non-traumatic, disabling neurological disease in young adults. It is estimated that approximately 2.3 million people have MS worldwide. While symptoms can vary, the most common symptoms of MS include blurred vision, numbness or tingling in the limbs and problems with strength and coordination. The relapsing forms of MS are the most common.

Merck KGaA, Darmstadt, Germany in Neurology and Immunology

News Release

Merck KGaA, Darmstadt, Germany, has a long-standing legacy in neurology and immunology, with significant R&D and commercial experience in multiple sclerosis (MS). The company`s current MS portfolio includes two products for the treatment of relapsing MS, with a robust pipeline focusing on discovering new therapies that have the potential to modulate key pathogenic mechanisms in MS. Merck KGaA, Darmstadt, Germany, aims to improve the lives of those living with MS, by addressing areas of unmet medical needs.

The company`s robust immunology pipeline focuses on discovering new therapies that have the potential to modulate key pathogenic mechanisms in chronic diseases such as MS, systemic lupus erythematosus, osteoarthritis and psoriasis.

All Merck KGaA, Darmstadt, Germany, press releases are distributed by e-mail at the same time they become available on the EMD Group Website. In case you are a resident of the USA or Canada please go to www.emdgroup.com/subscribe to register for your online subscription of this service as our geo-targeting requires new links in the email. You may later change your selection or discontinue this service.

About Merck KGaA, Darmstadt, Germany
Merck KGaA, Darmstadt, Germany, is a leading science and technology company in healthcare, life science and performance materials. Around 57,000 employees work to further develop technologies that improve and enhance life – from biopharmaceutical therapies to treat cancer or multiple sclerosis, cutting-edge systems for scientific research and production, to liquid crystals for smartphones and LCD televisions. In 2019, Merck KGaA, Darmstadt, Germany, generated sales of € 16.2 billion in 66 countries.

Scientific exploration and responsible entrepreneurship have been key to the company's technological and scientific advances. This is how Merck KGaA, Darmstadt, Germany, has thrived since its founding in 1668. The founding family remains the majority owner of the publicly listed company. Merck KGaA, Darmstadt, Germany, holds the global rights to the Merck name and brand. The only exceptions are the United States and Canada, where the business sectors of Merck operate as EMD Serono in healthcare, MilliporeSigma in life science, and EMD Performance Materials.