EMD Serono to Present Data Highlighting Investigational Cladribine Tablets at ACTRIMS 2018

-- Research will be presented evaluating the impact of Cladribine Tablets on the immune system

-- The company also announces it will file a regulatory submission for Cladribine Tablets with the FDA in Q2 2018

ROCKLAND, Mass., Feb. 1, 2018 /PRNewswire/ -- EMD Serono, the biopharmaceutical business of Merck KGaA, Darmstadt, Germany, in the US and Canada, today announced that six posters evaluating investigational Cladribine Tablets in multiple sclerosis (MS) will be presented at the Americas Committee for Treatment and Research in Multiple Sclerosis (ACTRIMS) Forum taking place February 1-3 in San Diego, California. The six posters evaluate the safety of Cladribine Tablets and its impact on the immune system via post hoc analyses of the CLARITY, CLARITY Extension, and ORACLE-MS trials, as well as the PREMIERE registry study.[1,2,3,4,5,6]

The company recently announced it will file a regulatory submission for Cladribine Tablets with the U.S. Food and Drug Administration in the second quarter of 2018. In August 2017, the European Commission granted marketing authorization for Cladribine Tablets, marketed as MAVENCLAD®, for the treatment of highly active relapsing forms of multiple sclerosis as defined

2017, Health Canada approved MAVENCLAD for the treatment of relapsing forms of MS.

"We are proud to share further clinical trial data during ACTRIMS 2018 evaluating the use of Cladribine Tablets in patients with multiple sclerosis. This adds to the body of research to help best understand the role of Cladribine Tablets as a potential future treatment option for appropriate patients who live with MS," said John Walsh, M.D., Vice President, Neurology & Immunology, US Medical Affairs at EMD Serono. "Our ongoing research underscores our commitment to developing new therapeutic options for patients with chronic and hard-to-treat conditions like MS."

The posters report on findings regarding Cladribine Tablets' selectivity and adaptive and innate immune system function and add further information about the safety profile.[1,2,3,4,5,6]

Attendees can learn more about EMD Serono's programs, pipeline and activities in neurology and immunology by visiting our medical booth #219. Booth activities include "I'm Balancing MS," an experience to help visitors better understand the balance between healthcare and lifestyle for those facing MS. For each participant EMD Serono will make a $100 donation to the Accelerated Cure Project for Multiple Sclerosis to support their mission to accelerate efforts toward a cure for multiple sclerosis by rapidly advancing research that determines its causes and mechanisms.

The following posters have been accepted for presentation at ACTRIMS 2018 Forum and will be presented on February 1, 6-8 p.m. PST (9-11 p.m. EST) in the Sapphire Ballroom, Hilton San Diego Bayfront:

Cladribine Tablets Presentations		
Poster Title	**Lead Author**	**Poster Number**
Effects of cladribine tablets on CD4+ T-cell subsets in the ORACLE-MS study: Results from an analysis of lymphocyte surface markers	O. Stuve	P059
Cladribine tablets produce selective and discontinuous reduction of B	O. Stuve	P060

Innate immune cell counts in patients with relapsing–remitting multiple sclerosis treated with cladribine tablets 3.5 mg/kg in CLARITY and CLARITY EXT	P. Soelberg-Sorensen	P061
Infections during periods of Grade 3 or 4 lymphopenia in patients taking cladribine tablets 3.5 mg/kg: data from an integrated safety analysis	S. Cook	P070
Long-term lymphocyte counts in patients with RRMS treated with cladribine tablets 3.5 mg/kg: Total lymphocytes, B-, and T-cell subsets	P. Soelberg-Sorensen	P084
Rates of lymphopenia in Years 1–4 in patients with relapsing multiple sclerosis treated annually with cladribine tablets 3.5 mg/kg	S. Cook	P086

About Cladribine Tablets

Cladribine Tablets is an investigational short-course oral therapy that is thought to selectively and periodically target lymphocytes thought to be integral to the pathological process of relapsing MS (RMS). Cladribine Tablets is currently under clinical investigation and not yet approved for the treatment for any use in the United States. In August 2017, the European Commission granted marketing authorization for Cladribine Tablets, marketed as MAVENCLAD®, for the treatment of highly active relapsing forms of multiple sclerosis as defined by clinical or imaging features, in the 28 countries of the EU in addition to Norway, Liechtenstein and Iceland. In December 2017, Health Canada approved MAVENCLAD for the treatment of relapsing forms of MS.

The clinical development program for Cladribine Tablets includes:

- The CLARITY (Cladribine Tablets Treating MS Orally) study: a two-year Phase III placebo-controlled study designed to evaluate the efficacy and safety of Cladribine Tablets as a monotherapy in patients with RRMS.
- The CLARITY extension study: a two-year Phase III placebo-controlled study following on from the CLARITY study, designed to evaluate the safety and efficacy of Cladribine Tablets over an extended administration for four years.
- The ORACLE MS (Oral Cladribine in Early MS) study: a two-year Phase III placebo-controlled study designed to evaluate the efficacy and safety of Cladribine Tablets as a

- The ONWARD (Oral Cladribine Added ON To Interferon beta-1a in Patients With Active Relapsing Disease) study: a Phase II placebo-controlled study designed primarily to evaluate the safety and tolerability of adding Cladribine Tablets treatment to patients with relapsing forms of MS, who have experienced breakthrough disease while on established interferon-beta therapy.
- PREMIERE (Prospective Observational Long-term Safety Registry of Multiple Sclerosis Patients Who Have Participated in Cladribine Clinical Studies) study: interim long-term follow-up data from the prospective registry, PREMIERE, to evaluate the safety and efficacy of Cladribine Tablets. This includes more than 10,000 patient years of data with over 2,700 patients included in the clinical trial program, and more than 10 years of observation in some patients.

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.

About EMD Serono, Inc.

EMD Serono is the biopharmaceutical business of Merck KGaA, Darmstadt, Germany, in the U.S. and Canada - a leading science and technology company - focused exclusively on specialty care. For more than 40 years, the business has integrated cutting-edge science, innovative products and industry-leading patient support and access programs. EMD Serono has deep expertise in neurology, fertility and endocrinology, as well as a robust pipeline of potential therapies in oncology, immuno-oncology and immunology as R&D focus areas. Today, the business has 1,300 employees around the country with commercial, clinical and research operations based in the company's home state of Massachusetts. www.emdserono.com

[1] Stuve O. ACTRIMS 2018 [Poster No. 060] Cladribine Tablets Produce Selective and Discontinuous Reduction of B and T Lymphocytes and Natural Killer Cells in Patients with Early and Relapsing Multiple Sclerosis (ORACLE-MS, CLARITY and CLARITY Extension).

[2] Cook S. ACTRIMS 2018 [Poster No. 086] Rates of Lymphopenia Year-by-year in Patients with Relapsing Multiple Sclerosis Treated and Retreated with Cladribine Tablets 3.5mg/kg.

[3] Soelberg-Sorensen P. ACTRIMS 2018 [Poster No. 061] Innate Immune Cell Counts in Patients with Relapsing-Remitting Multiple Sclerosis (RRMS) Treated with Cladribine Tablets 3.5 mg/kg in CLARITY and CLARITY Extension.

[5] Soelberg-Sorensen P. ACTRIMS 2018 [Poster No. 084] Long-Term Lymphocyte Counts in Patients with Relapsing-Remitting Multiple Sclerosis (RRMS) Treated with Cladribine Tablets 3.5 mg/kg: Total Lymphocytes, B and T Cell Subsets.

[6] Cook S. ACTRIMS 2018 [Poster No. 070] Infections During Periods of Grade 3 or 4 Lymphopenia in Patients Taking Cladribine Tablets 3.5 mg/kg: Data from an Integrated Safety Analysis.

Your Contact

Alice McGrail +1 781-681-2886

SOURCE EMD Serono

EMD Serono is the biopharmaceutical business of Merck KGaA, Darmstadt, Germany. This site contains information that is intended for residents of the United States only and is not meant to substitute for the advice provided by a medical professional. Always consult a physician if you have health concerns. Use and access of this site is subject to the terms and conditions as set out in our Legal Statement and Privacy Policy.

This site contains information that is intended for US residents only. Canadian residents should consult the EMD Inc. website at www.emdserono.ca for information on products and services approved in Canada.

SITEMAP

LEGAL STATEMENT

PRIVACY POLICY

CONTACT US

Merck KGaA, Darmstadt, Germany certified as one of the Top Employers North America 2018

-- North American businesses of Merck KGaA, Darmstadt, Germany, including EMD Serono, MilliporeSigma and EMD Performance Materials, recognized for second year in a row

-- Top Employers Institute honors leading employers worldwide

BOSTON and MISSISSAUGA, Ontario, Feb. 1, 2018 /PRNewswire/ -- For the second year in a row, the North American businesses of Merck KGaA, Darmstadt, Germany, a leading science and technology company, have been certified for the company's outstanding employee offerings by the independent Top Employers Institute.

EMD Serono, MilliporeSigma and EMD Performance Materials received this major employment recognition for showcasing the company's dedication to the development of its people.

"Attracting the best and brightest talent in key regions such as North America has been a fundamental part of what we do as a successful global company, throughout our 350-year history," said Udit Batra, Member of the Executive Board and CEO, Life Science at Merck KGaA,

"In all the company's sectors, including Life Science, we seek talent from many disciplines, such as digital and information technology, technical services, engineering and new areas such as artificial intelligence. The opportunities are endless."

Recently, the Life Science business opened a 280,000-square foot campus in Burlington, Massachusetts housing nearly 1,000 employees, designed to leverage the expertise and skills of the best talent in the Life Science industry.

Merck KGaA, Darmstadt, Germany, which is celebrating its 350th birthday this year, is one of a select group of companies to achieve the exclusive Top Employers North America 2018 certification. The company also achieved Top Employer status in Asia/Pacific, Europe, Latin America and the Middle East.

"We are honored to receive this official certification again and are committed to creating an environment where our talented employees are empowered to do their best work and build their careers," said Gary Zieziula, President and Managing Director of EMD Serono. "The contributions of our highly talented employees enable us to successfully deliver on our mission to create solutions and technologies that enhance the lives of people around the world."

The annual international research undertaken by the Top Employers Institute recognizes leading global employers who provide excellent employee conditions, nurture and talent develop throughout all levels of the organization, and strive to continuously optimize employment practices. To achieve certification from the Top Employer Institute, companies undergo a stringent research process in which they are assessed on criteria including talent strategy, workforce planning, leadership development and culture.

"We recognize the importance of fostering an inclusive and collaborative work environment aimed at not only utilizing our employees' existing skillsets, but also empowering them with the necessary tools to drive their development and fulfill their personal ambitions," said Luiz Vieira, President and Managing Director of EMD Performance Materials.

The Top Employers recognition follows the Massachusetts-based businesses of Merck KGaA, Darmstadt, Germany — MilliporeSigma and EMD Serono — being named to *The Boston Globe*'s annual "Top Places to Work" list in 2017.

About Merck KGaA, Darmstadt, Germany

Merck KGaA, Darmstadt, Germany, is a leading science and technology company in healthcare, life science and performance materials. Around 50,000 employees work to further develop technologies that improve and enhance life – from biopharmaceutical therapies to treat cancer or multiple sclerosis, to cutting-edge systems for scientific research and production, to liquid crystals for smartphones and LCD televisions. In 2016, Merck KGaA, Darmstadt, Germany, generated sales of € 15.0 billion in 66 countries.

Founded in 1668, Merck KGaA, Darmstadt, Germany, is the world's oldest pharmaceutical and chemical company. The founding family remains the majority owner of the publicly listed corporate group. 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 company operates as EMD Serono, MilliporeSigma and EMD Performance Materials.

Your Contact:
Melissa Beglin, +1 781 681 2609

SOURCE Merck KGaA, Darmstadt, Germany

EMD SERONO

COMPLIANCE & TRANSPARENCY

THERAPEUTIC AREAS

YOUR REQUESTS

EMD Serono is the biopharmaceutical business of Merck KGaA, Darmstadt, Germany. This site contains information that is intended for residents of the United States only and is not meant to substitute for the advice provided by a medical professional. Always consult a physician if you have health concerns. Use and access of this site is subject to the terms and conditions as set out in our Legal Statement and Privacy Policy.

This site contains information that is intended for US residents only. Canadian residents should consult the EMD Inc. website at www.emdserono.ca for information on products and services approved in Canada.

SITEMAP

LEGAL STATEMENT

PRIVACY POLICY

CONTACT US

Wendy Sussman Joins EMD Serono as Vice President of U.S. Healthcare Government & Public Affairs

ROCKLAND, Mass., March 6, 2018 /PRNewswire/ -- EMD Serono, the biopharmaceutical business of Merck KGaA, Darmstadt, Germany in the U.S. and Canada, today announced that Wendy Sussman has joined the organization as Vice President of U.S. Healthcare Government & Public Affairs. In this role, Ms. Sussman will lead the company's government policy strategy and advocacy at the federal and state level.

"Collaboration is critical across all healthcare stakeholders in order to continue to advocate for and deliver meaningful solutions for patients," said Gary Zieziula, President and Managing Director, EMD Serono. "With Wendy's wealth of knowledge and strategic experience in advocacy and government relations, I'm confident in her ability to further our efforts and strengthen EMD Serono's leadership in the biopharmaceutical industry."

to promote and protect key business priorities and tactics to advance the company's interests through legislative bodies, regulatory agencies, trade associations and advocacy groups. She previously worked as the Head of Governmental Affairs for Hospira where she represented corporate interests before Congress, and helped develop and execute federal, state, policy and alliance development strategies. Her extensive healthcare background also includes 12 years with CVS Caremark (now CVS Health) as the Vice President of Government Affairs.

Ms. Sussman succeeds Michael Ruggiero, who was recently appointed to a new position within Merck KGaA, Darmstadt, Germany, as the Vice President, Global Franchise Business Partners on the Healthcare Global Government and Public Affairs team.

Ms. Sussman holds a dual-degree from Lafayette College, Easton, PA in Government & Law and International Affairs.

About EMD Serono, Inc.

EMD Serono is the biopharmaceutical business of Merck KGaA, Darmstadt, Germany, in the U.S. and Canada - a leading science and technology company - focused exclusively on specialty care. For more than 40 years, the business has integrated cutting-edge science, innovative products and industry-leading patient support and access programs. EMD Serono has deep expertise in neurology, fertility and endocrinology, as well as a robust pipeline of potential therapies in oncology, immuno-oncology and immunology as R&D focus areas. Today, the business has 1,300 employees around the country with commercial, clinical and research operations based in the company's home state of Massachusetts. www.emdserono.com

About Merck KGaA, Darmstadt, Germany

Merck KGaA, Darmstadt, Germany, is a leading science and technology company in healthcare, life science and performance materials. Around 50,000 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 2016, Merck KGaA, Darmstadt, Germany, generated sales of €15.0 billion in 66 countries.

Founded in 1668, Merck KGaA, Darmstadt, Germany, is the world's oldest pharmaceutical and chemical company. The founding family remains the majority owner of the publicly listed corporate group. Merck KGaA, Darmstadt, Germany holds the global rights to the "Merck" name

Your Contact
Melissa Beglin 781-681-2609

SOURCE EMD Serono

COMPANY
LEADERSHIP TEAM
PARTNERING
PRESS
CONTACT US
COMPLIANCE & TRANSPARENCY

THERAPEUTIC AREAS

YOUR REQUESTS

conditions as set out in our Legal Statement and Privacy Policy.

This site contains information that is intended for US residents only. Canadian residents should consult the EMD Inc. website at www.emdserono.ca for information on products and services approved in Canada.

SITEMAP

LEGAL STATEMENT

PRIVACY POLICY

CONTACT US

EMD Serono to Collaborate with March of Dimes to Improve Health of Mothers and Babies

-- Three-year collaboration to focus on working mothers as a part of EMD Serono's support of the Healthy Women, Healthy Economies initiative

ROCKLAND, Mass., March 22, 2018 /PRNewswire/ -- EMD Serono, Inc., the biopharmaceutical business of Merck KGaA, Darmstadt, Germany in the U.S. and Canada, today announced that it will collaborate with March of Dimes to launch the March of Dimes Center for Social Science Research to inform evidence-based policymaking promoting the health of all mothers and babies.

Together – as part of EMD Serono's commitment to the Healthy Women, Healthy Economies initiative – EMD Serono and March of Dimes will conduct six research studies over the course of three years to better understand the relationship among economic and employer policies, women's health and productivity, and childbirth. The Center aims to create a greater capacity to better understand the influence of social

Additionally, with EMD Serono's help, March of Dimes will expand its Healthy Babies Healthy Business® workplace wellness program, which supports health benefits and policies for strong mothers and babies.

"Our March of Dimes collaboration is highly complementary to the Healthy Women, Healthy Economies initiative," said Belén Garijo, M.D., CEO Healthcare and member of the Executive Board of Merck KGaA, Darmstadt, Germany. "Both aim to support the health of women and their families, and at the same time, help create professional ecosystems that allow women to thrive."

The collaboration aims to advance the understanding that for many women, trying to balance caregiving responsibilities with workplace responsibilities has significant impacts on their own health and well-being.

Caregiving responsibilities also have an impact on economic success; over one in five[i] unpaid caregivers have had to reduce their paid hours at work to care for a family member. And, in line with the collaboration, government policies that support working mothers have been shown to improve both maternal health, including one study[ii] that found that women who took leaves longer than 12 weeks had fewer depressive symptoms. By finding ways to alleviate this problem, March of Dimes and EMD Serono hope to promote maternal health and healthy pregnancies, which in turn will help women achieve leadership positions and drive economic and social gains.

"It's crucial that we support mothers throughout every stage of their pregnancy and beyond," said Stacey D. Stewart, president of March of Dimes. "For 80 years, March of Dimes has helped millions of babies survive and thrive, and supporting mothers is integral to fulfilling our mission. As we build upon our legacy of impact and innovation, EMD Serono is a natural partner to help us advocate for policies that prioritize health."

The collaboration was announced at a panel event hosted by The Wilson Center titled "Balancing the Burden of Care." The event featured Belén Garijo and Stacey D. Stewart as panelists, as well as Grace Whiting, president and CEO of the National Alliance for Caregiving, and Gary Barker, president and CEO of Promundo.

U.S. and Canada - a leading science and technology company - focused exclusively on specialty care. For more than 40 years, the business has integrated cutting-edge science, innovative products and industry-leading patient support and access programs. EMD Serono has deep expertise in neurology, fertility and endocrinology, as well as a robust pipeline of potential therapies in oncology, immuno-oncology and immunology as R&D focus areas. Today, the business has 1,300 employees around the country with commercial, clinical and research operations based in the company's home state of Massachusetts. www.emdserono.com

About Healthy Women, Healthy Economies

Healthy Women, Healthy Economies strives to unleash the economic power of women by bringing governments, employers and other interested stakeholders together to help to improve women's health so women - and by extension their families - can join, thrive, rise in their communities and live better lives. Originally conceived in 2015 within the Asia-Pacific Economic Cooperation and in collaboration with the governments of the United States and the Philippines, Healthy Women, Healthy Economies aims to identify and implement policies that advance women's health and well-being to support their economic participation. Merck KGaA, Darmstadt, Germany is the founding private sector partner in Healthy Women, Healthy Economies and is expanding and making it part of our core commitment by supporting research to quantify the impact and forming collaborations to advocate for change. To learn more, please visit: https://www.emdgroup.com/en/company/responsibility/our-strategy/health/hwhe.html.

[i] Caregiving: The Impact on the Workplace, Health Advocate, 2010: http://bit.ly/1yjpqHV.
[ii] Family Leave After Childbirth
and the Mental Health of New Mothers. 23 April 2012.
http://i2.cdn.turner.com/cnn/2015/images/10/28/15-061_text.pdf.

Your Contact
Lisa Buffington 781-681-2340
Vice President U.S. Communications

SOURCE EMD Serono, Inc.

COMPANY

LEADERSHIP TEAM

PARTNERING

PRESS

CONTACT US

COMPLIANCE & TRANSPARENCY

THERAPEUTIC AREAS

YOUR REQUESTS

EMD Serono Highlights Commitment to Advance Multiple Sclerosis Treatment with Investigational Cladribine Tablets and Rebif® Data at AAN 2018

ROCKLAND, Mass., April 13, 2018 /PRNewswire/ -- EMD Serono, the biopharmaceutical business of Merck KGaA, Darmstadt, Germany, in the US and Canada, today announced data for Cladribine Tablets, an investigational treatment for multiple sclerosis (MS), and Rebif® (interferon beta-1a) will be presented at the American Academy of Neurology (AAN) 70th Annual Meeting, April 21-27, 2018, in Los Angeles.

Cladribine Tablets data to be presented includes poster presentations highlighting post-hoc analyses of the CLARITY, CLARITY Extension and ORACLE-MS trials evaluating safety and use in patients with MS, as well as the impact on B- and T-cells. Cladribine Tablets, marketed as MAVENCLAD® in the European Union (EU), is an investigational short-course oral therapy that is thought to preferentially target lymphocytes which may be integral to the pathological process of relapsing forms of MS (RMS). Cladribine Tablets is currently under clinical investigation and is not approved in the US.

MAVENCLAD® is now available in Germany, UK, Canada, Netherlands, Norway, Denmark, Sweden, Israel, and other markets. The Company is planning additional filings for regulatory approval including the United States.

Rebif data includes presentations analyzing no evidence of disease activity (NEDA), long-term disease activity assessed by the Magnetic Resonance Imaging in MS (MAGNIMS) score, new data on pregnancy outcomes for women being treated with interferon beta, as well as real-world evidence evaluating treatment adherence rates for patients treated with Rebif compared with dimethyl fumarate.

"We look forward to presenting data demonstrating advancement in our knowledge of MS, including further scientific information about Rebif, an important treatment option for relapsing forms of MS, and potential treatment options, such as investigational Cladribine Tablets, at the 2018 AAN Annual Meeting," said Luciano Rossetti, MD, Executive Vice President, Global Head of R&D for EMD Serono. "We are committed to better understanding MS and developing innovative solutions to improve the lives of patients and those affected by this disease."

Meeting attendees can learn more about the Company and participate in the following MS-specific interactive activities by visiting booth #1847:

- "I'm Balancing MS": Individuals can understand the balance between healthcare and lifestyle for those facing MS through a mobile art activity. For each participant, we will donate $100 to MS Fitness Challenge, a charity organization dedicated to educating and training people with MS on the benefits of exercise and nutrition.
- "Shine a Light": Individuals can create their own Light Trail art symbolizing what drives their commitment to fighting MS. Participation in the activity will drive a donation to MS Fitness Challenge.

Additionally, Exhibit Hall booth #1957 will host hands-on activities which will allow attendees to gain a better understanding of what it's like to have MS through virtual reality pods and simulation stations.

EMD Serono will also be hosting an Industry Therapeutic Update event entitled Evolving Perspectives and Innovations in Multiple Sclerosis on Wednesday, April 25 from 7:00 p.m.-10:00 p.m. PDT at the Platinum Ballroom in the JW Marriott Hotel in Los Angeles. Speakers include, Professor Amit Bar-Or, University of Pennsylvania, Philadelphia, PA, Professor

AAN Brain Health Fair

EMD Serono will exhibit its MS InsideOut experience at the AAN Brain Health Fair, a one-day-only event where attendees can learn about the brain and the field of neurology. The event takes place on Friday, April 20 from 10:00 a.m.-4:00 p.m. PDT at the Los Angeles Convention Center.

Presentations at AAN 2018 include the following accepted abstracts:

Cladribine Tablets Presentations			
Title	**Lead Author**	**Abstract/Poster #**	**Presentation Details**
Effects of Cladribine Tablets on CD4+ T-cell Subsets in the ORACLE-MS Study: Results from an Analysis of Lymphocyte Surface Markers	Leist T.	402	Session P1: Biomarkers and Experimental Studies for Multiple Sclerosis on April 22, 2018 On Display: 11:30 a.m. to 5:30 p.m. PDT Present: 4:00 p.m. to 5:30 p.m. PDT
Integrated Safety Analysis of Infections during Periods of Grade 3 or	Cook S.	407	Session P3: MS

			Development on April 24, 2018 On Display: 11:30 a.m. to 7:00 p.m. PDT Present: 5:30 p.m. to 7:00 p.m. PDT
Effectiveness of Lymphocyte-based Re-treatment Criteria in Minimizing the Incidence of Severe Sustained Lymphopenia During Treatment with Cladribine Tablets 3.5mg/kg	Cook S.	370	Session P5: MS Therapies: MOA, Safety and Complications on April 26, 2018 On Display: 11:30 a.m. to 7:00 p.m. PDT Present: 5:30 p.m. to 7:00 p.m. PDT
Long-term Lymphocyte Counts in Patients with RRMS Treated with	Soelberg-Sorensen P.	364	Session P5: MS

			and Complications on April 26, 2018 On Display: 11:30 a.m. to 7:00 p.m. PDT Present: 5:30 p.m. to 7:00 p.m. PDT
Selective and Discontinuous Reduction of B and T Lymphocytes and NK cells in Patients with Early and Relapsing MS (ORACLE-MS, CLARITY and CLARITY Extension) After Administration of Cladribine Tablets	Stuve O.	351	Session P5: MS Therapies: MOA, Safety and Complications on April 26, 2018 On Display: 11:30 a.m. to 7:00 p.m. PDT Present: 5:30 p.m. to 7:00 p.m. PDT
Rebif® (interferon beta-1a) Presentations			

Relapse in Patients with Multiple Sclerosis Newly Initiating scIFNβ1a Compared with Oral Disease-Modifying Drugs: A Real-World Assessment	Bowen J.	353	Session P1: Comparative Efficacy of Disease Modifying Therapies on April 22, 2018 On display: 11:30 a.m. to 5:30 p.m. PDT Present: 4:00 p.m. to 5:30 p.m. PDT
A Panel Survey Analysis of Adherence in Patients with Multiple Sclerosis Treated with scIFNβ1a or Dimethyl Fumarate	Perrin Ross A.	354	Session P1: Comparative Efficacy of Disease Modifying Therapies on April 22, 2018 On display: 11:30 a.m. to 5:30 p.m. PDT Present: 4:00 p.m. to 5:30 p.m. PDT

Multiple Sclerosis (MAGNIMS) Score Predicts Long-Term Clinical Disease Activity (CDA)-Free Status and Disability Progression in Patients Treated with Subcutaneous Interferon beta-1a (scIFNβ-1a)			Outcome Measures and Biomarkers on April 24, 2018, 4:18 p.m.-4:30 p.m. PDT
Evolution of New Lesions and its Temporal Patterns in Patients with Clinically Isolated Syndrome (CIS) Treated with Subcutaneous Interferon beta-1a (scIFNß-1a)	Vrenken H.	370	Session P3: MS and CNS Inflammatory Disease: Neuroimaging on April 24, 2018 On display: 11:30 a.m. to 7:00 p.m. PDT Present: 5:30 p.m. to 7:00 p.m. PDT
Risk of Stroke in Patients with Multiple Sclerosis Treated with Subcutaneous Interferon beta-1a	Sabidó-Espin M.	008	Session S36: MS Therapeutics and Clinical Research on April 25, 2018 4:54 p.m. to 5:06 p.m. PDT

Registry			and Multiple Sclerosis on April 25, 2018 On display: 11:30 a.m. to 7:00 p.m. PDT Present: 5:30 p.m. to 7:00 p.m. PDT
Impact of the Presence of Gadolinium-Enhancing (Gd+) Lesions at Baseline on No Evidence of Disease Activity (NEDA) Status in Patients Treated with Subcutaneous Interferon beta-1a (scIFNß-1a): A Post-hoc Analysis of REFLEXION	Freedman M.	387	Session P6: MS Therapeutics: Extension Studies on April 27, 2018 On display: 11:30 a.m. to 5:30 p.m. PDT Present: 4:00 p.m. to 5:30 p.m. PDT
Analysis of 6-month Confirmed Disability Progression in RRMS Patients Treated with Subcutaneous Interferon beta-1a	Wong S.L.	361	Session P6: MS Therapeutics III on April 27, 2018

			a.m. to 5:30 p.m. PDT Present: 4:00 p.m. to 5:30 p.m. PDT

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.

EMD Serono, Inc. and Multiple Sclerosis

For more than 20 years, EMD Serono has been relentlessly focused on understanding the journey people living with MS face in order to create a meaningful, positive experience for them and the broader MS community. However, there is still much that is unknown about this complex and unpredictable disease. EMD Serono is digging deeper to advance the science and reconstruct a new understanding of MS, inside and out. We are committed to delivering solutions that improve the lives of all those affected by MS. www.GetCloserToMS.com

About Cladribine Tablets

Cladribine Tablets is an investigational short-course oral therapy that is thought to selectively target lymphocytes which may be integral to the pathological process of relapsing MS (RMS). Cladribine Tablets is currently under clinical investigation and not approved for the treatment for any use in the United States. MAVENCLAD® has received marketing authorization in 35 countries including European Union member countries, Canada, Australia, Argentina, Israel, and the United Arab Emirates. MAVENCLAD® is now available in Germany, UK, Canada, Netherlands, Norway, Denmark, Sweden, Israel, and other markets. In December 2017, Health Canada approved MAVENCLAD for the treatment of relapsing forms of MS.

The clinical development program for Cladribine Tablets includes:

- The CLARITY (Cladribine Tablets Treating MS Orally) study: a two-year Phase III placebo-controlled study designed to evaluate the efficacy and safety of Cladribine Tablets as a

from the CLARITY study, designed to evaluate the safety and efficacy of Cladribine Tablets over an extended administration for four years.

- The ORACLE MS (Oral Cladribine in Early MS) study: a two-year Phase III placebo-controlled study designed to evaluate the efficacy and safety of Cladribine Tablets as a monotherapy in patients at risk of developing MS (patients who have experienced a first clinical event suggestive of MS).
- The ONWARD (Oral Cladribine Added ON To Interferon beta-1a in Patients With Active Relapsing Disease) study: a Phase II placebo-controlled study designed primarily to evaluate the safety and tolerability of adding Cladribine Tablets treatment to patients with relapsing forms of MS, who have experienced breakthrough disease while on established interferon-beta therapy.
- PREMIERE (Prospective Observational Long-term Safety Registry of Multiple Sclerosis Patients Who Have Participated in Cladribine Clinical Studies) study: interim long-term follow-up data from the prospective registry, PREMIERE, to evaluate the safety and efficacy of Cladribine Tablets. This includes more than 10,000 patient years of data with over 2,700 patients included in the clinical trial program, and more than 10 years of observation in some patients.

In the two-year CLARITY study, the most commonly reported adverse event (AE) in patients treated with Cladribine Tablets was lymphopenia. The incidence of infections was 48.3% with Cladribine Tablets and 42.5% with placebo, with 99.1% and 99.0% respectively rated mild-to-moderate by investigators.

About Rebif® (interferon beta-1a)

Rebif (interferon beta-1a) is used to treat relapsing forms of MS to decrease the frequency of relapses and delay the occurrence of some of the physical disability that is common in people with MS. The efficacy and safety of Rebif in controlled clinical trials beyond 2-years has not been established.

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.

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.

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.

There are no adequate and well-controlled studies in pregnant women. Rebif should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Version=

About EMD Serono, Inc.

EMD Serono is the biopharmaceutical business of Merck KGaA, Darmstadt, Germany, in the U.S. and Canada - a leading science and technology company - focused exclusively on specialty care. For more than 40 years, the business has integrated cutting-edge science, innovative products and industry-leading patient support and access programs. EMD Serono has deep expertise in neurology, fertility and endocrinology, as well as a robust pipeline of potential therapies in oncology, immuno-oncology and immunology as R&D focus areas. Today, the business has 1,300 employees around the country with commercial, clinical and research operations based in the company's home state of Massachusetts. www.emdserono.com

Your Contact

Alice McGrail 1-781-681-2886

SOURCE EMD Serono

Merck KGaA, Darmstadt, Germany, Presents New Osteoarthritis Data at OARSI 2018 World Congress

- Company to present 16 abstracts highlighting the momentum of its progress in osteoarthritis (OA) research and showcasing the company's leading OA pipeline
- Oral presentations on sprifermin offer further insights supporting its dose-response structural effect in patients with knee OA, observed in earlier studies

DARMSTADT, Germany, April 18, 2018 /PRNewswire/ -- Merck KGaA, Darmstadt, Germany, a leading science and technology company which operates its healthcare business in the U.S. and Canada as EMD Serono, today announced 16 abstracts, including two oral presentations, will be presented at the Osteoarthritis Research Society International (OARSI) 2018 World Congress, held April 26-29, 2018 in Liverpool, United Kingdom. The presence of Merck KGaA, Darmstadt, Germany at OARSI reflects the company's dedication to helping optimize outcomes for patients living with chronic progressive diseases, with the goal of developing novel disease-modifying therapies for osteoarthritis (OA).

Data of note includes an oral presentation of the three-year analysis of FORWARD, a five-year, multicenter Phase II study of sprifermin in OA of the knee. Results were consistent with the two-year results, which showed a statistically significant dose-dependent increase in cartilage

eighteen months after the last treatment cycle, cartilage thickness declined in all treatment arms as compared to year two. However, the difference observed at year two with sprifermin at the highest dose and frequency versus placebo was maintained at year three. The safety profile at year three was consistent with results observed at year two, where treatment emergent adverse events were balanced between groups and musculoskeletal and connective tissue disorders the most common.

"These data suggest the structural benefit of sprifermin at the highest dose was maintained in the third year and its long-term potential as a disease-modifying treatment for osteoarthritis will continue to be explored," said Dr. Marc C. Hochberg, primary investigator of the FORWARD study and Division Head, Rheumatology and Clinical Immunology, University of Maryland School of Medicine. "Osteoarthritis impacts an estimated 10 percent of the world's population over the age of 60[1] and represents an area of high unmet need for disease-modifying treatment options."

A second oral presentation features the results of an ex vivo study that showed sprifermin induced extra-cellular matrix remodelling and cartilage regeneration. In the study, long-term treatment with sprifermin continuously increased metabolic activity and type II collagen formation in human OA articular cartilage compared with placebo.

"We are committed to helping patients with osteoarthritis by elevating our understanding of the disease and continuing to invest in highly-targeted therapies," said Luciano Rossetti, Executive Vice President, Global Head of Research & Development at the biopharma business of Merck KGaA, Darmstadt, Germany. "Our intent is to provide true advancement to the field of osteoarthritis by developing therapeutic options with disease-modifying potential."

Additional presentations include: pre-clinical data for M6495, an ADAMTS-5 inhibiting nanobody moving into Phase I clinical development for OA; pre-clinical data for M1673, a GDF5 mutant for the potential treatment of OA; and research related to improving measures and patient recruitment in OA studies.

Accepted abstracts at the OARSI 2018 World Congress include:

Sprifermin				
Efficacy and Safety of Intra-Articular Sprifermin in Symptomatic Radiographic Knee Osteoarthritis: Pre-Specified Analysis of 3-Year Data From a 5-Year Randomized, Placebo-Controlled, Phase II Study with a 2 Year Treatment Phase	M Hochberg	32	Friday, April 27, 2:30 PM – 4:00 PM	Concurrent Session 3 – OA Clinical Trials and Treatment (Oral)
Articular Cartilage from OA Patients Show Extracellular Matrix Remodelling Over the Course of Treatment with Sprifermin (Recombinant Human Fibroblast Growth Factor 18)	A Bay-Jensen	65	Saturday, April 28, 10:45 AM – 12:15 PM	Plenary Session 5 – Growth Factors in OA: Opportunities for Intervention (Oral)
Intra-Articular Sprifermin Reduces Cartilage Loss in Addition to Increasing Cartilage Gain Independent of Femorotibial Location: A Post Hoc Analysis of a Randomized, Placebo-Controlled Phase II Clinical Trial	F Eckstein	551	Friday, April 27, 12:00-12:30 PM & 4:00-4:30 PM Saturday, April 28, 3:30-4:15 PM	Poster Sessions 1-3

In Vitro Characterization of the ADAMTS-5 Specific Nanobody M6495	D Werkmann	346	Friday, April 27, 12:30 -1:00 PM & 4:30-5:00 PM Saturday, April 28, 4:15 – 5:00 PM	Poster Sessions 1-3
Structural and Symptomatic Benefit of a Half-Live Extended Systemically Applied Anti-ADAMTS-5 Inhibitor M6495	C Brenneis	563	Friday, April 27, 12:00-12:30 PM & 4:00-4:30 PM Saturday, April 28, 3:30-4:15 PM	Poster Sessions 1-3
Pharmacokinetic and Pharmacodynamic Modelling of the Novel Anti-ADAMTS-5 Nanobody M6495 Using the Neo-Epitope Args as a Biomarker	J Pereira	343	Friday, April 27, 12:00-12:30 PM & 4:00-4:30 PM Saturday, April 28, 3:30-4:15 PM	Poster Sessions 1-3
The Anti-ADAMTS-5 Nanobody, M6495, Protects Against Cartilage Breakdown in Cartilage and Synovial Joint Tissue Explant Models	A Siebuhr	363	Friday, April 27, 12:00-12:30 PM & 4:00-4:30 PM Saturday, April 28, 3:30-4:15 PM	Poster Sessions 1-3
Study Design of a Phase I, Placebo-Controlled, First-In-Human Trial To Assess Safety and Tolerability, Immunogenecity, and Pharmacokinetics and	A Bihlet	522	Friday, April 27, 12:30 -1:00 PM & 4:30-5:00 PM Saturday, April 28, 4:15 – 5:00 PM	Poster Sessions 1-3

the Anti-ADAMTS-5 Nanobody, M6495, in Healthy Male Subjects				
M1673 (GDF5 mutant)				
M1673 (GDF5 mutant) Increases Matrix Production in Primary Porcine and Human Osteoarthritic Chondrocytes	T Mang	138	Friday, April 27, 12:30 -1:00 PM & 4:30-5:00 PM Saturday, April 28, 4:15 – 5:00 PM	Poster Sessions 1-3
A GDF5 Mutant Induces Chondrogenesis in Mesenchymal Stem Cells Similarly to GDF5 Wildtype But Shows a Decreased Osteogenic Potential	T Mang	125	Friday, April 27, 12:00-12:30 PM & 4:00-4:30 PM Saturday, April 28, 3:30-4:15 PM	Poster Sessions 1-3
Osteoarthritis Research				
C1M, C2M, C3M, PRO-C2, and CRPM in Serum Reflect Different Potential Pathogenetic Domains of Osteoarthritis, Data from Check	A Bay-Jensen	349	Friday, April 27, 12:00-12:30 PM & 4:00-4:30 PM Saturday, April 28, 3:30-4:15 PM	Poster Sessions 1-3
Recruitment Procedure Maximising Inclusion of Progressors in OA Clinical Studies Based on Existing Cohorts: Approach-Consortium Data Analysis	P Widera	521	Friday, April 27, 12:00-12:30 PM & 4:00-4:30 PM Saturday, April 28, 3:30-4:15 PM	Poster Sessions 1-3

APPROACH-consortium: Development to Predict Osteoarthritis Progression in Patients across Populations			4:00-4:30 PM Saturday, April 28, 3:30-4:15 PM	
"APPROACH" Study: A 2-Year, European, Cohort Study to Describe, Validate and Predict Phenotypes of Knee Osteoarthritis By Use Of Clinical, Imaging and Biochemical Markers	E van Helvoort	515	Friday, April 27, 12:00-12:30 PM & 4:00-4:30 PM Saturday, April 28, 3:30-4:15 PM	Poster Sessions 1-3
Two Year Tibiofemoral Joint Cartilage Loss is Weakly Correlated With Increased Pain Among Knees With Lower Baseline Cartilage Thickness	C Kwoh	474	Friday, April 27, 12:30 -1:00 PM & 4:30-5:00 PM Saturday, April 28, 4:15 – 5:00 PM	Poster Sessions 1-3
Pain Medication Reporting and Patient-Reported Outcomes in the Years Prior to Knee Replacement: Challenges to Assessing Symptomatic Experiences	C Kwoh	455	Friday, April 27, 12:00-12:30 PM & 4:00-4:30 PM Saturday, April 28, 3:30-4:15 PM	Poster Sessions 1-3

For more information about the data to be presented, please access the OARSI app. Also, visit the Merck KGaA, Darmstadt, Germany booth at this year's Congress to learn more about the company's commitment to advancing innovation in OA.

(OA) of the knee. It is a truncated recombinant human FGF-18 protein thought to induce chondrocyte proliferation and increased extra-cellular matrix (ECM) production, with the potential of promoting cartilage growth and repair. Sprifermin is currently in Phase II studies.

About M6495

M6495 is in clinical development to investigate its potential as a treatment for osteoarthritis (OA). Administered subcutaneously, M6495 is a selective nanobody thought to inhibit a disintegrin and metalloproteinase with thrombospondin motifs 5 (ADAMTS-5), a metalloproteinase crucial for cartilage matrix destruction as an early and key event in developing OA, with the potential for providing structural improvement and rapid pain relief for all OA joints. M6495 is currently being evaluated in a first-in-man Phase I study in healthy subjects.

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 again for your online subscription of this service as our newly introduced 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. More than 52,000 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 2017, Merck KGaA, Darmstadt, Germany, generated sales of € 15.3 billion in 66 countries.

Founded in 1668, Merck KGaA, Darmstadt, Germany, is the world's oldest pharmaceutical and chemical company. The founding family remains the majority owner of the publicly listed corporate group. 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 company operates as EMD Serono, MilliporeSigma and EMD Performance Materials.

[1] Arthritis Facts & Figures. Arthritis Foundation. https://www.arthritis.org/Documents/Sections/About-Arthritis/arthritis-facts-stats-figures.pdf.

Your Contact
Brenda Mulligan +1 (978) 821-5345

SOURCE Merck KGaA, Darmstadt, Germany

conditions as set out in our Legal Statement and Privacy Policy.

This site contains information that is intended for US residents only. Canadian residents should consult the EMD Inc. website at www.emdserono.ca for information on products and services approved in Canada.

SITEMAP

LEGAL STATEMENT

PRIVACY POLICY

CONTACT US

EMD Serono R&D Building Earns First WELL Gold Certification™ in U.S. for New & Existing Building Project

EXPLORE MORE

-- Prestigious building distinction reflects company's commitment to employee health and wellness

BILLERICA, Mass., April 23, 2018 /PRNewswire/ -- EMD Serono, the biopharmaceutical business of Merck KGaA, Darmstadt, Germany in the U.S. and Canada, today announced that its R&D facility's Sagamore Building in Billerica, Massachusetts has been awarded WELL Certification at the Gold level by the International WELL Building Institute™ (IWBI™), underscoring the company's commitment to employee health and well-being. The Sagamore is the first building to receive WELL Gold Certification for New and Existing Buildings in the U.S. This prestigious distinction was awarded through IWBI's WELL Building Standard™ (WELL), which is the premier building standard focused on enhancing people's health and wellness through built environments.

An employee's physical workplace is one of the top three factors affecting performance and job satisfaction[1]. The WELL Building Standard™ encourages the design of buildings with a human-centered approach, leveraging a research-based certification system that measures the human health and wellness of occupants based on building design and construction.

our collaborative and knowledge-sharing culture," said Anthony Meenaghan, Senior Director, Facilities Management and Engineering, Environmental Health & Safety, EMD Serono. "Offering employees an environment where they can do their best work plays an important role in bringing meaningful solutions to people with difficult-to-treat diseases."

At EMD Serono's R&D campus in Billerica – one of the company's four global R&D hubs – more than 500 employees work to accelerate R&D innovation in oncology, immuno-oncology, and immunology. The Sagamore Building was completed last year to further expand the R&D campus, featuring innovative labs, open office space, bleacher seating, huddle rooms and technology-free quiet zones across three buildings and approximately 275,000 square feet.

Created through seven years of rigorous research and development working with leading physicians, scientists, and industry professionals, the WELL Building Standard is a performance-based system that marries best practices in design and construction with evidence-based medical and scientific research. WELL is grounded in a body of medical research that explores the connection between the buildings where we spend more than 90 percent of our time and the health and wellness impact on us as occupants. To be awarded WELL Certification by IWBI, the Sagamore Building underwent rigorous testing and a final evaluation carried out by Green Business Certification Inc. (GBCI), which is the third-party certification body for WELL, to ensure it met all WELL Certified™ Gold Level performance requirements. WELL Certification ensures that the built environment is designed to improve the nutrition, fitness, mood, sleep patterns and performance of its occupants.

"The work of innovative building projects such as the Sagamore Building is helping propel the healthy building movement forward," said Rick Fedrizzi, chairman and CEO of IWBI™. "As the newest member of the family of WELL Certified™ projects, the Sagamore Building is a strong representation of our growing movement."

Beyond being recognized with WELL Certification at the Gold level for a new and existing building project in the U.S., the Sagamore Building received Platinum LEED certification in 2015.

[1] The Gensler Design + Performance Index, The US Workplace Survey (2006).

U.S. and Canada - a leading science and technology company - focused exclusively on specialty care. For more than 40 years, the business has integrated cutting-edge science, innovative products and industry-leading patient support and access programs. EMD Serono has deep expertise in neurology, fertility and endocrinology, as well as a robust pipeline of potential therapies in oncology, immuno-oncology and immunology as R&D focus areas. Today, the business has 1,300 employees around the country with commercial, clinical and research operations based in the company's home state of Massachusetts. www.emdserono.com

About Merck KGaA, Darmstadt, Germany

Merck KGaA, Darmstadt, Germany, is a leading science and technology company in healthcare, life science and performance materials. Around 50,000 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 2017, Merck KGaA, Darmstadt, Germany, generated sales of € 15.3 billion in 66 countries.

Founded in 1668, Merck KGaA, Darmstadt, Germany, is the world's oldest pharmaceutical and chemical company. The founding family remains the majority owner of the publicly listed corporate group. 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 company operates as EMD Serono, MilliporeSigma and EMD Performance Materials.

Contact
Melissa Beglin 781-681-2609

SOURCE EMD Serono

14th Annual EMD Serono Specialty Digest™ Educates Health Plans on Latest Trends in Unmet Payer Needs and Patient-Centric Services

- Digest's Launch at 2018 Asembia Specialty Pharmacy Summit Reveals Increase in Physician Collaboration, Infusion Site-of-Care Programs

ROCKLAND, Mass., April 30, 2018 /PRNewswire/ -- EMD Serono, the biopharmaceutical business of Merck KGaA, Darmstadt, Germany, in the U.S. and Canada, today announced the launch of the 14th edition of the EMD Serono Specialty Digest™ at the Asembia Specialty Pharmacy Summit in Las Vegas, NV. The Digest is an annual industry resource that provides market data on pharmacy benefit manager (PBM) and health insurance plans' management of biopharmaceuticals and identifies common trends occurring across plans. The Digest is available to those who request a copy at https://specialtydigestemdserono.com.

"This year's Specialty Digest reveals noteworthy findings – particularly the increase of infusion site-of-care programs and rise in physician collaboration for cancer treatment development – that we believe will serve as an important benchmarking tool in this highly complex managed care environment," said Robert Truckenmiller, Senior Vice President, Market Access & Customer Solutions, EMD Serono. "Similar to previous years, our Specialty Digest shares insights on

health plan decisions that better meet the needs of patients."

The 14th edition EMD Serono Specialty Digest outlines the results of a survey of 59 commercial health plans representing nearly 100 million covered lives in 2017. Among the interesting trends identified this year:

- **Payer Strategies to Manage Specialty Drugs:** Since 2013, there was a 135 percent increase in health plans that are using site-of-care programs - hospitals, community offices, ambulatory infusion suites, or home-based settings. Of those that do not have a site-of-care program, more than half plan to implement one in the next 12 months.
- **Challenges and Opportunities in Oncology:** Today, 84 percent of plans now collaborate with physicians, including oncologists, to develop cancer treatment pathways, while only 38 percent did so in 2016; Plans are now concentrating on collaborating rather than solely focusing on use of third party organizations and/or internally-developed pathways.
- **Benefits Assessment for Multiple Sclerosis (MS):** Seventy-six percent of plans cover injectable drugs under the pharmacy benefit only. Furthermore, most plans (78 percent) require injectable drugs for MS to be dispensed through a contracted specialty pharmacy provider (SPP).

"Compiling the changes and trends in health plan decision making offers a unique opportunity for decision makers to see the big picture of how plans are impacting care," indicated Kevin Host, Pharmaceutical Strategies Group. "This year, we were pleased to see an increase in focus on access, goals to improve disease remission rates and other trends that will benefit patients."

Originally developed in 2004 to serve as a reference and benchmarking tool for managed care decision makers, the EMD Serono Specialty Digest has been accessed and used annually by thousands of stakeholders, including health plans, pharmacy benefit managers, employers, specialty pharmacies, and pharmaceutical companies.

Findings are available in the full text of the EMD Serono Specialty Digest, at https://specialtydigestemdserono.com.

About EMD Serono, Inc.

EMD Serono is the biopharmaceutical business of Merck KGaA, Darmstadt, Germany, in the U.S. and Canada - a leading science and technology company - focused exclusively on specialty care. For more than 40 years, the business has integrated cutting-edge science, innovative

therapies in oncology, immuno-oncology and immunology as R&D focus areas. Today, the business has 1,300 employees around the country with commercial, clinical and research operations based in the company's home state of Massachusetts. www.emdserono.com

About Merck KGaA, Darmstadt, Germany

Merck KGaA, Darmstadt, Germany, is a leading science and technology company in healthcare, life science and performance materials. Around 50,000 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 2017, Merck KGaA, Darmstadt, Germany, generated sales of € 15.3 billion in 66 countries.

Founded in 1668, Merck KGaA, Darmstadt, Germany, is the world's oldest pharmaceutical and chemical company. The founding family remains the majority owner of the publicly listed corporate group. 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 company operates as EMD Serono, MilliporeSigma and EMD Performance Materials.

Your Contact

Melissa Beglin, 781-681-2609

SOURCE EMD Serono

EMD Serono to Present MS Data and Debut New Patient Resources at CMSC 2018

EXPLORE MORE

- Presentations for investigational Cladribine Tablets include analyses of NEDA and MRI outcomes in patients with relapsing MS
- MS in the 21st Century to debut 'My MS Priorities,' a new tool to help improve patient-HCP dialogue
- Continued company support for CMSC initiatives: MS Teamworks and the June Halper MS Scholarship

ROCKLAND, Mass., May 29, 2018 /PRNewswire/ -- EMD Serono, the biopharmaceutical business of Merck KGaA, Darmstadt, Germany, in the U.S. and Canada, today announced that six abstracts including two poster presentations on Cladribine Tablets, an investigational treatment for relapsing multiple sclerosis (RMS), will be presented at the 32nd Annual Meeting of the Consortium of Multiple Sclerosis Centers (CMSC), taking place from May 30 – June 2, 2018, in Nashville, TN.

Poster presentations for Cladribine Tablets include evaluations of no evidence of disease activity (NEDA) and radiological outcomes in RMS patients from the CLARITY trial. Cladribine Tablets, marketed as MAVENCLAD® outside of the U.S., is an investigational short-course oral therapy that is thought to preferentially target lymphocytes, which may be integral to the pathological

"We look forward to presenting data at CMSC 2018 evaluating the use of Cladribine Tablets in patients with relapsing forms of multiple sclerosis," said John Walsh, Vice President, Neurology & Immunology (N&I), U.S. Medical Affairs for EMD Serono. "This data is a further testament to our commitment to understanding MS in a deeper way and building a better future for the MS community."

Additional poster presentations include analyses of health economics and outcomes research (HEOR) data on the diagnosis and treatment of infertility and live birth rates in women with or without MS, and the prevalence of comorbidities in patients with or without MS. A mapping study comparing the availability of educational resources for MS patients across different geographical regions will also be shared at the meeting.

Meeting attendees can learn more about EMD Serono and its support of the MS community by participating in the following interactive activities at booth #522:

- "I'm Balancing MS": Individuals can learn about the balance between healthcare and lifestyle for those facing MS through a mobile art activity. For each participant, EMD Serono will make a donation to the MS Foundation.
- "Shine a Light": Individuals can create their own Light Trail art symbolizing what drives their commitment to fighting MS.
- "Sage on the Stage": Subject matter experts will provide brief presentations sharing their insights on emerging issues of importance around MS.

The Company will also sponsor booth #500, which is focused on MS in the 21st Century (MS21), an initiative comprised of an international steering group of healthcare professionals (HCPs) and patient advocates showcasing its newly developed consultation tool, 'My MS Priorities.' This priority planner aims to assist with improving patient engagement, enhancing mutual trust between patients and HCPs, and encouraging a more open dialogue. MS21 will host a series of short workshops at the exhibit throughout Wednesday, May 30 and Thursday, May 31 to introduce this tool to attendees.

Partnering with CMSC

Additionally, EMD Serono is proud to support the June Halper MS Nursing Scholarship, sponsored by The Foundation of the Consortium of Multiple Sclerosis Centers (FCMSC). The

EMD Serono is pleased to sustain its support of the CMSC's MS Teamworks online program, an educational web-based series that launched at the CMSC annual meeting in 2017. The 14-18 minute episodes have a wide range of speakers and are designed help the MS community prepare for clinical appointments, gain knowledge when they are between appointments, and ensure accurate and state-of-the-art education to all those affected by MS. The targeted talks feature practical answers and solutions to common questions and concerns surrounding topics such as symptoms, child rearing, where and how to seek care, and self-care leading to wellness. The program is continuing to expand in 2018 with new video content. For more information visit: http://msteamworks.com/.

The following abstracts were accepted for presentation at the CMSC 2018 Annual Meeting:

Cladribine Tablets Presentations			
Title	**Lead Author**	**Abstract/Poster #**	**Presentation Date/Time**
Effects of Cladribine Tablets on MRI Outcomes in High Disease Activity (HDA) Patients with Relapsing Multiple Sclerosis (RMS) in the CLARITY Study	G. Giovannoni	DX10	May 31, 2018 6:30 – 7:30 p.m. CDT
A Post Hoc Analysis of No Evidence of Disease Activity (NEDA) in Patients with Highly Active RMS Who Were Treated with Cladribine Tablets in CLARITY	G. Giovannoni	DX11	May 31, 2018 6:30 – 7:30 p.m. CDT
HEOR Presentations			
Diagnosis of Infertility and Infertility Treatment in Women	M.K. Houtchens	MD06	May 31, 2018 6:30 – 7:30 p.m. CDT

Live Birth Rates by Infertility Treatment in Women With and Without Multiple Sclerosis	M.K. Houtchens	QL07	May 31, 2018 6:30 – 7:30 p.m. CDT
Prevalence of Comorbidities in Patients With and Without Multiple Sclerosis by Age and Sex: A US Retrospective Claims Database Analysis	K. Kresa-Reahl	EG04	May 31, 2018 6:30 – 7:30 p.m. CDT
Educational Resources for MS			
A Mapping Study Comparing Educational Resources for Multiple Sclerosis Patients across the USA, Latin America, Middle East and Asia-Pacific Regions	D. Langdon	IS02	May 31, 2018 6:30 – 7:30 p.m. CDT

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.

EMD Serono, Inc. and Multiple Sclerosis

For more than 20 years, EMD Serono has been relentlessly focused on understanding the journey people living with MS face in order to create a meaningful, positive experience for them and the broader MS community. However, there is still much that is unknown about this complex and unpredictable disease. EMD Serono is digging deeper to advance the science and

About Cladribine Tablets

Cladribine Tablets is an investigational short-course oral therapy that is thought to selectively target lymphocytes which may be integral to the pathological process of relapsing MS (RMS). Cladribine Tablets is currently under clinical investigation and not approved for the treatment for any use in the United States. MAVENCLAD® has received marketing authorization in 35 countries including European Union member countries, Canada, Australia, Argentina, Israel, and the United Arab Emirates. MAVENCLAD® is now available in Germany, UK, Canada, Netherlands, Norway, Denmark, Sweden, Israel, and other markets. In December 2017, Health Canada approved MAVENCLAD® for the treatment of relapsing forms of MS.

The clinical development program for Cladribine Tablets includes:

- The CLARITY (Cladribine Tablets Treating MS Orally) study: a two-year Phase III placebo-controlled study designed to evaluate the efficacy and safety of Cladribine Tablets as a monotherapy in patients with RRMS.
- The CLARITY extension study: a two-year Phase III placebo-controlled study following on from the CLARITY study, designed to evaluate the safety and efficacy of Cladribine Tablets over an extended administration for four years.
- The ORACLE MS (Oral Cladribine in Early MS) study: a two-year Phase III placebo-controlled study designed to evaluate the efficacy and safety of Cladribine Tablets as a monotherapy in patients at risk of developing MS (patients who have experienced a first clinical event suggestive of MS).
- The ONWARD (Oral Cladribine Added ON To Interferon beta-1a in Patients With Active Relapsing Disease) study: a Phase II placebo-controlled study designed primarily to evaluate the safety and tolerability of adding Cladribine Tablets treatment to patients with relapsing forms of MS, who have experienced breakthrough disease while on established interferon-beta therapy.
- PREMIERE (Prospective Observational Long-term Safety Registry of Multiple Sclerosis Patients Who Have Participated in Cladribine Clinical Studies) study: interim long-term follow-up data from the prospective registry, PREMIERE, to evaluate the safety and efficacy of Cladribine Tablets. This includes more than 10,000 patient years of data with over 2,700 patients included in the clinical trial program, and more than 10 years of observation in some patients.

In the two-year CLARITY study, the most commonly reported adverse event (AE) in patients treated with Cladribine Tablets was lymphopenia. The incidence of infections was 48.3% with

About EMD Serono, Inc.

EMD Serono is the biopharmaceutical business of Merck KGaA, Darmstadt, Germany, in the U.S. and Canada - a leading science and technology company - focused exclusively on specialty care. For more than 40 years, the business has integrated cutting-edge science, innovative products and industry-leading patient support and access programs. EMD Serono has deep expertise in neurology, fertility and endocrinology, as well as a robust pipeline of potential therapies in oncology, immuno-oncology and immunology as R&D focus areas. Today, the business has 1,300 employees around the country with commercial, clinical and research operations based in the company's home state of Massachusetts. www.emdserono.com

Your Contact

Alice McGrail 1-781-681-2886

SOURCE EMD Serono

THERAPEUTIC AREAS

YOUR REQUESTS

World MS Day 2018: Call for Greater Curiosity to Drive Understanding of the Disease and Future Innovation

- **Launch of #MSInsideOut campaign, aimed at providing a deeper understanding of multiple sclerosis (MS)**
- **Donation to the MS International Federation (MSIF)* of up to € 20,000**
- **Shift.ms to Executive Produce a documentary to highlight stories and unique perspectives within the MS community**

Darmstadt, Germany, May 30, 2018 – Merck KGaA, Darmstadt, Germany, a leading science and technology company, today announced its support of World MS Day 2018 and MS International Federation (MSIF)'s #BringingUsCloser campaign through a new campaign, #MSInsideOut, to support the multiple sclerosis (MS) community and deepen understanding of the disease. The initiative will involve a collaboration with Shift.ms, the social network for people with MS, who will be Executive Producers on a new documentary, which will feature unique perspectives from the MS community. The documentary will premiere at the 34th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) in Berlin, Germany in October.

In addition, for every use of the hashtag #MSInsideOut on Twitter until June 8, Merck KGaA, Darmstadt, Germany will donate €1 (up to €20,000) towards MSIF's research fellowship

"To create further advances it is critical that we continuously ask questions, listen and learn," said Rehan Verjee, Chief Marketing and Strategy Officer at the Biopharma business of Merck KGaA, Darmstadt, Germany. "We are committed to truly understanding MS from the inside-out, and more importantly, helping others do the same."

"We are pleased to be working as Executive Producers on this new documentary in an effort to shine a light on the untold stories of MS," said George Pepper, Co-founder and Director, Shift.ms. "In line with our broader mission at Shift.ms, the aim of this documentary is to highlight the positive stories of our members, as well as the elements of MS that still remain under-represented. We hope that by bringing these stories out in the open we will be able to address the challenges that remain and drive further innovation to tackle these barriers."

For most people living with MS, a diagnosis occurs in the prime of their lives, ages 20-40[i], and MS produces significant physical disability within 20 to 25 years in more than 30% of patients[ii]. Despite advances in MS care, a deeper understanding of the unique challenges both patients and care partners face is needed.

Last year, Merck KGaA, Darmstadt, Germany announced the largest global MS care partner study to date in partnership with the International Alliance of Carer Organizations (IACO). Findings from previous research have shown that problems identified among care partners include anxiety, depression, insomnia and pain, along with concerns about the financial impact of MS for families[iii]. These data, which will be published at ECTRIMS in Berlin, Germany, October 10–12, 2018, further demonstrate the need for a deeper understanding of those affected by MS and their care partners.

Merck KGaA, Darmstadt, Germany, a company celebrating its 350th anniversary in 2018, has played an important role in innovation, as well as supporting the MS community more broadly, for more than two decades. Curiosity has always been the force that drives Merck KGaA, Darmstadt, Germany and will continue to motivate the Company to apply its expertise in science and technology to achieve human progress.

In addition, today, MS in the 21st Century, a Merck KGaA, Darmstadt, Germany-sponsored initiative, is launching a website that will support the facilitation of discussions between patients and healthcare professionals, available at www.msinthe21stcentury.com.

LinkedIn from World MS Day onwards to view, like and share stories that will help others better understand MS.

* For every use of the hashtag #MSInsideOut until June 8, Merck KGaA, Darmstadt, Germany will donate €1 towards MSIF's ongoing research fellowship program– to mark the Company's commitment to MS over the last two decades.

About Multiple Sclerosis (MS)

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.

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 again for your online subscription of this service as our newly introduced geo-targeting requires new links in the email. You may later change your selection or discontinue this service.

About World MS Day 2018

World MS Day is officially marked on the last Wednesday of May. Events and campaigns take place throughout the month of May. It brings the global MS community together to share stories, raise awareness and campaign with and for everyone affected by multiple sclerosis. In 2009, the MS International Federation (MSIF) and its members initiated the first World MS Day. Campaigns are rolled out globally which focus on a different theme each year. The theme for World MS Day 2018 is 'Bringing Us Closer'.

About Shift.ms

Shift.ms - www.Shift.ms - is the social network for people with multiple sclerosis. Founded by MSers, for MSers, the charity supports many thousands of recently diagnosed people across the world as they make sense of MS. It's independent and it's free.

About Merck KGaA, Darmstadt, Germany

Merck KGaA, Darmstadt, Germany, is a leading science and technology company in healthcare, life science and performance materials. Almost 53,000 employees work to further develop

crystals for smartphones and LCD televisions. In 2017, Merck KGaA, Darmstadt, Germany, generated sales of € 15.3 billion in 66 countries.

Founded in 1668, Merck KGaA, Darmstadt, Germany, is the world's oldest pharmaceutical and chemical company. The founding family remains the majority owner of the publicly listed corporate group. 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 company operates as EMD Serono, MilliporeSigma and EMD Performance Materials.

---

[i] National Institute of Neurology Disorders and Strokes. Multiple Sclerosis: Hope Through Research. http://www.ninds.nih.gov/disorders/multiple_sclerosis/detail_multiple_sclerosis.htm. Accessed May 3, 2016.

[ii] Luzzio C, Dangond F. Multiple Sclerosis. Medscape. http://emedicine.medscape.com/article/1146199-overview. Accessed February 22, 2017.

[iii] Kantar Health. May 2017. NATIONAL HEALTH AND WELLNESS SURVEY, 2016 [EU]. New York, NY

For further information: Erin-Marie Beals, +1 781-681-2850

EMD SERONO

COMPLIANCE & TRANSPARENCY

THERAPEUTIC AREAS

YOUR REQUESTS

EMD Serono is the biopharmaceutical business of Merck KGaA, Darmstadt, Germany. This site contains information that is intended for residents of the United States only and is not meant to substitute for the advice provided by a medical professional. Always consult a physician if you have health concerns. Use and access of this site is subject to the terms and conditions as set out in our Legal Statement and Privacy Policy.

This site contains information that is intended for US residents only. Canadian residents should consult the EMD Inc. website at www.emdserono.ca for information on products and services approved in Canada.

SITEMAP

LEGAL STATEMENT

PRIVACY POLICY

CONTACT US

Cheryl Schwartz Joins EMD Serono as Head of U.S. Fertility and Endocrinology

Rockland, Massachusetts, July 31, 2018 – EMD Serono, the biopharmaceutical business of Merck KGaA, Darmstadt, Germany in the U.S. and Canada, today announced that Cheryl Schwartz joined the company as Senior Vice President and Head of U.S. Fertility and Endocrinology. In this role, Ms. Schwartz will oversee the strategic direction of EMD Serono's Fertility, Fertility Technologies and Endocrinology businesses in the U.S.

"EMD Serono has long been a leader in the Fertility and Endocrinology spaces, showing unwavering commitment to these communities for more than 20 years by offering medications, devices, technologies and services," said Gary Zieziula, President and Managing Director of EMD Serono. "We are thrilled to welcome Cheryl, a seasoned healthcare executive with a proven track record of success whose experience aligns with our own commitment to meeting the needs of patients."

Prior to joining EMD Serono, Ms. Schwartz held positions of increasing responsibility at Pfizer Inc., where she most recently served as General Manager of the U.S. Biosimilars business. In this role, she led Pfizer's efforts to successfully commercialize a broad portfolio of assets for the emerging US Biosimilars market. Previously, Ms. Schwartz also served as Vice President and Global Commercial Lead in Pfizer Vaccines supporting Prevnar 13®, and a range of other U.S.

Laboratories and Oxford Health Plans.

Ms. Schwartz holds an MBA from the Kellogg School of Management at Northwestern University and a bachelor's degree from the University of Michigan-Ann Arbor.

Prevnar 13 is a registered trademark of Wyeth LLC

About EMD Serono, Inc.

EMD Serono - the biopharmaceutical business of Merck KGaA, Darmstadt, Germany, in the U.S. and Canada – is engaged in the discovery, research and development of medicines for patients with difficult to treat diseases. The business is committed to transforming lives by developing and delivering meaningful solutions that help address the therapeutic and support needs of individual patients. Building on a proven legacy and deep expertise in neurology, fertility and endocrinology, EMD Serono is developing potential new oncology and immuno-oncology medicines while continuing to explore potential therapeutic options for diseases such as psoriasis, lupus and multiple sclerosis. Today, the business has approximately 1,300 employees around the country with commercial, clinical and research operations based in the company's home state of Massachusetts. www.emdserono.com

About Merck KGaA, Darmstadt, Germany

Merck KGaA, Darmstadt, Germany, is a leading science and technology company in healthcare, life science and performance materials. Around 50,000 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 2017, Merck KGaA, Darmstadt, Germany, generated sales of € 15.3 billion in 66 countries.

Founded in 1668, Merck KGaA, Darmstadt, Germany, is the world's oldest pharmaceutical and chemical company. The founding family remains the majority owner of the publicly listed corporate group. 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 company operates as EMD Serono, MilliporeSigma and EMD Performance Materials.

COMPANY

LEADERSHIP TEAM

PARTNERING

PRESS

CONTACT US

COMPLIANCE & TRANSPARENCY

THERAPEUTIC AREAS

YOUR REQUESTS

Rehan Verjee to Lead EMD Serono as Company Advances its Innovative Medicines Strategy in North America

(1)

ROCKLAND, Mass., Aug. 31, 2018 /PRNewswire/ -- EMD Serono, the biopharmaceutical business of Merck KGaA, Darmstadt, Germany in the U.S. and Canada, today announced that Rehan Verjee has been appointed President of EMD Serono and Global Head of Innovative Medicine Franchises, Merck KGaA, Darmstadt, Germany.

"Uniting the leadership of North America with our Global Innovative Medicine Franchises will increasingly put North America at the heart of our strategy," said Belén Garijo, Member of the Executive Board and CEO Healthcare at Merck KGaA, Darmstadt, Germany. "Rehan's leadership experience and track record of working across commercial and R&D makes him perfectly suited to ensure we are well positioned

For the past three years, Mr. Verjee has been the Executive Vice President, Chief Marketing and Strategy Officer, Healthcare, at Merck KGaA, Darmstadt, Germany, accountable for the global specialty franchises of Infertility, Oncology, and Neurology & Immunology, together with Global Market Access, Business Development, Strategy and Portfolio Management and the Medical Device and Services Unit. Prior to that, Mr. Verjee led the Canadian business as Managing Director.

In his new role, Mr. Verjee will take accountability for the U.S. and Canada biopharmaceutical business, while maintaining global accountability for the Oncology and Neurology & Immunology Franchises. He will assume full responsibility of the new position starting September 1, 2018.

"EMD Serono employees have played a significant role in advancing the treatment of several difficult-to-treat diseases. I look forward to continuing to advance our efforts in these areas and building on this heritage with the introduction of new medicines that hold real promise for even more patients," said Mr. Verjee.

Mr. Verjee succeeds Gary Zieziula, who has successfully led the business first as Chief Commercial Officer since January, 2014, and then as President, from January, 2016 until the present. Mr. Zieziula will remain with EMD Serono through the end of 2018 in support of the transition.

Mr. Verjee joined Merck KGaA, Darmstadt, Germany in 2004, holding management positions of increasing responsibility before joining the organization's Healthcare Executive Committee as Executive Vice President, Chief Marketing and Strategy Officer in October 2015. Mr. Verjee holds a master's in Molecular and Cellular Biochemistry from the University of Oxford in the U.K. He will relocate from Germany to the company's U.S. Headquarters in Rockland, Massachusetts.

About EMD Serono, Inc.

EMD Serono - the biopharmaceutical business of Merck KGaA, Darmstadt, Germany, in the U.S. and Canada – is engaged in the discovery, research and development of medicines for patients with difficult to treat diseases. The business is committed to transforming lives by developing and delivering meaningful solutions that help address the therapeutic and support needs of individual patients. Building on a proven legacy and deep expertise in neurology, fertility and endocrinology, EMD Serono is developing potential new oncology and immuno-oncology

psoriasis, lupus and multiple sclerosis. Today, the business has approximately 1,300 employees around the country with commercial, clinical and research operations based in the company's home state of Massachusetts. www.emdserono.com

About Merck KGaA, Darmstadt, Germany

Merck KGaA, Darmstadt, Germany, is a leading science and technology company in healthcare, life science and performance materials. Around 53,000 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 2017, Merck KGaA, Darmstadt, Germany, generated sales of € 15.3 billion in 66 countries.

Founded in 1668, Merck KGaA, Darmstadt, Germany, is the world's oldest pharmaceutical and chemical company. The founding family remains the majority owner of the publicly listed corporate group. 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 company operates as EMD Serono, MilliporeSigma and EMD Performance Materials.

Media contact:
Lisa Buffington 781-681-2340

SOURCE EMD Serono

LEADERSHIP TEAM

PARTNERING

PRESS

CONTACT US

COMPLIANCE & TRANSPARENCY

THERAPEUTIC AREAS

YOUR REQUESTS

SITEMAP

LEGAL STATEMENT

PRIVACY POLICY

CONTACT US

Merck KGaA, Darmstadt, Germany Data at ESMO 2018 Congress Highlight Multiple Therapeutics with Potential to Transform Cancer Care

EXPLORE MORE

- First presentation of Phase III data for avelumab (plus axitinib) in previously untreated, advanced kidney cancer
- New and updated data for bifunctional immunotherapy M7824
- Results from Phase II trials for tepotinib, including in EGFR TKI-resistant NSCLC
- Additional pipeline data feature abstracts for a further four innovative agents across multiple tumor types with a significant patient need

ESMO Abstract #

Avelumab: LBA6_PR, 659P, 1290P, 1291P, 1282P, 877P; **M7824 (TGF β-trap/anti-PD-L1):** 1048O, 1463P, 1931P, 757P, 643P, 642P, 661P; **tepotinib (MET kinase inhibitor):**

Darmstadt, Germany, October 9, 2018 – Merck KGaA, Darmstadt, Germany, a leading science and technology company which operates its healthcare business in the U.S. and Canada as EMD Serono, today announced that new data from a variety of high-priority clinical development programs will be presented at the ESMO 2018 Congress (European Society for Medical Oncology Annual Meeting), October 19–23, 2018, Munich, Germany.

In the year that Merck KGaA, Darmstadt, Germany celebrates its 350-year anniversary, abstracts at the congress represent a company record with eight therapeutic agents across 14 tumor types, reinforcing Merck KGaA, Darmstadt, Germany's position at the forefront of clinical development in oncology.

"Our data at this year's European Society for Medical Oncology Congress expand our understanding of avelumab in renal cell carcinoma and other tumors, and demonstrate the headway we are making with our pipeline, including bifunctional immunotherapy M7824 and tepotinib," said Luciano Rossetti, Global Head of Research & Development for the Biopharma business of Merck KGaA, Darmstadt, Germany. "We look forward to many more years of real and significant progress towards our vision of transforming the management and treatment of cancer."

Data from the Phase III study JAVELIN Renal 101, evaluating avelumab* in combination with axitinib, compared with sunitinib as initial therapy for patients with advanced renal cell carcinoma (RCC), will be presented for the first time during the Presidential Symposium at ESMO on Sunday, October 21, 2018 at 5:20 PM – 5:35 PM CEST. Avelumab is being jointly developed and commercialized with Pfizer. The results represent the first positive Phase III immunotherapy trial in combination with a tyrosine kinase inhibitor (TKI) in any tumor type, supporting Merck KGaA, Darmstadt, Germany's interest in the potential use of avelumab in combination with currently approved therapies and novel agents. These results will be submitted for publication in a peer-reviewed journal. Other updates include new avelumab data in Merkel cell carcinoma (MCC) and advanced gastric or gastroesophageal junction (GEJ) cancer.

(SCCHN), biliary tract cancer, esophageal squamous cell carcinoma and esophageal adenocarcinoma. In addition, updated data for M7824 in patients with gastric cancer and non-small cell lung cancer (NSCLC) will be shared. M7824, discovered in-house at Merck KGaA, Darmstadt, Germany, is an investigational bifunctional immunotherapy designed to combine a transforming growth factor β (TGF-β) trap by 'fusing' it with the anti-programmed death ligand-1 (PD-L1) mechanism. To date more than 650 patients with various types of solid tumors have been treated across the program with M7824 and the safety profile is consistent with that observed with other PD-1/PD-L1 inhibitors and previously described skin lesions (keratoacanthomas, SCC, hyperkeratosis) associated with TGF-β-inhibiting therapies.

Data for tepotinib** include results from three Phase II trials in epidermal growth factor receptor (EGFR) TKI-resistant NSCLC and advanced hepatocellular carcinoma, providing further evidence of this precision medicine's potential clinical activity in a range of tumors. Tepotinib, discovered in-house at Merck KGaA, Darmstadt, Germany, is an investigational, oral MET inhibitor that is designed to selectively inhibit the oncogenic MET receptor signaling caused by *MET* (gene) alterations or MET protein overexpression.

Additional pipeline abstracts feature updated data from Merck KGaA, Darmstadt, Germany's comprehensive DNA damage response (DDR) portfolio. These include results from a Phase I trial investigating M6620 (formerly VX-970) in combination with gemcitabine in patients with advanced NSCLC, and combined data from two Phase I trials of DNA-dependent protein kinase inhibitor, M3814. Results will also be shared from a Phase I/II trial of M7583, a Bruton's TKI, in patients with B-cell malignancies, as well as a retrospective analysis of the Phase I/II Poseidon study investigating abituzumab in patients with metastatic colorectal cancer (mCRC).

Data to be presented at the congress for Erbitux® will add to the growing body of real-world evidence supporting the therapy's role as a standard of care in RAS wild-type mCRC and first-line recurrent or metastatic SCCHN (R/M SCCHN), and for patients with locally advanced SCCHN (LA SCCHN) who may not be able to tolerate cisplatin-based regimens in full.

*Avelumab is under clinical investigation for the treatment of RCC, MCC, CRC, gastric and GEJ cancer, and has not been demonstrated to be safe and effective for these indications. There is no guarantee that avelumab will be approved for RCC, CRC, gastric or GEJ cancer by any health authority worldwide.

any use anywhere in the world.

Tepotinib, M7824, M3814, M7583, M6620 and abituzumab are under clinical investigation and have not been proven to be safe and effective. There is no guarantee any product will be approved in the sought-after indication by any health authority worldwide.

Notes to Editors

Key abstracts supported by Merck KGaA, Darmstadt, Germany, slated for presentation are listed below. In addition, a number of investigator-sponsored studies have been accepted (not listed).

Title	Lead Author	Abstract #	Presentation Date / Time (CEST)	Location
Avelumab				
Late-Breaking Abstracts				
JAVELIN Renal 101: a randomized, phase 3 study of avelumab + axitinib vs sunitinib as first-line treatment of advanced renal cell carcinoma (aRCC)	R Motzer	LBA6_PR	Sun, Oct 21, 4:30 – 6:10 PM (5:20 – 5:35 PM lecture time)	Hall A2 – Room 18

Poster Sessions				
Avelumab (anti–PD-L1) in Japanese patients with advanced gastric or gastroesophageal junction cancer (GC/GEJC): updated results from the phase 1b JAVELIN Solid Tumor JPN trial	T Doi	659P	Sun, Oct 21, 12:45 – 1:45 PM	Hall A3 – Poster Area Networking Hub
Avelumab in European patients (pts) with metastatic Merkel cell carcinoma (mMCC): experience from an ad hoc expanded access program (EAP)	P Nathan	1290P	Sun, Oct 21, 12:45 – 1:45 PM	Hall A3 – Poster Area Networking Hub
Cost-effectiveness (CE) of avelumab vs standard care (SC) for the	M Bharmal	1291P	Sun, Oct 21, 12:45 – 1:45 PM	Hall A3 – Poster Area Networking Hub

with metastatic Merkel cell carcinoma (mMCC)				
Responder analysis based on patient-reported outcomes (PROs) and clinical endpoints (CEPs) in patients (pts) with metastatic Merkel cell carcinoma (mMCC) treated with avelumab	SP D'Angelo	1282P	Sun, Oct 21, 12:45 – 1:45 PM	Hall A3 – Poster Area Networking Hub
First-line (1L) or second-line (2L) avelumab monotherapy in patients (pts) with advanced renal cell carcinoma (aRCC) enrolled in the phase 1b JAVELIN Solid Tumor trial	UN Vaishampayan	877P	Mon, Oct 22, 12:45 – 1:45 PM	Hall A3 – Poster Area Networking Hub

Title	Lead Author	Abstract #	Presentation Date / Time (CEST)	Location
M7824 (TGF β-trap/anti-PD-L1)				
Proffered Paper Session				
M7824 (MSB0011359C), a bifunctional fusion protein targeting PD-L1 and TGF-β, in patients (pts) with advanced SCCHN: results from a phase 1 cohort	BC Cho	1048O	Mon, Oct 22, 2:45 – 4:15 PM (3:00 PM lecture time)	ICM, Room 14B
Poster Sessions				
Updated results of M7824 (MSB0011359C), a bifunctional fusion protein targeting TGF-β and PD-L1, in	L Paz-Ares	1463P	Sat, Oct 20, 12:30 – 1:30 PM	Hall A3 – Poster Area Networking Hub

Assessment of PD1/ PD-L1 colocalization in hepatocellular carcinoma (HCC) using brightfield double labeling and quantitative digital image analysis	T Mrowiec	1931P	Sun, Oct 21, 12:45 – 1:45 PM	Hall A3 – Poster Area Networking Hub
M7824 (MSB0011359C), a bifunctional fusion protein targeting PD-L1 and TGF-β, in Asian patients with pretreated biliary tract cancer: preliminary results from a phase 1 trial	C Yoo	757P	Sun, Oct 21, 12:45 – 1:45 PM	Hall A3 – Poster Area Networking Hub
M7824 (MSB0011359C), a bifunctional fusion protein targeting PD-L1	B Tan	643P	Sun, Oct 21, 12:45 – 1:45 PM	Hall A3 – Poster Area Networking Hub

post-platinum esophageal adenocarcinoma (EAC): preliminary results from a phase 1 cohort				
Phase 1 study results from an esophageal squamous cell carcinoma (ESCC) cohort treated with M7824 (MSB0011359C), a bifunctional fusion protein targeting transforming growth factor β (TGF-β) and PD-L1	CC Lin	642P	Sun, Oct 21, 12:45 – 1:45 PM	Hall A3 – Poster Area Networking Hub
Updated results from a phase 1 trial of M7824 (MSB0011359C), a bifunctional fusion protein targeting PD-L1 and TGF-β, in	YJ Bang	661P	Sun, Oct 21, 12:45 – 1.45 PM	Hall A3 – Poster Area Networking Hub

recurrent or refractory gastric cancer				

Title	Lead Author	Abstract #	Presentation Date / Time (CEST)	Location
Tepotinib				
Proffered Paper Session				
Phase 2 study of tepotinib + gefitinib (TEP+GEF) in MET-positive (MET+)/epidermal growth factor receptor (EGFR)-mutant (MT) non-small lung cancer (NSCLC)	YL Wu	1377O	Fri, Oct 19, 4:00 – 5:30 PM (4:51 PM lecture time)	Hall A2, Room 18
Poster Discussion				

tepotinib vs sorafenib in Asian patients (pts) with advanced hepatocellular carcinoma (HCC)	BY Ryoo	621PD	Fri, Oct 19, 3:45 – 5:30 PM (4:25 PM lecture time)	Hall B3, Room 21
Poster Session				
Phase 2 efficacy and safety data for the MET inhibitor tepotinib in patients (pts) with sorafenib-treated advanced hepatocellular carcinoma (HCC)	T Decaens	698P	Sun, Oct 21, 12:45 – 1:45 PM	Hall A3 – Poster Area Networking Hub

Title	Lead Author	Abstract #	Presentation Date / Time (CEST)	Location
M6620				
Poster Session				

expansion data for M6620 (formerly VX-970), a first-in-class ATR inhibitor, combined with gemcitabine (Gem) in patients (pts) with advanced non-small cell lung cancer (NSCLC)			PM	Area Networking Hub

Title	Lead Author	Abstract #	Presentation Date / Time (CEST)	Location
M3814				
Poster Session				
Safety, clinical	M Mau-	1845P	Sat, Oct 20,	Hall A3 –

biomarker evaluation of the DNA-dependent protein kinase (DNAPK) inhibitor M3814: results from two phase I trials				Networking Hub

Title	Lead Author	Abstract #	Presentation Date / Time (CEST)	Location
M7583				
Poster Session				
Phase I/II, first in human trial with M7583, a Bruton's tyrosine kinase inhibitor	W Jurczak	1014PD	Sun, Oct 21, 4:30 – 5:45 PM	Hall B3 – Room 21

B cell malignancies				

Title	Lead Author	Abstract #	Presentation Date / Time (CEST)	Location
Abituzumab				
Poster session				
Patient selection for targeting integrin with abituzumab in patients with metastatic colorectal cancer (mCRC). A retrospective analysis of the randomized phase I/II Poseidon study	R Laeufle	487P	Sun, Oct 21, 12:45 – 1:45 PM	Hall A3 – Poster Area Networking Hub

About Avelumab

Avelumab is a human anti-programmed death ligand-1 (PD-L1) antibody. Avelumab has been shown in preclinical models to engage both the adaptive and innate immune functions. By blocking the interaction of PD-L1 with PD-1 receptors, avelumab has been shown to release the suppression of the T cell-mediated antitumor immune response in preclinical models.[1-3] Avelumab has also been shown to induce NK cell-mediated direct tumor cell lysis via antibody-dependent cell-mediated cytotoxicity (ADCC) in vitro.[3-5] In November 2014, Merck KGaA, Darmstadt, Germany and Pfizer announced a strategic alliance to co-develop and co-commercialize avelumab.

Avelumab is currently being evaluated in the JAVELIN clinical development program, which involves at least 30 clinical programs, including seven Phase III trials, and more than 8,600 patients across more than 15 different tumor types. For a comprehensive list of all avelumab trials, please visit clinicaltrials.gov.

Approved Indications in the US

The US Food and Drug Administration (FDA) granted accelerated approval for avelumab (BAVENCIO®) for the treatment of (i) adults and pediatric patients 12 years and older with metastatic Merkel cell carcinoma (mMCC) and (ii) patients with locally advanced or metastatic urothelial carcinoma (mUC) who have disease progression during or following platinum-containing chemotherapy, or have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy. These indications are approved under accelerated approval based on tumor response rate and duration of response. Continued approval for these indications may be contingent upon verification and description of clinical benefit in confirmatory trials.

Important Safety Information from the US FDA Approved Label

BAVENCIO can cause **immune-mediated pneumonitis**, including fatal cases. Monitor patients for signs and symptoms of pneumonitis, and evaluate suspected cases with radiographic imaging. Administer corticosteroids for Grade 2 or greater pneumonitis. Withhold BAVENCIO for moderate (Grade 2) and permanently discontinue for severe (Grade 3), life-threatening (Grade

with Grade 3.

BAVENCIO can cause **immune-mediated hepatitis**, including fatal cases. Monitor patients for abnormal liver tests prior to and periodically during treatment. Administer corticosteroids for Grade 2 or greater hepatitis. Withhold BAVENCIO for moderate (Grade 2) immune-mediated hepatitis until resolution and permanently discontinue for severe (Grade 3) or life-threatening (Grade 4) immune-mediated hepatitis. Immune-mediated hepatitis was reported in 0.9% (16/1738) of patients, including two (0.1%) patients with Grade 5, and 11 (0.6%) with Grade 3.

BAVENCIO can cause **immune-mediated colitis**. Monitor patients for signs and symptoms of colitis. Administer corticosteroids for Grade 2 or greater colitis. Withhold BAVENCIO until resolution for moderate or severe (Grade 2 or 3) colitis, and permanently discontinue for life-threatening (Grade 4) or recurrent (Grade 3) colitis upon reinitiation of BAVENCIO. Immune-mediated colitis occurred in 1.5% (26/1738) of patients, including seven (0.4%) with Grade 3.

BAVENCIO can cause **immune-mediated endocrinopathies**, including adrenal insufficiency, thyroid disorders, and type 1 diabetes mellitus.

Monitor patients for signs and symptoms of **adrenal insufficiency** during and after treatment, and administer corticosteroids as appropriate. Withhold BAVENCIO for severe (Grade 3) or life-threatening (Grade 4) adrenal insufficiency. Adrenal insufficiency was reported in 0.5% (8/1738) of patients, including one (0.1%) with Grade 3.

Thyroid disorders can occur at any time during treatment. Monitor patients for changes in thyroid function at the start of treatment, periodically during treatment, and as indicated based on clinical evaluation. Manage hypothyroidism with hormone replacement therapy and hyperthyroidism with medical management. Withhold BAVENCIO for severe (Grade 3) or life-threatening (Grade 4) thyroid disorders. Thyroid disorders, including hypothyroidism, hyperthyroidism, and thyroiditis, were reported in 6% (98/1738) of patients, including three (0.2%) with Grade 3.

Type 1 diabetes mellitus including diabetic ketoacidosis: Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Withhold BAVENCIO and administer antihyperglycemics or insulin in patients with severe or life-threatening (Grade ≥ 3) hyperglycemia, and resume treatment when metabolic control is achieved. Type 1 diabetes

BAVENCIO can cause **immune-mediated nephritis and renal dysfunction**. Monitor patients for elevated serum creatinine prior to and periodically during treatment. Administer corticosteroids for Grade 2 or greater nephritis. Withhold BAVENCIO for moderate (Grade 2) or severe (Grade 3) nephritis until resolution to Grade 1 or lower. Permanently discontinue BAVENCIO for life-threatening (Grade 4) nephritis. Immune-mediated nephritis occurred in 0.1% (1/1738) of patients.

BAVENCIO can result in **other severe and fatal immune-mediated adverse reactions** involving any organ system during treatment or after treatment discontinuation. For suspected immune-mediated adverse reactions, evaluate to confirm or rule out an immune-mediated adverse reaction and to exclude other causes. Depending on the severity of the adverse reaction, withhold or permanently discontinue BAVENCIO, administer high-dose corticosteroids, and initiate hormone replacement therapy, if appropriate. Resume BAVENCIO when the immune-mediated adverse reaction remains at Grade 1 or lower following a corticosteroid taper. Permanently discontinue BAVENCIO for any severe (Grade 3) immune-mediated adverse reaction that recurs and for any life-threatening (Grade 4) immune-mediated adverse reaction. The following clinically significant immune-mediated adverse reactions occurred in less than 1% of 1,738 patients treated with BAVENCIO: myocarditis with fatal cases, myositis, psoriasis, arthritis, exfoliative dermatitis, erythema multiforme, pemphigoid, hypopituitarism, uveitis, Guillain-Barré syndrome, and systemic inflammatory response.

BAVENCIO can cause severe (Grade 3) or life-threatening (Grade 4) **infusion-related reactions**. Patients should be premedicated with an antihistamine and acetaminophen prior to the first 4 infusions and for subsequent doses based upon clinical judgment and presence/severity of prior infusion reactions. Monitor patients for signs and symptoms of infusion-related reactions, including pyrexia, chills, flushing, hypotension, dyspnea, wheezing, back pain, abdominal pain, and urticaria. Interrupt or slow the rate of infusion for mild (Grade 1) or moderate (Grade 2) infusion-related reactions. Permanently discontinue BAVENCIO for severe (Grade 3) or life-threatening (Grade 4) infusion-related reactions. Infusion-related reactions occurred in 25% (439/1738) of patients, including three (0.2%) patients with Grade 4 and nine (0.5%) with Grade 3.

BAVENCIO can cause **fetal harm** when administered to a pregnant woman. Advise patients of the potential risk to a fetus including the risk of fetal death. Advise females of childbearing

human milk. Advise a lactating woman **not to breastfeed** during treatment and for at least 1 month after the last dose of BAVENCIO due to the potential for serious adverse reactions in breastfed infants.

The most common adverse reactions (all grades, ≥ 20%) in patients with **metastatic Merkel cell carcinoma (MCC)** were fatigue (50%), musculoskeletal pain (32%), diarrhea (23%), nausea (22%), infusion-related reaction (22%), rash (22%), decreased appetite (20%), and peripheral edema (20%).

Selected treatment-emergent laboratory abnormalities (all grades, ≥ 20%) in patients with **metastatic MCC** were lymphopenia (49%), anemia (35%), increased aspartate aminotransferase (34%), thrombocytopenia (27%), and increased alanine aminotransferase (20%).

The most common adverse reactions (all grades, ≥ 20%) in patients with locally advanced or **metastatic urothelial carcinoma (UC)** were fatigue (41%), infusion-related reaction (30%), musculoskeletal pain (25%), nausea (24%), decreased appetite/hypophagia (21%), and urinary tract infection (21%).

Selected laboratory abnormalities (Grades 3-4, ≥ 3%) in patients with **locally advanced or metastatic UC** were hyponatremia (16%), increased gamma-glutamyltransferase (12%), lymphopenia (11%), hyperglycemia (9%), increased alkaline phosphatase (7%), anemia (6%), increased lipase (6%), hyperkalemia (3%), and increased aspartate aminotransferase (3%).

Please see full US Prescribing Information and Medication Guide available at http://www.BAVENCIO.com.

About M7824

M7824 is an investigational bifunctional immunotherapy that is designed to bring together a TGF-β trap and 'fuse' it with the anti-PD-L1 mechanism. M7824 is designed to simultaneously block the two immunosuppressive pathways – targeting both pathways aims to control tumor growth by potentially restoring and enhancing anti-tumor responses. M7824 is currently in Phase I studies for solid tumors.

About Tepotinib

14 skipping mutations and *MET* amplifications, or MET protein overexpression. It is a precision medicine and is designed to have a highly selective mechanism of action.

About M6620

M6620 (previously known as VX-970) is an investigational small-molecule thought to inhibit ataxia telangiectasia and Rad3-related protein (ATR). ATR is believed to be a key sensor for DNA damage, activating the DNA damage checkpoint and leading to cell cycle arrest. Inhibition of ATR could potentially enhance the efficacy of DNA-damaging agents, but is also being investigated as a monotherapy against tumors with high levels of replication stress induced by overexpression of oncogenes.

About M3814

M3814 is an investigational small-molecule which is thought to inhibit DNA-dependent protein kinase (DNA-PK). DNA-PK is a key enzyme for non-homologous end-joining (NHEJ), an important DNA double-strand break (DSB) repair pathway. Clinical studies investigating combinations of M3814 with other commonly used DNA-damaging agents such as radiotherapy and chemotherapy are underway.

About M7583

M7583 is an investigational therapy that is thought to be a highly selective covalent inhibitor of Bruton's tyrosine kinase (BTKi) designed to minimize off-target effects.

About Abituzumab

Abituzumab is an investigational pan-αv integrin inhibiting monoclonal antibody thought to show activity against αvβ1, 3, 5, 6 and 8 integrin heterodimers. Merck KGaA, Darmstadt, Germany entered into a development agreement with the SFJ Pharmaceuticals Group for abituzumab in metastatic colorectal cancer (mCRC). This collaboration will allow Merck KGaA, Darmstadt, Germany and SFJ to develop the potential of abituzumab in a targeted way, focusing on a patient population that may benefit from the treatment the most.

About Erbitux® (cetuximab)

chemotherapy treatments in that it specifically targets and binds to the EGFR. This binding inhibits the activation of the receptor and the subsequent signal-transduction pathway, which results in reducing both the invasion of normal tissues by tumor cells and the spread of tumors to new sites. It is also believed to inhibit the ability of tumor cells to repair the damage caused by chemotherapy and radiotherapy and to inhibit the formation of new blood vessels inside tumors, which appears to lead to an overall suppression of tumor growth. Based on in vitro evidence, Erbitux also targets cytotoxic immune effector cells towards EGFR expressing tumor cells (antibody dependent cell-mediated cytotoxicity, ADCC).

The most commonly reported side effect with Erbitux is an acne-like skin rash. In approximately 5% of patients, hypersensitivity reactions may occur during treatment with Erbitux; about half of these reactions are severe.

Erbitux has already obtained market authorization in over 100 countries world-wide for the treatment of RAS wild-type metastatic colorectal cancer and for the treatment of squamous cell carcinoma of the head and neck (SCCHN). Merck KGaA, Darmstadt, Germany licensed the right to market Erbitux, a registered trademark of ImClone LLC, outside the U.S. and Canada from ImClone LLC, a wholly-owned subsidiary of Eli Lilly and Company, in 1998.

References

1. Dolan DE, Gupta S. PD-1 pathway inhibitors: changing the landscape of cancer immunotherapy. Cancer Control 2014;21:231–7.
2. Dahan R et al. FcγRs modulate the anti-tumor activity of antibodies targeting the PD-1/PD-L1 axis. Cancer Cell 2015;28:285–95.
3. Boyerinas B et al. Antibody-dependent cellular cytotoxicity activity of a novel anti-PD-L1 antibody avelumab (MSB0010718C) on human tumor cells. Cancer Immunol Res 2015;3:1148–57.
4. Kohrt HE et al. Combination strategies to enhance antitumor ADCC. Immunotherapy 2012;4:511–27.
5. Hamilton G, Rath B. Avelumab: combining immune checkpoint inhibition and antibody-dependent cytotoxicity. Expert Opin Biol Ther 2017;17:515–23.

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 again for your online

About Merck KGaA, Darmstadt, Germany

Merck KGaA, Darmstadt, Germany, is a leading science and technology company in healthcare, life science and performance materials. Almost 53,000 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 2017, Merck KGaA, Darmstadt, Germany, generated sales of € 15.3 billion in 66 countries.

Founded in 1668, Merck KGaA, Darmstadt, Germany, is the world's oldest pharmaceutical and chemical company. The founding family remains the majority owner of the publicly listed corporate group. 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 company operates as EMD Serono, MilliporeSigma and EMD Performance Materials.

For further information: Brenda Mulligan +1 978 821 5345; Investor relations +49 6151 72 3321

EMD SERONO

THERAPEUTIC AREAS

YOUR REQUESTS

EMD Serono is the biopharmaceutical business of Merck KGaA, Darmstadt, Germany. This site contains information that is intended for residents of the United States only and is not meant to substitute for the advice provided by a medical professional. Always consult a physician if you have health concerns. Use and access of this site is subject to the terms and conditions as set out in our Legal Statement and Privacy Policy.

This site contains information that is intended for US residents only. Canadian residents should consult the EMD Inc. website at www.emdserono.ca for information on products and services approved in Canada.

SITEMAP

LEGAL STATEMENT

PRIVACY POLICY

CONTACT US

Global Survey and Documentary Film Expose Emotional Impact of Multiple Sclerosis

- Merck KGaA, Darmstadt, Germany-sponsored survey developed in collaboration with IACO and Eurocarers reveals lifelong effects of caring for a loved one with MS
- #MSInsideOut documentary film, executively produced by Shift.ms, provides artistic take on the experiences of those impacted by MS

ROCKLAND, Mass., Oct. 11, 2018 /PRNewswire/ -- EMD Serono, the biopharmaceutical business of Merck KGaA, Darmstadt, Germany, in the U.S. and Canada, today announced the publication of results from a global Company-sponsored multiple sclerosis (MS) carer survey, as well as the premiere of the #MSInsideOut documentary, *Seeing MS from the Inside Out,* executive produced by Shift.ms, a social network for people with MS, at the 34th Congress of the European Committee for Treatment and Research In Multiple Sclerosis (ECTRIMS), in Berlin, Germany.

The '*Living with Multiple Sclerosis: The Carer's Perspective*' report was developed in collaboration with The International Alliance of Carer Organizations (IACO) and Eurocarers to examine the experiences of 1,050 MS carers across seven countries (U.S., Canada, U.K., France, Germany, Italy and Spain). The survey found that almost half (48%) of those surveyed

years or more.

Additional key findings from the carer survey included:

- 43% and 28% of carers surveyed reported an impact on their emotional/mental health and physical health, respectively
- 34% said being an MS carer impacted their financial situation, more than a third (36%) stated they had to take time off work, and as a result, 84% of those carers reported their work and career being impacted
- Only 15% of carers surveyed connected with other carers or patient organizations to help cope with the challenges of their role

"MS can be a devastating disease for both patients and carers, with the responsibilities assumed by carers over an extended length of time and intensifying as the disease progresses. Carers can experience a profound impact on their physical and emotional health, finances, and employment," said Nadine Henningsen, Board Chair, IACO. "Not surprisingly, the survey results reinforced the large number of young people who are becoming carers – often in a formative time of their life."

As part of the *#MSInsideOut* campaign, an initiative aimed at providing a deeper understanding of MS, the MS Inside Out documentary film, '*Seeing MS from the Inside Out',* will be premiered. Developed with Shift.ms as executive producers, it is the first global documentary film to pair artists and people from across the MS community, with a view to interpreting the experiences and perspectives of those impacted by MS through art.

"In line with our broader mission at Shift.ms, the aim of this documentary is to highlight the individual stories in a unique and innovative way across the MS community, digging deeper into the elements of MS that remain under-represented with a view of interpreting the unmet needs of those impacted by MS through art," said George Pepper, Co-founder and CEO, Shift.ms. "By bringing these stories out into the open we will be able to address those challenges that remain, opening lines of communication and ultimately raising awareness of MS."

The documentary follows three stories: Maria Florencia, a person living with MS from Argentina, Jon Strum, a caregiver from the U.S., and Dr. Luigi Lavorgna, a healthcare professional from Italy. Each were paired with a local visual artist to bring their stories to life through an

The premiere will take place at 12:00 – 1:30 pm EST today on October 11, during ECTRIMS 2018.

"We are extremely proud to highlight the unmet needs in the community through our work with Shift.ms, IACO and Eurocarers which expose the experiences of different members of the MS community, including the perspective of MS carers, whose voices have traditionally not been heard as strongly," said Andrew Paterson, Senior Vice President, Global Head of Neurology and Immunology, at the biopharma business of Merck KGaA, Darmstadt, Germany. "Forming part of our ongoing company-wide commitment to carers, and connecting with the broader Embracing Carers initiative, the outcomes from both the survey and documentary film highlight the need for additional support and awareness. We therefore encourage and call upon the MS community to take these findings and identify ways in which they can better assist both MS carers and patients."

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.

EMD Serono, Inc. and Multiple Sclerosis

For more than 20 years, EMD Serono has been relentlessly focused on understanding the journey people living with MS face in order to create a meaningful, positive experience for them and the broader MS community. However, there is still much that is unknown about this complex and unpredictable disease. EMD Serono is digging deeper to advance the science and reconstruct a new understanding of MS, inside and out. We are committed to delivering solutions that improve the lives of all those affected by MS. www.GetCloserToMS.com

and Canada – is engaged in the discovery, research and development of medicines for patients with difficult to treat diseases. The business is committed to transforming lives by developing and delivering meaningful solutions that help address the therapeutic and support needs of individual patients. Building on a proven legacy and deep expertise in neurology, fertility and endocrinology, EMD Serono is developing potential new oncology and immuno-oncology medicines while continuing to explore potential therapeutic options for diseases such as psoriasis, lupus and multiple sclerosis. Today, the business has approximately 1,300 employees around the country with commercial, clinical and research operations based in the company's home state of Massachusetts. www.emdserono.com

About Embracing Carers

Embracing Carers is a global initiative led by Merck KgaA, Darmstadt, Germany in collaboration with leading caregiver organizations around the world designed to increase awareness, discussion, and action about the often-overlooked needs of caregivers. Given that caregivers need support and often do not know where to turn for help, Embracing Carers was created to help fill that void.

About IACO

The International Alliance of Carer Organizations (IACO) is a global coalition of 15 member nations committed to building a global understanding and respect for the vital role of family carers. Recognized as an official NGO by the United Nations, IACO works to improve the quality of life and support the needs of carers, through international partnerships and advocacy that strengthens and honors the voice of carers. To learn more, visit www.internationalcarers.org.

About Eurocarers

Eurocarers is the European umbrella organisation representing informal carers and their organizations, irrespective of the particular age or health need of the person they are caring for. Eurocarers works to raise awareness of the significant contribution made by carers to care systems while ensuring that all relevant policies across Europe take account of their needs and preferences. To learn more, visit www.eurocarers.org.

About Shift.ms

Shift.ms - www.Shift.ms - is the social network for people with multiple sclerosis. Founded by

About *#MSInsideOut*

#MSInsideOut is a campaign supported by EMD Serono which focuses on understanding the journeys people living with MS face and telling the inside story of the disease. For more than 20 years, EMD Serono has been relentlessly focused on understanding the journey people living with MS face to create a meaningful, positive experience for them and the broader MS Community. With the *#MSInsideOut* campaign EMD Serono aims to better understand MS and, importantly, enable others to do the same.

Your Contact
Alice McGrail 1-781-681-2886

SOURCE EMD Serono

EMD Serono is the biopharmaceutical business of Merck KGaA, Darmstadt, Germany. This site contains information that is intended for residents of the United States only and is not meant to substitute for the advice provided by a medical professional. Always consult a physician if you have health concerns. Use and access of this site is subject to the terms and conditions as set out in our Legal Statement and Privacy Policy.

This site contains information that is intended for US residents only. Canadian residents should consult the EMD Inc. website at www.emdserono.ca for information on products and services approved in Canada.

SITEMAP

LEGAL STATEMENT

PRIVACY POLICY

CONTACT US

Merck KGaA, Darmstadt, Germany, Presents Updated Results for Bifunctional Immunotherapy M7824 at ESMO 2018 Congress

EXPLORE MORE

- **New data include first disclosure of results for M7824 in advanced squamous cell carcinoma of the head and neck, biliary tract cancer and esophageal cancers**
- **Updated data also being presented include non-small cell lung cancer and gastric cancer**
- **M7824 is a bifunctional immunotherapy designed to bring together transforming growth factor-β and anti-PD-L1 mechanisms**

ESMO Abstract #

M7824 (TGF β-trap/anti-PD-L1): 10480, 1463P, 757P, 643P, 642P, 661P, 1931P

as EMD Serono, today announced new and updated results from expansion cohorts of two ongoing M7824 Phase I clinical trials (NCT02517398 and NCT02699515) at the ESMO (European Society for Medical Oncology) 2018 Congress in Munich, October. New data presented include the first presentation of results for M7824 in advanced squamous cell carcinoma of the head and neck (SCCHN), biliary tract cancer (BTC) and esophageal cancers (esophageal squamous cell carcinoma [ESCC] and esophageal adenocarcinoma [EAC]). In addition, updated data for M7824 in non-small cell lung cancer (NSCLC) and gastric cancer add to the growing evidence for M7824's clinical anti-tumor activity in a number of challenging cancers.

"We are excited to share encouraging updated and new data for M7824, including four additional difficult-to-treat cancers," said Luciano Rossetti, Executive Vice President, Head of Global Research & Development for the Biopharma business of Merck KGaA, Darmstadt, Germany. "The results we've seen to date will enable us to target those tumors and settings with the highest potential to impact people living with cancer, as we move into the next stage of our development program with this bifunctional immunotherapy."

New data from an ongoing Phase I expansion cohort (32 patients, NCT02517398) showed signs of promising early clinical activity in patients with refractory metastatic second-line SCCHN, especially in HPV-positive SCCHN patients. As presented during the Proffered Paper Head and Neck cancers session, the overall response rate (ORR) was 15.6%, with a numerically higher ORR in HPV-positive patients (36.4%, 4/11 patients experienced a partial response), with two additional delayed responses resulting in a 54.5% clinical response rate for the HPV-positive population. At ASCO 2018, data from the dose escalation cohort of a Phase I, open-label study in advanced HPV-associated cancers (including SCCHN) were presented in collaboration with the National Cancer Institute, which showed that M7824 delivered an ORR of 41.7% in HPV-positive tumors. These new data from the SCCHN expansion cohort add to the evidence of encouraging activity in HPV-positive tumors. A total of 11 patients (34.4%) experienced Grade 3 treatment-related adverse events (TRAEs) and no Grade 4 or 5 TRAEs were seen. The most common TRAEs were rash (18.8%), asthenia (15.6%), pruritus (15.6%), hypothyroidism (15.6%), increased alanine aminotransferase (12.5%), increased aspartate aminotransferase (12.5%) and skin neoplasm (12.5%).

Updated results (now with longer follow-up and independent review committee [IRC] assessed data) from an ongoing Phase I trial (NCT02517398) in patients with previously treated,

expressing tumors (cut-off of ≥80% using the 73-10 assay; ≥80% cut-off with 73-10 assay is most comparable to ≥50% cut-off with the 22C3 test based on internal comparability studies), ORR was 85.7% (6/7 patients). Grade 3 TRAEs occurred in 23 patients (28.8%) and Grade 4 TRAEs occurred in 2 patients (2.5%): hypokalemia and decreased blood magnesium and increased amylase and lipase levels. The most common TRAEs were pruritus (21.3%), maculopapular rash (18.8%), decreased appetite (12.5%), asthenia (11.3%) and rash (10.0%).

New data from an ongoing expansion cohort (NCT02699515) in Asian patients with BTC who had progressed after platinum-based first-line treatment, demonstrated clinical activity with M7824 treatment. The ORR among the total of 30 patients was 20%, as assessed by IRC. Responses were observed across all PD-L1 levels and duration of response ranged from 8.3 months to 13.9+ months. Grade 3 or higher TRAEs were experienced by 10 patients (33.3%). The most common TRAEs were rash (10%) and lipase increase (10%). Three deaths due to adverse events were reported: one due to septic shock (bacteremia, etiology unknown) and two due to interstitial lung disease (ILD; reported term: interstitial pneumonitis). Both patients with ILD were Japanese, which is consistent with the higher incidence of drug-induced ILD observed among Japanese patients compared with the non-Japanese population.[1]

Three additional posters featuring new data from two cohorts of ongoing Phase I studies in patients with ESCC and advanced EAC (studies NCT02699515 and NCT02517398 respectively) and updated data in gastric cancer (NCT02699515) were also presented. These data provide further indications of the potential of M7824 in cancers with significant unmet needs.

To date more than 650 patients with various types of solid tumors have been treated across the program with M7824. The safety profile is consistent with that observed with other PD-1/PD-L1 inhibitors. Previously described rash/skin lesions (keratoacanthomas, SCC, hyperkeratosis) associated with transforming growth factor-β (TGF-β) inhibiting therapies have also been observed.

Merck KGaA, Darmstadt, Germany, has recently initiated a trial to investigate M7824 compared with pembrolizumab as a first-line treatment in patients with PD-L1 expressing advanced NSCLC. The multicenter, randomized, open-label, controlled study is evaluating the safety and efficacy of M7824 versus pembrolizumab as monotherapy treatment.

immunosuppressive pathways, M7824 is thought to control tumor growth by potentially restoring and enhancing anti-tumor responses. M7824 is an important part of a novel combination approach that seeks to harness the power of the immune system and address the tremendously complex nature of difficult-to-treat tumors.

Notes to Editors

Accepted abstracts supported by Merck KGaA, Darmstadt, Germany slated for presentation are listed below. In addition, a number of investigator-sponsored studies were accepted (not listed).

Title	Lead Author	Abstract #	Presentation Date / Time (CEST)	Location
M7824 (TGF β-trap/anti-PD-L1)				
Proffered Paper Session				
M7824 (MSB0011359C), a bifunctional fusion protein targeting PD-L1 and TGF-β, in patients (pts) with advanced SCCHN: results from a phase 1 cohort	BC Cho	1048O	Mon, Oct 22, 2:45 – 4:15 PM (3:00 PM lecture time)	ICM, Room 14B

Updated results of M7824 (MSB0011359C), a bifunctional fusion protein targeting TGF-β and PD-L1, in second-line (2L) NSCLC	L Paz-Ares	1463P	Sat, Oct 20, 12:30 – 1:30 PM	Hall A3 – Poster Area Networking Hub
Assessment of PD1/ PD-L1 colocalization in hepatocellular carcinoma (HCC) using brightfield double labeling and quantitative digital image analysis	T Mrowiec	1931P	Sun, Oct 21, 12:45 – 1:45 PM	Hall A3 – Poster Area Networking Hub
M7824 (MSB0011359C), a bifunctional fusion protein targeting PD-L1 and TGF-β, in Asian patients with pretreated biliary tract cancer:	C Yoo	757P	Sun, Oct 21, 12:45 – 1:45 PM	Hall A3 – Poster Area Networking Hub

phase 1 trial				
M7824 (MSB0011359C), a bifunctional fusion protein targeting PD-L1 and TGF-β, in patients with post-platinum esophageal adenocarcinoma (EAC): preliminary results from a phase 1 cohort	B Tan	643P	Sun, Oct 21, 12:45 – 1:45 PM	Hall A3 – Poster Area Networking Hub
Phase 1 study results from an esophageal squamous cell carcinoma (ESCC) cohort treated with M7824 (MSB0011359C), a bifunctional fusion protein targeting transforming growth factor β (TGF-β) and PD-L1	CC Lin	642P	Sun, Oct 21, 12:45 – 1:45 PM	Hall A3 – Poster Area Networking Hub

from a phase 1 trial of M7824 (MSB0011359C), a bifunctional fusion protein targeting PD-L1 and TGF-β, in patients with pretreated recurrent or refractory gastric cancer	YJ Bang	661P	Sun, Oct 21, 12:45 – 1.45 PM	Hall A3 – Poster Area Networking Hub

About M7824

M7824 is an investigational bifunctional immunotherapy that is designed to bring together a TGF-β trap and 'fuse' it with the anti-PD-L1 mechanism. M7824 is designed to simultaneously block the two immunosuppressive pathways – targeting both pathways aims to control tumor growth by potentially restoring and enhancing anti-tumor responses. M7824 is currently in Phase I studies for solid tumors.

About Biliary Tract Cancer (BTC)

BTC is a collective term for a group of rare and aggressive gastrointestinal cancers, made up of intrahepatic cholangiocarcinoma (iCC), extrahepatic cholangiocarcinoma (eCC), and gallbladder carcinoma (GBC).[2,3,4] Surgery is the only curative treatment, but most patients present with advanced disease and therefore have a limited survival.[4] Approximately 140,000 cases of BTC are estimated to occur annually world-wide.[5] However, incidence of BTC varies in different parts of the world: the incidence of cholangiocarcinomas is rising in the Western world, with reports of up to 2 in 100,000. By contrast, in Asian countries, the incidence is much higher.[3] GBC also has an incidence of 2 in 100,000, but is much more prevalent in parts of South America.[3] Collectively these cancers present late in the majority of patients and long-term outcomes for resectable patients are poor with median survival in the advanced setting less than 1 year.[4,6,7,8]

www.emdgroup.com/subscribe to register online, 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. Almost 53,000 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 2017, Merck KGaA, Darmstadt, Germany, generated sales of € 15.3 billion in 66 countries.

Founded in 1668, Merck KGaA, Darmstadt, Germany, is the world's oldest pharmaceutical and chemical company. The founding family remains the majority owner of the publicly listed corporate group. Merck KGaA, Darmstadt, Germany holds the global rights to the "Merck" name and brand except in the United States and Canada, where the company operates as EMD Serono, MilliporeSigma and EMD Performance Materials.

References

1. Hanaoka M et al, eds. Drug-Induced Lung Injury. Singapore: Springer; 2017. https://www.springer.com/us/book/9789811044656
2. Blair A B et al. Immunotherapy as a treatment for biliary tract cancers: A review of approaches with an eye to the future. Current Problems in Cancer (2017) https://doi.org/10.1016/j.currproblcancer.2017.10.004
3. Goldstein D et al. New molecular and immunotherapeutic approaches in biliary cancer. ESMO Open (2017). Published online 2017 Mar 27. doi: https://dx.doi.org/10.1136%2Fesmoopen-2016-000152
4. Jain A et al. Molecular profiling of biliary tract cancer: a target rich disease. Journal of Gastrointestinal Oncology (2016) 7(5): 797–803. https://dx.doi.org/10.21037%2Fjgo.2016.09.01
5. Global Burden of Disease Study 2013. The Lancet 2015;385(9963):117–171.
6. GBD. Mortality and causes of death collaborators. global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990-2013: a systematic analysis for the global burden of disease study 2013. Lancet 2013;2015:117–71
7. Marcano-Bonilla et al. Biliary tract cancers: epidemiology, molecular pathogenesis and genetic risk associations. Chin Clin Oncol 2016;5:61. no 5.

Oncol 2010;28:3331–40. http://dx.doi.org/10.1200/JCO.2009.27.4787

For further information: Brenda Mulligan +1 978 821 5345

COMPANY
LEADERSHIP TEAM
PARTNERING
PRESS
CONTACT US
COMPLIANCE & TRANSPARENCY

THERAPEUTIC AREAS

YOUR REQUESTS

EMD Serono and Can Do MS Deliver Educational Programs and Support Groups to Multiple Sclerosis Caregivers

ROCKLAND, Mass., Oct. 25, 2018 /PRNewswire/ -- Embracing Carers™, the global initiative designed to increase awareness and action about the often-overlooked needs of caregivers, today announced a new collaboration with Can Do Multiple Sclerosis to fill the shortage of resources focused on the unique needs, concerns, and unmet challenges of MS Care Partners.

Under the collaboration, Can Do MS is creating online support groups and educational programs dedicated to helping caregivers understand the impact of MS-related mood and cognitive changes on relationships, communication and everyday life activities. The initiative will also support the caregiver in learning to prioritize his or her own well-being while maintaining a satisfying relationship with his or her partner receiving care.

The main components of this educational program series include:

- **Online Support Groups**: Four one-hour long online support group sessions facilitated by psychologist Roz Kalb, Ph.D. will facilitate communication, shared experiences challenges and learnings among caregivers.

- **Webinar Series:** A special three-part Webinar series designed to recognize and support MS caregivers with interactive education materials on critical issues such as achieving a satisfying partnership with his or her partner receiving care, including the need for shared decision making, and intimacy.

"Across the world, many caregivers are supporting partners, family members, or other loved ones living with MS, and they often do not know where to turn for help or resources," said Terrie Livingston, Head of Patient Outcomes and Solutions at EMD Serono. "By partnering with Can Do MS, one of the leaders in providing resources for MS patients and those who care for them, we hope that we can help these caregivers support their loved ones and have fulfilling relationships while ensuring they also care for themselves."

"Caregivers are the often-unrecognized lynchpin in our health care system," Livingston continued. "It is one of the most substantial public health issues of our time, and we want to highlight their challenges while helping them get the support they need. We do this by collaborating with organizations like Can Do MS to drive visibility and create innovative opportunities for health care system integration."

"MS caregivers play a fundamental role in caring for MS patients, and it is important that we include them in our conversations about how to help those living with this disease" said Anne Gilbert, Director of Programs at Can Do MS. "We have developed an extensive library of materials and information for MS patients, and this new collaboration will produce valuable materials targeted specifically toward the caregiver community. We hope to make a difference in the lives of millions who have been diagnosed with multiple sclerosis around the world."

The first online support group session began in late September with more content becoming available every day. To learn more, visit https://www.cando-ms.org/multiple-sclerosis-programs/embracing-carers.

About Embracing Carers™

Embracing Carers™ is a global initiative led by EMD Serono, in collaboration with leading caregiver organizations around the world, designed to increase awareness, discussion, and action about the often-overlooked needs of caregivers. Given that caregivers need support and often do not know where to turn for help, Embracing Carers™ was created to fill that void.

education programs on exercise, nutrition, symptom management, and motivation to help families living with MS thrive. For more information, visit the organization's website at www.CanDo-MS.org or call 800-367-3101.

About EMD Serono

EMD Serono - the biopharmaceutical business of Merck KGaA, Darmstadt, Germany, in the U.S. and Canada – is engaged in the discovery, research and development of medicines for patients with difficult to treat diseases. The business is committed to transforming lives by developing and delivering meaningful solutions that help address the therapeutic and support needs of individual patients. Building on a proven legacy and deep expertise in neurology, fertility and endocrinology, EMD Serono is developing potential new oncology and immuno-oncology medicines while continuing to explore potential therapeutic options for diseases such as psoriasis, lupus and multiple sclerosis. Today, the business has approximately 1,300 employees around the country with commercial, clinical and research operations based in the company's home state of Massachusetts. www.emdserono.com.

Your Contact

Lisa Buffington 1 781 681 2340

SOURCE EMD Serono

EMD Serono Launches Community-Based Program to Advance Understanding of the Impact of Multiple Sclerosis on Patients and Caregivers

- MS On My Mind is part of the company's #MSInsideOut global campaign, aimed at providing a deeper understanding of MS around the world

- Renowned artist, MS patient and advocate Lydia Emily Archibald will bring individuals' experiences with MS to life via art at MSIsOnMyMind.com

- EMD Serono will support the MS community and advocacy organizations in addressing needs identified by the initiative

ROCKLAND, Mass., Oct. 31, 2018 /PRNewswire/ -- EMD Serono, the biopharmaceutical business of Merck KGaA, Darmstadt, Germany, in the U.S. and Canada, announces the launch of MS On My Mind (MSOMM), a new initiative to raise awareness of the emotional toll and multi-faceted impact MS has on patients and their caregivers.

MSOMM encourages people living with MS to authentically reveal the reality of their lives by visiting MSIsOnMyMind.com to complete the sentence, "MS is on my mind when _____." These real-life experiences of gratitude or struggle, of accomplishment or challenge can

website.

The content shared by the MS community will serve as inspiration for nationally-renowned artist and MSOMM creative director Lydia Emily (Lydia Emily Archibald), who was diagnosed with MS in 2014, to create thought-provoking artwork, illustrating the personal impact on people with the condition.

"MS is on my mind when I need to strap paintbrushes to my hands in order to paint, but I am grateful that I can still continue doing what I love," said Ms. Archibald. "That's why I'm encouraging the MS community to share their experiences – whether it's times when they are celebrating successes or dealing with the challenges of the disease. I'll use the submissions we receive as inspiration for artwork that reflects the many ways MS impacts individuals."

In 2019, as part of the initiative's second phase, EMD Serono will partner with MS advocacy and caregiver organizations as well as the larger MS community to develop actionable resources and programming based on patients' real-life experiences in hopes of improving the lives of people living with MS and caregivers.

"We want to learn from the MS community and work hand-in-hand to make a positive difference," said Rehan Verjee, President, EMD Serono, Global Head of Innovative Medicine Franchises, Merck KGaA, Darmstadt, Germany. "This adds to our renewed commitment to continue to advance the science of MS in the hopes of one day finding a way to stop MS."

Recently, as a part of the #MSInsideOut campaign, the company premiered the documentary film, 'Seeing MS from the Inside Out', at the 34th Congress of the European Committee for Treatment and Research In Multiple Sclerosis (ECTRIMS), in Berlin, Germany. Developed with Shift.ms as executive producers, it is the first global documentary film to pair artists, including Lydia Emily, and people from across the MS community, with a view to interpreting the experiences and perspectives of those impacted by MS through art.

MS is a chronic, inflammatory condition of the central nervous system affecting approximately 2.3 million people worldwide. Visit MSIsOnMyMind.com to learn more and tell us about when MS is on your mind.

or Canada please go to www.emdgroup.com/subscribe to register again for your online subscription of this service as our newly introduced geo-targeting requires new links in the email. You may later change your selection or discontinue this service.

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.

EMD Serono, Inc. and Multiple Sclerosis

For more than 20 years, EMD Serono has been relentlessly focused on understanding the journey people living with MS face in order to create a meaningful, positive experience for them and the broader MS community. However, there is still much that is unknown about this complex and unpredictable disease. EMD Serono is digging deeper to advance the science and reconstruct a new understanding of MS, inside and out. We are committed to delivering solutions that improve the lives of all those affected by MS. www.GetCloserToMS.com

About Embracing Carers

Embracing Carers is a global initiative led by Merck KGaA, Darmstadt, Germany in collaboration with leading caregiver organizations around the world designed to increase awareness, discussion, and action about the often-overlooked needs of caregivers. Given that caregivers need support and often do not know where to turn for help, Embracing Carers was created to help fill that void.

About EMD Serono, Inc.

EMD Serono - the biopharmaceutical business of Merck KGaA, Darmstadt, Germany, in the U.S. and Canada – is engaged in the discovery, research and development of medicines for patients with difficult to treat diseases. The business is committed to transforming lives by developing and delivering meaningful solutions that help address the therapeutic and support needs of individual patients. Building on a proven legacy and deep expertise in neurology, fertility and endocrinology, EMD Serono is developing potential new oncology and immuno-oncology medicines while continuing to explore potential therapeutic options for diseases such as psoriasis, lupus and multiple sclerosis. Today, the business has approximately 1,300 employees around the country with commercial, clinical and research operations based in the comm

About Shift.ms

Shift.ms - www.Shift.ms - is the social network for people with multiple sclerosis. Founded by MSers, for MSers, the charity supports many thousands of recently diagnosed people across the world as they make sense of MS. It's independent and it's free.

About #MSInsideOut

#MSInsideOut is a campaign supported by EMD Serono which focuses on understanding the journeys people living with MS face and telling the inside story of the disease. For more than 20 years, EMD Serono has been relentlessly focused on understanding the journey people living with MS face to create a meaningful, positive experience for them and the broader MS Community. With the #MSInsideOut campaign EMD Serono aims to better understand MS and, importantly, enable others to do the same.

Your Contact
Alice McGrail 1-781-681-2886

SOURCE EMD Serono

THERAPEUTIC AREAS

YOUR REQUESTS

Merck KGaA, Darmstadt, Germany Announces FDA Orphan Drug Designation for Bifunctional Immunotherapy M7824 in Biliary Tract Cancer

- **FDA grants M7824, an investigational bifunctional immunotherapy, orphan drug designation in biliary tract cancer**
- **First regulatory designation for M7824 following recent presentation of first clinical data in BTC**
- **BTC is a group of rare, aggressive gastrointestinal cancers associated with limited treatment options and poor outcomes**

Darmstadt, Germany, December 10, 2018 – Merck KGaA, Darmstadt, Germany, a leading science and technology company, which operates its healthcare business in the U.S. and Canada as EMD Serono, today announced that the US Food and Drug Administration (FDA) has granted orphan drug designation (ODD) to M7824, the first regulatory designation for the bifunctional immunotherapy, for the treatment of biliary tract cancer (BTC). The FDA orphan drug designation follows the recent presentation of the first clinical data for M7824 in BTC at

transforming growth factor-β and anti-PD-L1 immune escape mechanisms.

BTC is a collective term for a group of rare and aggressive gastrointestinal cancers, including intrahepatic cholangiocarcinoma (ICC), extrahepatic cholangiocarcinoma (ECC), and gallbladder carcinoma (GBC).[1] Approximately 16,000 cases of BTC are estimated to occur every year in the US and collectively these cancers present late in the majority of patients. [1, 2] Treatment options are limited and the median survival rate in the advanced setting is less than one year, objective tumor response with commonly used chemotherapy is typically less than 10% with short duration of response. [1,3,5]

"Biliary tract cancer is a rare, notoriously hard-to-treat tumor where existing treatment approaches, such as surgery or chemotherapy, are either not viable or simply don't deliver acceptable patient outcomes," said Luciano Rossetti, Head of Global Research & Development at the Biopharma business of Merck KGaA, Darmstadt, Germany. "As the first regulatory designation for M7824, Merck KGaA, Darmstadt, Germany is excited about the potential of this new class of immunotherapy in a number of challenging cancers and settings."

The first clinical data for M7824 in BTC, presented at the ESMO congress in October, demonstrated clinical activity in Asian patients who had progressed after platinum-based first-line treatment. The ORR among the total of 30 patients was 20%, as assessed by IRC, and responses were observed across PD-L1 levels with a duration of response ranging from 8.3 months to 13.9+ months. Grade 3 or higher TRAEs were experienced by 10 patients (33.3%) and the most common Grade 3 TRAEs were rash (10%) and lipase increase (10%).

FDA Orphan Drug Designation (ODD) is granted to medicines intended to treat rare diseases or disorders that affect fewer than 200,000 people in the US, or those that affect more than 200,000 people but are unlikely to recover the costs of developing and marketing the drug. Medicines that meet the FDA's ODD criteria qualify for a number of incentives to help support advancement.

M7824 is an investigational bifunctional immunotherapy that combines a TGF-β trap with the anti-PD-L1 mechanism in one fusion protein. Designed to combine co-localized blocking of the two immunosuppressive pathways, M7824 is thought to control tumor growth by potentially restoring and enhancing anti-tumor responses. M7824 is an important part of a novel combination approach that seeks to harness the power of the immune system and address the

BTC, M7824 is being studied in solid tumor indications, including non-small cell lung, HPV associated tumors and gastrointestinal cancers, such as gastric cancer, esophageal squamous cell carcinoma and esophageal adenocarcinoma.

About M7824

M7824 is an investigational bifunctional immunotherapy that is designed to combine a TGF-β trap with the anti-PD-L1 mechanism in one fusion protein. M7824 is designed to combine co-localized blocking of the two immunosuppressive pathways – targeting both pathways aims to control tumor growth by potentially restoring and enhancing anti-tumor responses. M7824 is currently in Phase I studies for solid tumors, as well as a trial to investigate M7824 compared with pembrolizumab as a first-line treatment in patients with PD-L1 expressing advanced NSCLC. The multicenter, randomized, open-label, controlled study is evaluating the safety and efficacy of M7824 versus pembrolizumab as a monotherapy treatment.

About the FDA Orphan Designation

FDA orphan drug designation is granted to drugs intended to treat rare diseases or disorders that affect fewer than 200,000 people in the US, or those that affect more than 200,000 people, but are unlikely to recover the costs of developing and marketing the drug. Orphan drug designation by the FDA qualifies the sponsor for incentives provided for in the Orphan Drug Act, which can include protocol assistance for clinical trials, prescription drug user fee waivers, tax incentives and seven years of market exclusivity. The granting of an orphan drug designation does not alter the standard regulatory requirement to establish the safety and effectiveness of a drug through adequate and well-controlled studies to support approval. The orphan drug designation for M7824 applies only to BTC.

About Biliary Tract Cancer (BTC)

BTC is a collective term for a group of rare and aggressive gastrointestinal cancers, including intrahepatic cholangiocarcinoma (iCC), extrahepatic cholangiocarcinoma (eCC), and gallbladder carcinoma (GBC).[1] Surgery is the only curative treatment, but most patients present with advanced disease and therefore have a limited survival.[1] Approximately 140,000 cases of BTC are estimated to occur annually world-wide.[2] However, incidence of BTC varies in different parts of the world: the incidence of cholangiocarcinomas is rising in the Western world, with reports of up to 2 in 100,000[4]. By contrast, in Asian countries, the incidence is much higher.[4] GBC also has an incidence of 2 in 100,000, but is much more prevalent in parts of South America.[4]

References

1. Blair A B et al. Immunotherapy as a treatment for biliary tract cancers: A review of approaches with an eye to the future. Current Problems in Cancer (2018) https://www.sciencedirect.com/science/article/pii/S0147027217301083?via%3Dihub Accessed November 2018
2. Global Burden of Disease Study 2013. The Lancet 2015;385(9963):117–171.
3. Hezel AF et al. Genetics of biliary tract cancers and emerging targeted therapies. J Clin Oncol 2010;28:3531–40. http://dx.doi.org/10.1200/JCO.2009.27.4787 Accessed November 2018
4. Goldstein D et al. New molecular and immunotherapeutic approaches in biliary cancer. ESMO Open (2017). Published online 2017 Mar 27. doi: https://dx.doi.org/10.1136%2Fesmoopen-2016-000152 Accessed November 2018
5. Lamarca A, et al. Ann Oncol. 2014;25(12):2328–2338.

About Merck KGaA, Darmstadt, Germany

Merck KGaA, Darmstadt, Germany, a vibrant science and technology company, operates across healthcare, life science and performance materials. Around 51,000 employees work to make a positive difference to millions of people's lives every day by creating more joyful and sustainable ways to live. From advancing gene editing technologies and discovering unique ways to treat the most challenging diseases to enabling the intelligence of devices – the company is everywhere. In 2017, Merck KGaA, Darmstadt, Germany, generated sales of € 15.3 billion in 66 countries.

For further information: Media Relations: friederike.segeberg@merckgroup.com, Phone: +49 6151 72-6328; Investor Relations: investor.relations@emdgroup.com, Phone: +49 6151 72-3321

This site contains information that is intended for US residents only. Canadian residents should consult the EMD Inc. website at www.emdserono.ca for information on products and services approved in Canada.

Merck KGaA, Darmstadt, Germany Presents Data on Bifunctional Immunotherapy M7824 at ASCO 2018 Gastrointestinal Cancers Symposium

Company to present three abstracts on M7824, its investigational early phase PD-L1/TGF-β bifunctional immuno-oncology asset

Noteworthy data includes encouraging preliminary expansion cohort data in gastric cancer

Darmstadt, Germany, January 16, 2018 – Merck KGaA, Darmstadt, Germany, a leading science and technology company which operates its healthcare business in the U.S. and Canada as EMD Serono, today announced three abstracts on M7824, an investigational early phase PD-L1/TGF-β bifunctional immuno-oncology asset, will be presented at the American Society of Clinical Oncology 2018 Gastrointestinal Cancers Symposium, January 19–21, 2018, in San Francisco, California. These data provide preliminary evidence that combining the anti-PD-L1 mechanism

"The data at ASCO GI includes some of the first tumor-specific preliminary cohort data for M7824, with encouraging results in gastric cancer," said Luciano Rossetti, M.D., Executive Vice President, Global Head of Research & Development at the Biopharma business of Merck KGaA, Darmstadt, Germany. "The data adds to our deepening knowledge of the therapeutic potential of this bi-functional immunotherapy, allowing us to further sharpen our focus on indications where we have the highest potential to make a real difference for patients."

In 31 heavily pretreated Asian patients with recurrent or refractory unresectable advanced gastric and gastroesophageal adenocarcinoma and unselected for PD-L1 status, preliminary data show initial clinical activity based on investigator-assessed best overall response (BOR), with an unconfirmed overall response rate (ORR) of 25.8%, confirmed ORR of 19.4% and a disease control rate of 35.5% observed. The safety profile was in line with that anticipated in such a heavily pretreated population. More information for all of the data presented at ASCO GI is included below.

Merck KGaA, Darmstadt, Germany, is committed to exploring an array of targets and taking creative scientific approaches to developing novel therapies for hard-to- treat cancers. With the belief that rational combination is the key to the future of new and more efficacious treatment options, Merck KGaA, Darmstadt, Germany, has a particular focus on combination therapies, whether it be with chemotherapy/radiotherapy, other targeted therapies and/or immunotherapies from its own or external portfolios. The strength of Merck KGaA, Darmstadt, Germany's promising oncology development program and growing presence in the field of immuno-oncology demonstrates how the company is re-imagining the way cancer care is delivered.

M7824 ASCO GI Abstracts

Abstract 100 – M7824 (MSB0011359C), a bifunctional fusion protein targeting PD- L1 and TGF-β, in Asian patients with pretreated recurrent or refractory gastric cancer: preliminary results from a phase 1 trial

• In 31 heavily pretreated Asian patients with recurrent or refractory unresectable advanced gastric and gastroesophageal adenocarcinoma and unselected for PD- L1 status, preliminary

35.5% observed: For confirmed responses, 1 patient had a confirmed complete response (ongoing at 5.4+ months), 5 had a confirmed partial response (4 still ongoing at 1.5+, 3.6+, 5.4+ and 6.9+ months) and 6 patients had stable disease

• The safety profile was in line with that anticipated in such a heavily pretreated population. A total of 15 patients (48.4%) experienced treatment-related adverse events (TRAEs), most commonly maculopapular rash (22.6%). Seven patients reported ≥grade 3 TRAEs, including rash, anemia and diarrhea. One patient died following an AE considered possibly treatment-related (reported as "sudden death") – the investigator cited suspected rupture of preexisting thoracic aortic aneurysm as other probable cause

• Biomarker analysis to identify patient subpopulations are ongoing and will be reported at a later time point

Abstract 762 – M7824 (MSB0011359C), a bifunctional fusion protein targeting PD- L1 and TGF-β, in patients with heavily pretreated CRC: preliminary results from a phase I trial

• In 32 heavily pretreated patients with recurrent or refractory unresectable advanced colorectal cancer (CRC), preliminary data showed a confirmed PR (ongoing at 8.3 months) in one patient, who had CRC that was microsatellite stable (MSS), consensus molecular subtype (CMS) 4, KRAS mutant (mt) and PD-L1+

• The safety profile was in line with that anticipated in such a heavily pretreated patient population. Four patients (12.5%) experienced grade 3 TRAEs: adrenal insufficiency, anemia, blood bilirubin increased, enteritis (leading to discontinuation) and fatigue. There were no grade ≥4 TRAEs or treatment-related deaths

Abstract 764 – M7824 (MSB0011359C), a bifunctional fusion protein targeting PD- L1 and TGF-β, in Asian patients with advanced solid tumors

• Fourteen heavily pretreated patients received M7824 at 3, 10 or 20 mg/kg q2w until confirmed progressive disease, unacceptable toxicity or trial withdrawal. The median duration of

• Signs of clinical activity were seen across all dose levels, and maximum tolerated dose was not reached. Two patients had a confirmed partial response (CRC [associated with Lynch syndrome] and ovarian cancer) and 3 patients had confirmed stable disease (gastric, gastroesophageal junction and adenoid cystic cancer)

• A total of 3 patients (21.4%) reported ≥grade 3 TRAEs, including hyponatremia, increased blood creatine phosphokinase and hypopituitarism. Two of these patients discontinued treatment following grade 3 TRAEs (intracranial tumor hemorrhage and reversible hypoacusis)

About M7824

M7824 is an investigational bifunctional immunotherapy that is designed to bring together the anti-PD- L1 mechanism and 'fuse' it with a transforming growth factor β (TGF-β) trap. M7824 is designed to simultaneously block the two immuno-inhibitory pathways – targeting both pathways aims to control tumor growth by potentially restoring and enhancing anti-tumor responses. By combining two targeting mechanisms against cancer cells in one molecule, it also aims to increase safety and efficacy, compared to monotherapy approaches.

About Merck KGaA, Darmstadt, Germany

Merck KGaA, Darmstadt, Germany, is a leading science and technology company in healthcare, life science and performance materials. Around 50,000 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 2016, Merck KGaA, Darmstadt, Germany, generated sales of € 15.0 billion in 66 countries. Founded in 1668, Merck KGaA, Darmstadt, Germany, is the world's oldest pharmaceutical and chemical company. The founding family remains the majority owner of the publicly listed corporate group. 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 company operates as EMD Serono, MilliporeSigma and EMD Performance Materials.

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 again for your online

For further information: Brenda Mulligan +1 978 821 5345

COMPANY

LEADERSHIP TEAM

PARTNERING

PRESS

CONTACT US

COMPLIANCE & TRANSPARENCY

THERAPEUTIC AREAS

YOUR REQUESTS

BAVENCIO® (avelumab) Plus INLYTA® (axitinib) Significantly Improved Progression-Free Survival in Previously Untreated Patients with Advanced Renal Cell Carcinoma in Phase III Study

Not intended for UK-based media

First positive Phase III immunotherapy trial in combination with a tyrosine kinase inhibitor (TKI) in any tumor type

Results significant in both PDL1+ and all-comer populations

Alliance plans to pursue a regulatory submission in the US and discussions with other health authorities based on interim results for progression-free survival

Trial will continue for the other primary endpoint of overall survival; detailed results to be submitted for presentation at an upcoming medical congress

Merck KGaA, Darmstadt, Germany, and Pfizer Inc. (NYSE: PFE) today announced positive top-line results from the pivotal Phase III JAVELIN Renal 101 study evaluating BAVENCIO® (avelumab) **in combination with INLYTA® (axitinib)**, compared with SUTENT® (sunitinib) as initial therapy for patients with advanced renal cell carcinoma (RCC). As part of a planned interim analysis, an independent Data Monitoring Committee confirmed that the trial showed a statistically significant improvement in progression-free survival (PFS) by central review for patients treated with the combination whose tumors had programmed death ligand-1–positive (PD-L1+) expression greater than 1% (primary objective), as well as in the entire study population regardless of PD-L1 tumor expression (secondary objective). According to the statistical analysis plan, if PFS was statistically significant in the PD-L1+ subgroup, then PFS in the entire study population was to be analyzed for statistical significance. JAVELIN Renal 101 will continue as planned to the final analysis for the other primary endpoint of overall survival (OS). No new safety signals were observed, and adverse events for BAVENCIO, INLYTA and SUTENT in this trial were consistent with the known safety profiles for all three medicines. The alliance intends to pursue a regulatory submission in the US based on these interim results, and these results will be discussed with global health authorities. A detailed analysis will also be submitted for presentation at an upcoming medical congress.

"JAVELIN Renal 101 is the first positive Phase III study combining an immune checkpoint blocker with a TKI, supporting the potential of BAVENCIO and INLYTA as a new cancer treatment approach for patients with advanced RCC," said Chris Boshoff, M.D., Ph.D., Senior Vice President and Head of Immuno-Oncology, Early Development and Translational Oncology, Pfizer Global Product Development. "These positive results reinforce Pfizer's long-standing heritage in advancing standards of care for people with RCC, and we look forward to discussing these data in greater detail with health authorities."

In December 2017, the US Food and Drug Administration (FDA) granted Breakthrough Therapy Designation for BAVENCIO in combination with INLYTA for treatment-naïve patients with advanced RCC. Despite available therapies, the outlook for patients with advanced RCC remains poor.1 Approximately 20% to 30% of patients are first diagnosed at the metastatic stage.2 The five-year survival rate for patients with metastatic RCC is approximately 12%.1
"We are encouraged by these data which illustrate the impact of BAVENCIO in combination with INLYTA as a potential first-line treatment for people with advanced RCC, a serious and life-threatening cancer," said Luciano Rossetti, M.D., Executive Vice President, Global Head of Research & Development at the Biopharma business of Merck KGaA, Darmstadt, Germany,

focus of the overall JAVELIN clinical development program."

JAVELIN Renal 101 is a global Phase III, multicenter, randomized (1:1) study investigating the efficacy and safety of BAVENCIO in combination with INLYTA as a first-line treatment option compared with SUTENT monotherapy in 886 patients with advanced RCC across all risk groups. The primary objectives are to demonstrate that BAVENCIO in combination with INLYTA is superior to SUTENT monotherapy in prolonging PFS or OS in patients with PD-L1+ tumors. BAVENCIO was administered at 10 mg/kg IV every two weeks in combination with INLYTA at 5 mg orally twice daily; SUTENT was administered at 50 mg orally once daily, four weeks on/two weeks off.

*The combination of BAVENCIO and INLYTA is under clinical investigation for advanced RCC, and there is no guarantee this combination will be approved for advanced RCC by any health authority worldwide. In the US, INLYTA is approved as monotherapy for the treatment of advanced RCC after failure of one prior systemic therapy. INLYTA is also approved by the European Medicines Agency (EMA) for use in the EU in adult patients with advanced RCC after failure of prior treatment with SUTENT or a cytokine.

About the JAVELIN Clinical Development Program

The clinical development program for BAVENCIO, known as JAVELIN, involves at least 30 clinical programs, eight Phase III trials and more than 8,600 patients evaluated across more than 15 different tumor types. In addition to RCC, these tumor types include breast, gastric/gastro-esophageal junction, head and neck, Hodgkin's lymphoma, melanoma, mesothelioma, Merkel cell carcinoma, non-small cell lung cancer, ovarian and urothelial carcinoma.

About Renal Cell Carcinoma

RCC is the most common form of kidney cancer, accounting for about 2% to 3% of all cancers in adults.3,4 The most common type of RCC is clear cell carcinoma, accounting for approximately 70% of all cases.3 In 2012, there were approximately 338,000 new cases of RCC diagnosed worldwide, with an estimated 63,340 cases expected in the US alone in 2018.3,5 Incidence varies substantially worldwide, with generally higher rates seen in North America and Central/Eastern Europe.5

shown in preclinical models to engage both the adaptive and innate immune functions. By blocking the interaction of PD-L1 with PD-1 receptors, BAVENCIO has been shown to release the suppression of the T cell-mediated antitumor immune response in preclinical models.6-8 BAVENCIO has also been shown to induce NK cell-mediated direct tumor cell lysis via antibody-dependent cell-mediated cytotoxicity (ADCC) in vitro.8-10 In November 2014, Merck KGaA, Darmstadt, Germany, and Pfizer announced a strategic alliance to co-develop and co-commercialize BAVENCIO.

Approved Indications

The FDA granted accelerated approval for BAVENCIO for the treatment of (i) adults and pediatric patients 12 years and older with metastatic Merkel cell carcinoma (mMCC) and (ii) patients with locally advanced or metastatic urothelial carcinoma (mUC) who have disease progression during or following platinum-containing chemotherapy, or have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy. These indications are approved under accelerated approval based on tumor response rate and duration of response. Continued approval for these indications may be contingent upon verification and description of clinical benefit in confirmatory trials.

BAVENCIO is also approved by the European Medicines Agency (EMA) for use in the EU as a monotherapy for the treatment of adult patients with mMCC.

Important Safety Information from the US FDA Approved Label

BAVENCIO can cause **immune-mediated pneumonitis**, including fatal cases. Monitor patients for signs and symptoms of pneumonitis, and evaluate suspected cases with radiographic imaging. Administer corticosteroids for Grade 2 or greater pneumonitis. Withhold BAVENCIO for moderate (Grade 2) and permanently discontinue for severe (Grade 3), life-threatening (Grade 4), or recurrent moderate (Grade 2) pneumonitis. Pneumonitis occurred in 1.2% (21/1738) of patients, including one (0.1%) patient with Grade 5, one (0.1%) with Grade 4, and five (0.3%) with Grade 3.

BAVENCIO can cause **immune-mediated hepatitis**, including fatal cases. Monitor patients for abnormal liver tests prior to and periodically during treatment. Administer corticosteroids for Grade 2 or greater hepatitis. Withhold BAVENCIO for moderate (Grade 2) immune-mediated hepatitis until resolution and permanently discontinue for severe (Grade 3) or life-threatening (Grade 4) immune-mediated hepatitis. Immune-mediated hepatitis was reported in 0.9%

BAVENCIO can cause immune-mediated colitis. Monitor patients for signs and symptoms of colitis. Administer corticosteroids for Grade 2 or greater colitis. Withhold BAVENCIO until resolution for moderate or severe (Grade 2 or 3) colitis, and permanently discontinue for life-threatening (Grade 4) or recurrent (Grade 3) colitis upon reinitiation of BAVENCIO. Immune-mediated colitis occurred in 1.5% (26/1738) of patients, including seven (0.4%) with Grade 3.

BAVENCIO can cause **immune-mediated endocrinopathies**, including adrenal insufficiency, thyroid disorders, and type 1 diabetes mellitus.

Monitor patients for signs and symptoms of **adrenal insufficiency** during and after treatment, and administer corticosteroids as appropriate. Withhold BAVENCIO for severe (Grade 3) or life-threatening (Grade 4) adrenal insufficiency. Adrenal insufficiency was reported in 0.5% (8/1738) of patients, including one (0.1%) with Grade 3.

Thyroid disorders can occur at any time during treatment. Monitor patients for changes in thyroid function at the start of treatment, periodically during treatment, and as indicated based on clinical evaluation. Manage hypothyroidism with hormone replacement therapy and hyperthyroidism with medical management. Withhold BAVENCIO for severe (Grade 3) or life-threatening (Grade 4) thyroid disorders. Thyroid disorders, including hypothyroidism, hyperthyroidism, and thyroiditis, were reported in 6% (98/1738) of patients, including three (0.2%) with Grade 3.

Type 1 diabetes mellitus including diabetic ketoacidosis: Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Withhold BAVENCIO and administer antihyperglycemics or insulin in patients with severe or life-threatening (Grade ≥ 3) hyperglycemia, and resume treatment when metabolic control is achieved. Type 1 diabetes mellitus without an alternative etiology occurred in 0.1% (2/1738) of patients, including two cases of Grade 3 hyperglycemia.

BAVENCIO can cause **immune-mediated nephritis and renal dysfunction**. Monitor patients for elevated serum creatinine prior to and periodically during treatment. Administer corticosteroids for Grade 2 or greater nephritis. Withhold BAVENCIO for moderate (Grade 2) or severe (Grade 3) nephritis until resolution to Grade 1 or lower. Permanently discontinue BAVENCIO for life-threatening (Grade 4) nephritis. Immune-mediated nephritis occurred in 0.1% (1/1738) of patients.

immune-mediated adverse reactions, evaluate to confirm or rule out an immune-mediated adverse reaction and to exclude other causes. Depending on the severity of the adverse reaction, withhold or permanently discontinue BAVENCIO, administer high-dose corticosteroids, and initiate hormone replacement therapy, if appropriate. Resume BAVENCIO when the immune-mediated adverse reaction remains at Grade 1 or lower following a corticosteroid taper. Permanently discontinue BAVENCIO for any severe (Grade 3) immune-mediated adverse reaction that recurs and for any life-threatening (Grade 4) immune-mediated adverse reaction. The following clinically significant immune-mediated adverse reactions occurred in less than 1% of 1,738 patients treated with BAVENCIO: myocarditis with fatal cases, myositis, psoriasis, arthritis, exfoliative dermatitis, erythema multiforme, pemphigoid, hypopituitarism, uveitis, Guillain-Barré syndrome, and systemic inflammatory response.

BAVENCIO can cause severe (Grade 3) or life-threatening (Grade 4) **infusion-related reactions**. Patients should be premedicated with an antihistamine and acetaminophen prior to the first 4 infusions and for subsequent doses based upon clinical judgment and presence/severity of prior infusion reactions. Monitor patients for signs and symptoms of infusion-related reactions, including pyrexia, chills, flushing, hypotension, dyspnea, wheezing, back pain, abdominal pain, and urticaria. Interrupt or slow the rate of infusion for mild (Grade 1) or moderate (Grade 2) infusion-related reactions. Permanently discontinue BAVENCIO for severe (Grade 3) or life-threatening (Grade 4) infusion-related reactions. Infusion-related reactions occurred in 25% (439/1738) of patients, including three (0.2%) patients with Grade 4 and nine (0.5%) with Grade 3.

BAVENCIO can cause **fetal harm** when administered to a pregnant woman. Advise patients of the potential risk to a fetus including the risk of fetal death. Advise females of childbearing potential to use effective contraception during treatment with BAVENCIO and for at least 1 month after the last dose of BAVENCIO. It is not known whether BAVENCIO is excreted in human milk. Advise a lactating woman **not to breastfeed** during treatment and for at least 1 month after the last dose of BAVENCIO due to the potential for serious adverse reactions in breastfed infants.

The most common adverse reactions (all grades, ≥ 20%) in patients with **metastatic Merkel cell carcinoma** (MCC) were fatigue (50%), musculoskeletal pain (32%), diarrhea (23%), nausea (22%), infusion-related reaction (22%), rash (22%), decreased appetite (20%), and peripheral edema (20%).

aminotransferase (34%), thrombocytopenia (27%), and increased alanine aminotransferase (20%).

The most common adverse reactions (all grades, ≥ 20%) in patients with locally advanced or **metastatic urothelial carcinoma** (UC) were fatigue (41%), infusion-related reaction (30%), musculoskeletal pain (25%), nausea (24%), decreased appetite/hypophagia (21%), and urinary tract infection (21%).

Selected laboratory abnormalities (Grades 3-4, ≥ 3%) in patients with **locally advanced or metastatic UC** were hyponatremia (16%), increased gamma-glutamyltransferase (12%), lymphopenia (11%), hyperglycemia (9%), increased alkaline phosphatase (7%), anemia (6%), increased lipase (6%), hyperkalemia (3%), and increased aspartate aminotransferase (3%).

Please see full US Prescribing Information and Medication Guide available at http://www.BAVENCIO.com.

About INLYTA® (axitinib)

INLYTA is an oral therapy that is designed to inhibit tyrosine kinases, including vascular endothelial growth factor (VEGF) receptors 1, 2 and 3; these receptors can influence tumor growth, vascular angiogenesis and progression of cancer (the spread of tumors). In the US, INLYTA is approved for the treatment of advanced renal cell carcinoma (RCC) after failure of one prior systemic therapy. INLYTA is also approved by the European Medicines Agency (EMA) for use in the EU in adult patients with advanced RCC after failure of prior treatment with sunitinib or a cytokine.

INLYTA Important Safety Information

Hypertension including **hypertensive crisis** has been observed. Blood pressure should be well controlled prior to initiating INLYTA. Monitor for hypertension and treat as needed. For persistent hypertension, despite use of antihypertensive medications, reduce the dose. Discontinue INLYTA if hypertension is severe and persistent despite use of antihypertensive therapy and dose reduction of INLYTA, and discontinuation should be considered if there is evidence of hypertensive crisis.

Hemorrhagic events, including fatal events, have been reported. INLYTA has not been studied in patients with evidence of untreated brain metastasis or recent active gastrointestinal bleeding and should not be used in those patients. If any bleeding requires medical intervention, temporarily interrupt the INLYTA dose.

Cardiac failure has been observed and can be fatal. Monitor for signs or symptoms of cardiac failure throughout treatment with INLYTA. Management of cardiac failure may require permanent discontinuation of INLYTA.

Gastrointestinal perforation and fistula, including death, have occurred. Use with caution in patients at risk for gastrointestinal perforation or fistula. Monitor for symptoms of gastrointestinal perforation or fistula periodically throughout treatment.

Hypothyroidism requiring thyroid hormone replacement has been reported. Monitor thyroid function before initiation of, and periodically throughout, treatment.

No formal studies of the effect of INLYTA on **wound healing** have been conducted. Stop INLYTA at least 24 hours prior to scheduled surgery.

Reversible Posterior Leukoencephalopathy Syndrome (RPLS) has been observed. If signs or symptoms occur, permanently discontinue treatment.

Monitor for **proteinuria** before initiation of, and periodically throughout, treatment. For moderate to severe proteinuria, reduce the dose or temporarily interrupt treatment.

Liver enzyme elevation has been observed during treatment with INLYTA. Monitor ALT, AST, and bilirubin before initiation of, and periodically throughout, treatment.

For patients with moderate **hepatic impairment**, the starting dose should be decreased. INLYTA has not been studied in patients with severe hepatic impairment.

Women of childbearing potential should be advised of potential hazard to the fetus and to avoid becoming **pregnant** while receiving INLYTA.

Avoid strong **CYP3A4/5 inducers** and, if possible, avoid moderate CYP3A4/5 inducers.

The most common (≥20%) adverse events (AEs) occurring in patients receiving INLYTA (all grades, vs sorafenib) were diarrhea (55% vs 53%), hypertension (40% vs 29%), fatigue (39% vs 32%), decreased appetite (34% vs 29%), nausea (32% vs 22%), dysphonia (31% vs 14%), hand-foot syndrome (27% vs 51%), weight decreased (25% vs 21%), vomiting (24% vs 17%), asthenia (21% vs 14%), and constipation (20% vs 20%).
The most common (≥10%) grade 3/4 AEs occurring in patients receiving INLYTA (vs sorafenib) were hypertension (16% vs 11%), diarrhea (11% vs 7%), and fatigue (11% vs 5%).
The most common (≥20%) lab abnormalities occurring in patients receiving INLYTA (all grades, vs sorafenib) included increased creatinine (55% vs 41%), decreased bicarbonate (44% vs 43%), hypocalcemia (39% vs 59%), decreased hemoglobin (35% vs 52%), decreased lymphocytes (absolute) (33% vs 36%), increased ALP (30% vs 34%), hyperglycemia (28% vs 23%), increased lipase (27% vs 46%), increased amylase (25% vs 33%), increased ALT (22% vs 22%), and increased AST (20% vs 25%).
For more information and full Prescribing Information, visit www.INLYTA.com.

SUTENT Important Safety Information
Boxed Warning/Hepatotoxicity has been observed in clinical trials and postmarketing experience. Hepatotoxicity may be severe, and in some cases fatal. Monitor hepatic function and interrupt, reduce, or discontinue dosing as recommended. Fatal liver failure has been observed. Monitor liver function tests before initiation of treatment, during each cycle of treatment, and as clinically indicated. Interrupt SUTENT for Grade 3 or 4 drug-related hepatic adverse reactions and discontinue if there is no resolution. Do not restart SUTENT if patients subsequently experience severe changes in liver function tests or have signs and symptoms of liver failure.

Cardiovascular events, including myocardial ischemia, myocardial infarction, left ventricular ejection fraction declines to below the lower limit of normal and cardiac failure including death have occurred. Monitor patients for signs and symptoms of congestive heart failure. Discontinue SUTENT for clinical manifestations of congestive heart failure. In patients without cardiac risk factors, a baseline evaluation of ejection fraction should be considered. Baseline

SUTENT can cause **QT Prolongation** in a dose-dependent manner, which may lead to an increased risk for ventricular arrhythmias including **Torsades de Pointes**, which has been seen in <0.1% of patients. Monitor patients that are at a higher risk for developing QT interval prolongation, including those with a history of QT interval prolongation, patients who are taking antiarrhythmics, or patients with relevant pre-existing cardiac disease, bradycardia, or electrolyte disturbances. Consider monitoring of electrocardiograms and electrolytes. Concomitant treatment with strong CYP3A4 inhibitors may increase sunitinib plasma concentrations and dose reduction of SUTENT should be considered.

Hypertension may occur. Monitor blood pressure and treat as needed with standard antihypertensive therapy. In cases of severe hypertension, temporary suspension of SUTENT is recommended until hypertension is controlled.

Hemorrhagic events, including tumor-related hemorrhage, and viscus perforation (both with fatal events) have occurred. These events may occur suddenly, and in the case of pulmonary tumors, may present as severe and life-threatening hemoptysis or pulmonary hemorrhage. Perform serial complete blood counts (CBCs) and physical examinations.

Cases of **tumor lysis syndrome** (TLS) (some fatal) have been reported. Patients generally at risk of TLS are those with high tumor burden prior to treatment. Monitor these patients closely and treat as clinically indicated.

Thrombotic microangiopathy (TMA), including thrombotic thrombocytopenic purpura and hemolytic uremic syndrome, sometimes leading to renal failure or a fatal outcome, has been reported in patients who received SUTENT as monotherapy and in combination with bevacizumab. Discontinue SUTENT in patients developing TMA. Reversal of the effects of TMA has been observed after treatment was discontinued.

Proteinuria and nephrotic syndrome have been reported. Some of these cases have resulted in renal failure and fatal outcomes. Monitor patients for the development or worsening of proteinuria. Perform baseline and periodic urinalysis during treatment, with follow-up measurement of 24-hour urine protein as clinically indicated. Interrupt treatment for 24-hour urine protein ≥3 grams. Discontinue for repeat episodes of protein ≥3 grams despite dose reductions or nephrotic syndrome.

epidermal necrolysis (TEN), some of which were fatal. If signs or symptoms of EM, SJS, or TEN are present, discontinue SUTENT treatment. If a diagnosis of SJS or TEN is suspected, treatment must not be restarted.

Necrotizing fasciitis, including fatal cases, has been reported, including of the perineum and secondary to fistula formation. Discontinue SUTENT in patients who develop necrotizing fasciitis.

Thyroid dysfunction may occur. Monitor thyroid function in patients with signs and/or symptoms suggestive of thyroid dysfunction, including hypothyroidism, hyperthyroidism, and thyroiditis, and treat per standard medical practice.

Hypoglycemia may occur. SUTENT can result in symptomatic hypoglycemia, which may lead to a loss of consciousness or require hospitalization. Reductions in blood glucose levels may be worse in patients with diabetes. Check blood glucose levels regularly during and after discontinuation of treatment with SUTENT. Assess if antidiabetic drug dosage needs to be adjusted to minimize the risk of hypoglycemia.

Osteonecrosis of the jaw (ONJ) has been reported. Consider preventive dentistry prior to treatment with SUTENT. If possible, avoid invasive dental procedures, particularly in patients receiving intravenous bisphosphonate therapy.

Impaired wound healing has occurred with SUTENT. Temporary interruption of therapy with SUTENT is recommended in patients undergoing major surgical procedures. There is limited clinical experience regarding the timing of reinitiation of therapy following major surgical intervention. Therefore, the decision to resume SUTENT therapy following a major surgical intervention should be based upon clinical judgment of recovery from surgery.

Embryo fetal toxicity and reproductive potential

Females - SUTENT can cause fetal harm when administered to pregnant women. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with SUTENT and for 4 weeks following the final dose.

Males - Based on findings in animal reproduction studies, advise male patients with female partners of reproductive potential to use effective contraception during treatment with SUTENT and for 7 weeks after the last dose.

Lactation: Because of the potential for serious adverse reactions in breastfed infants from SUTENT, advise a lactating woman not to breastfeed during treatment with SUTENT and for at least 4 weeks after the last dose.

Venous thromboembolic events: In patients treated with SUTENT (N=7527) for GIST, advanced RCC, adjuvant treatment of RCC and pNET, 3.5% of patients experienced a venous thromboembolic event; 2.2% Grade 3-4.

There have been (<1%) reports, some fatal, of subjects presenting with seizures and radiological evidence of **reversible posterior leukoencephalopathy syndrome (RPLS)**. Patients with seizures and signs/symptoms consistent with RPLS, such as hypertension, headache, decreased alertness, altered mental functioning, and visual loss, including cortical blindness, should be controlled with medical management including control of hypertension. Temporary suspension of SUTENT is recommended; following resolution, treatment may be resumed at the discretion of the treating healthcare provider.

Pancreatic function: In a trial of patients receiving adjuvant treatment for RCC, 1 patient (<1%) on SUTENT and none on placebo experienced pancreatitis.

CYP3A4 inhibitors and inducers: Dose adjustments are recommended when SUTENT is administered with CYP3A4 inhibitors or inducers. During treatment with SUTENT, patients should not drink grapefruit juice, eat grapefruit, or take St. John's Wort.

Most common ARs & most common grade 3/4 ARs (adjuvant RCC): The **most common ARs** reported in ≥20% of patients receiving SUTENT for adjuvant treatment of RCC and more commonly than in patients given placebo (all grades, vs placebo) were mucositis/stomatitis (61% vs 15%), diarrhea (57% vs 22%), fatigue/asthenia (57% vs 34%), hand-foot syndrome (50% vs 10%), hypertension (39% vs 14%), altered taste (38% vs 6%), nausea (34% vs 15%), dyspepsia (27% vs 7%), abdominal pain (25% vs 9%), hypothyroidism/TSH increased (24% vs 4%), rash (24% vs 12%), hair color changes (22% vs 2%). **The most common grade 3/4 ARs** reported in ≥5% of patients receiving SUTENT for adjuvant treatment of RCC and more commonly than in patients given placebo (vs placebo) were hand-foot syndrome (16% vs <1%), fatigue/asthenia (8% vs 2%), hypertension (8% vs 1%), and mucositis/stomatitis (6% vs 0%).

neutropenia (13%), thrombocytopenia (5%), leukopenia (3%), lymphopenia (3%), elevated alanine aminotransferase (2%), elevated aspartate aminotransferase (2%), hyperglycemia (2%), and hyperkalemia (2%).

Most common ARs & most common grade 3/4 ARs (advanced RCC): The **most common ARs** reported in ≥20% of patients receiving SUTENT for treatment-naïve metastatic RCC (all grades, vs IFNα) were diarrhea (66% vs 21%), fatigue (62% vs 56%), nausea (58% vs 41%), anorexia (48% vs 42%), altered taste (47% vs 15%), mucositis/stomatitis (47% vs 5%), pain in extremity/limb discomfort (40% vs 30%), vomiting (39% vs 17%), bleeding, all sites (37% vs 10%), hypertension (34% vs 4%), dyspepsia (34% vs 4%), arthralgia (30% vs 19%), abdominal pain (30% vs 12%), rash (29% vs 11%), hand-foot syndrome (29% vs 1%), back pain (28% vs 14%), cough (27% vs 14%), asthenia (26% vs 22%), dyspnea (26% vs 20%), skin discoloration/yellow skin (25% vs 0%), peripheral edema (24% vs 5%), headache (23% vs 19%), constipation (23% vs 14%), dry skin (23% vs 7%), fever (22% vs 37%), and hair color changes (20% vs <1%). **The most common grade 3/4 ARs** reported in ≥5% of patients with RCC receiving SUTENT (vs IFNα) were fatigue (15% vs 15%), hypertension (13% vs <1%), asthenia (11% vs 6%), diarrhea (10% vs <1%), hand-foot syndrome (8% vs 0%), dyspnea (6% vs 4%), nausea (6% vs 2%), back pain (5% vs 2%), pain in extremity/limb discomfort (5% vs 2%), vomiting (5% vs 1%), and abdominal pain (5% vs 1%).

Most common grade 3/4 lab abnormalities (advanced RCC): The **most common grade 3/4 lab abnormalities** (occurring in ≥5% of patients with RCC receiving SUTENT vs IFNα) included lymphocytes (18% vs 26%), lipase (18% vs 8%), neutrophils (17% vs 9%), uric acid (14% vs 8%), platelets (9% vs 1%), hemoglobin (8% vs 5%), sodium decreased (8% vs 4%), leukocytes (8% vs 2%), glucose increased (6% vs 6%), phosphorus (6% vs 6%), and amylase (6% vs 3%).

Most common ARs & most common grade 3/4 ARs (imatinib-resistant or -intolerant GIST): The **most common ARs** reported in ≥20% of patients with GIST and more commonly with SUTENT than placebo (all grades, vs placebo) were diarrhea (40% vs 27%), anorexia (33% vs 29%), skin discoloration (30% vs 23%), mucositis/stomatitis (29% vs 18%), asthenia (22% vs 11%), altered taste (21% vs 12%), and constipation (20% vs 14%). **The most common grade 3/4 ARs** reported in ≥4% of patients with GIST receiving SUTENT (vs placebo) were asthenia (5% vs 3%), hand-foot syndrome (4% vs 3%), diarrhea (4% vs 0%), and hypertension (4% vs0%).

receiving SUTENT vs placebo) included lipase (10% vs 7%), neutrophils (10% vs 0%), amylase (5% vs 3%), and platelets (5% vs 0%).

Most common ARs & most common grade 3/4 ARs (advanced pNET): The **most common ARs** reported in ≥20% of patients with advanced pNET and more commonly with SUTENT than placebo (all grades, vs placebo) were diarrhea (59% vs 39%), stomatitis/oral syndromes (48% vs 18%), nausea (45% vs 29%), abdominal pain (39% vs 34%), vomiting (34% vs 31%), asthenia (34% vs 27%), fatigue (33% vs 27%), hair color changes (29% vs 1%), hypertension (27% vs 5%), hand-foot syndrome (23% vs 2%), bleeding events (22% vs 10%), epistaxis (21% vs 5%), and dysgeusia (21% vs 5%). **The most common grade 3/4 ARs r**eported in ≥5% of patients with advanced pNET receiving SUTENT (vs placebo) were hypertension (10% vs 1%), hand-foot syndrome (6% vs 0%), stomatitis/oral syndromes (6% vs 0%), abdominal pain (5% vs 10%), fatigue (5% vs 9%), asthenia (5% vs 4%), and diarrhea (5% vs 2%).

Most common grade 3/4 lab abnormalities (advanced pNET): The **most common grade 3/4 lab abnormalities** (occurring in ≥5% of patients with advanced pNET receiving SUTENT vs placebo) included decreased neutrophils (16% vs 0%), increased glucose (12% vs 18%), increased alkaline phosphatase (10% vs 11%), decreased phosphorus (7% vs 5%), decreased lymphocytes (7% vs 4%), increased creatinine (5% vs 5%), increased lipase (5% vs 4%), increased AST (5% vs 3%), and decreased platelets (5% vs 0%).

Please see full Prescribing Information, including BOXED WARNING and Medication Guide, for SUTENT® (sunitinib malate) at www.SUTENT.com.

About SUTENT® (sunitinib malate)

Sunitinib is a small molecule that inhibits multiple receptor tyrosine kinases, some of which are implicated in tumor growth, pathologic angiogenesis, and metastatic progression of cancer. Sunitinib was evaluated for its inhibitory activity against a variety of kinases (>80 kinases) and was identified as an inhibitor of platelet-derived growth factor receptors (PDGFRα and PDGFRβ), vascular endothelial growth factor receptors (VEGFR1, VEGFR2 and VEGFR3), stem cell factor receptor (KIT), Fms-like tyrosine kinase-3 (FLT3), colony stimulating factor receptor Type 1 (CSF-1R), and the glial cell-line derived neurotrophic factor receptor (RET).

cell carcinoma (RCC); the adjuvant treatment of adult patients at high risk of recurrent RCC following nephrectomy; the treatment of progressive, well-differentiated pancreatic neuroendocrine tumors (pNET) in patients with unresectable locally advanced or metastatic disease.

For more information, please contact **Friederike Segeberg**
+49 6151 72 6328
Email

About Merck KGaA, Darmstadt, Germany

Merck KGaA, Darmstadt, Germany, is a leading science and technology company in healthcare, life science and performance materials. Almost 53,000 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 2017, Merck KGaA, Darmstadt, Germany, generated sales of € 15.3 billion in 66 countries.

Founded in 1668, Merck KGaA, Darmstadt, Germany, is the world's oldest pharmaceutical and chemical company. The founding family remains the majority owner of the publicly listed corporate group. Merck KGaA, Darmstadt, Germany holds the global rights to the "Merck" name and brand except in the United States and Canada, where the company operates as EMD Serono, MilliporeSigma and EMD Performance Materials.

Pfizer Inc.: Working together for a healthier world®

At Pfizer, we apply science and our global resources to bring therapies to people that extend and significantly improve their lives. We strive to set the standard for quality, safety and value in the discovery, development and manufacture of health care products. Our global portfolio includes medicines and vaccines as well as many of the world's best-known consumer health

our time. Consistent with our responsibility as one of the world's premier innovative biopharmaceutical companies, we collaborate with health care providers, governments and local communities to support and expand access to reliable, affordable health care around the world. For more than 150 years, we have worked to make a difference for all who rely on us. We routinely post information that may be important to investors on our website at www.pfizer.com. In addition, to learn more, please visit us on www.pfizer.com and follow us on Twitter at @Pfizer and @Pfizer_News, LinkedIn, YouTube and like us on Facebook at Facebook.com/Pfizer.

PFIZER DISCLOSURE NOTICE

The information contained in this release is as of September 11, 2018. Pfizer assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments.

This release contains forward-looking information about BAVENCIO (avelumab), including a potential new indication for BAVENCIO in combination with INLYTA (axitinib) for the treatment of patients with advanced renal cell carcinoma (the "Potential Indication"), the alliance between Merck KGaA, Darmstadt, Germany, and Pfizer involving anti-PD-L1 and anti-PD-1 therapies, and clinical development plans, including their potential benefits, that involves substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Risks and uncertainties include, among other things, uncertainties regarding the commercial success of BAVENCIO; the uncertainties inherent in research and development, including the ability to meet anticipated clinical study commencement and completion dates and regulatory submission dates, as well as the possibility of unfavorable study results, including unfavorable new clinical data and additional analyses of existing clinical data and uncertainties regarding whether the other primary endpoint of JAVELIN Renal 101 will be met; risks associated with interim data; the risk that clinical trial data are subject to differing interpretations, and, even when we view data as sufficient to support the safety and/or effectiveness of a product candidate, regulatory authorities may not share our views and may require additional data or may deny approval altogether; whether regulatory authorities will be satisfied with the design of and results from our clinical studies; whether and when any drug applications may be filed for BAVENCIO in any jurisdictions for the Potential Indication or for any other potential indications for BAVENCIO,

combination therapies or other product candidates may approve any such applications, which will depend on the assessment by such regulatory authorities of the benefit-risk profile suggested by the totality of the efficacy and safety information submitted; decisions by regulatory authorities regarding labeling and other matters that could affect the availability or commercial potential of BAVENCIO, combination therapies or other product candidates, including the Potential Indication and competitive developments.

A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2017, and in its subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information and Factors That May Affect Future Results", as well as in its subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and Exchange Commission and available at www.sec.gov and www.pfizer.com.

References

1. National Cancer Institute: SEER Stat Fact Sheets: Kidney and renal pelvis. Available from: http://seer.cancer.gov/statfacts/html/kidrp.html. Accessed July 2018.

2. Ljungberg B, Campbell S and Cho H. The Epidemiology of Renal Cell Carcinoma. Eur Urol. 2011;60:615-621.

3. American Cancer Society. What is kidney cancer? Available from: https://www.cancer.org/cancer/kidney-cancer/about.html. Accessed July 2018.

4. Escudier B, Porta C, Schmidinger M et al Renal cell carcinoma: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Annal Oncol. 2014; 25(Suppl3):iii49-iii56.

5. World Cancer Research Fund International: Kidney cancer statistics. Available from: http://www.wcrf.org/int/cancer-facts-figures/data-specific-cancers/kidney-cancer-statistics. Accessed July 2018.

6. Dolan DE, Gupta S. PD-1 pathway inhibitors: changing the landscape of cancer immunotherapy. Cancer Control. 2014;21(3):231-237.

8. Boyerinas B, Jochems C, Fantini M, et al. Antibody-dependent cellular cytotoxicity activity of a novel anti-PD-L1 antibody avelumab (MSB0010718C) on human tumor cells. Cancer Immunol Res. 2015;3(10):1148-1157.

9. Kohrt HE, Houot R, Marabelle A, et al. Combination strategies to enhance antitumor ADCC. Immunotherapy. 2012;4(5):511-527.

10. Hamilton G, Rath B. Avelumab: combining immune checkpoint inhibition and antibody-dependent cytotoxicity. Expert Opin Biol Ther. 2017;17(4):515-523.

Luciano-Rossetti.jpg
(2 MB)

EMD Serono

EMD Serono is the biopharmaceutical business of Merck KGaA, Darmstadt, Germany. This site contains information that is intended for residents of the United States only and is not meant to substitute for the advice provided by a medical professional. Always consult a physician if you have health concerns. Use and access of this site is subject to the terms and conditions as set out in our Legal Statement and Privacy Policy.

This site contains information that is intended for US residents only. Canadian residents should consult the EMD Inc. website at www.emdserono.ca for information on products and services approved in Canada.

SITEMAP

LEGAL STATEMENT

PRIVACY POLICY

CONTACT US

Embracing Carers™ expands support for caregivers worldwide

EXPLORE MORE

- **Increasing global reach of Embracing Carers™ to include Brazil and China**
- **Supporting the development of an advocacy resource which aims to improve the global state of care**

Darmstadt – Merck KGaA, Darmstadt, Germany, which operates its biopharmaceutical business in the U.S. and Canada as EMD Serono, today announced the continued expansion of Embracing Carers™. The global initiative, led by Merck KGaA, Darmstadt, Germany in collaboration with leading carer organizations around the world, seeks to increase awareness, discussion, and action about the often-overlooked needs of carers. At the one-year anniversary since the launch of the global movement, Embracing Carers™ has made tangible progress in building awareness and implementing practical solutions to support caregivers.

"Caregivers are a hidden pillar within the healthcare system," said Belén Garijo, Member of the Executive Board and CEO Healthcare at Merck KGaA, Darmstadt, Germany. "They are critical contributors to the health and wellbeing of patients, which very often affects the carer's health as well as financial, personal and professional development. We at Merck KGaA, Darmstadt, Germany are committed to support the needs of caregivers and to help raise awareness of their role as a global health priority."

Increasing Global Awareness

- Working with leading advocacy organizations and stakeholders, Embracing Carers™ has launched in Brazil. An in-country survey showed that despite unpaid caregivers feeling supported by family and finding their role rewarding, their role impacts their own physical and mental health.
- Embracing Carers™ will also undertake a dedicated roundtable meeting with health, advocacy and academic leaders in Shanghai, China. The discussion will explore the opportunities to support caregivers within China, and how Embracing Carers™ along with its national and international advisors can increase support and recognition of the crucial role that caregivers play in the country.
- To help the many thousands of un-identified caregivers around the world, Embracing Carers™ is launching an international social media campaign via Facebook that aims to tell carer stories to help individuals who are yet to identify as a carer to reflect on their own daily lives.

Engaging Healthcare Systems and Activating Policy

With support from Embracing Carers™, the International Alliance of Carer Organizations (IACO) will publish a Global State of Care Report, which has been developed to provide a global assessment of unpaid carer needs and best practices across Australia, Canada, France, Germany, India, Italy, Spain, United Kingdom and the United States. The report will be launched at the International Forum on Care and Caregiving in Toronto, Canada on November 22, 2018.

"Recognition and support of caregivers is a global priority. Since its launch, Embracing Carers™ has made positive steps to bring visibility and advance actions for caregivers, said Nadine Henningsen, IACO Board Chair. "IACO, along with the other strategic advisors, will continue to guide Embracing Carers™ and leverage advocacy resources, such as the Global State of Care report, to continue building on this momentum."

Broadening Stakeholder Engagement to Foster Best Practice

IACO, with the support of Embracing Carers™, is developing a series of Innovative Carer Practices (ICPs) that will showcase evidence-informed practices that enhance the quality and effectivenesss of integrated care for caregivers to identify, spread and scale promising practices for caregivers. ICPs from France, Ireland, Taiwan, and the United Kingdom will be showcased across the world throughout 2018 and 2019.

Embracing Carers™ has provided support to leading patient organizations who are leading efforts targeted to patients and caregivers globally.

Embracing Carers™ is a global movement led by Merck KGaA, Darmstadt, Germany in collaboration with leading carer organizations around the world to increase awareness and discussion about the often-overlooked needs of caregivers. The initiative plays a major role in raising awareness about the importance of caregivers as a global health priority. For more information on Embracing Carers™, visit our website at www.embracingcarers.com

Launched in 2017, Embracing Carers™ is a global initiative led by Merck KGaA, Darmstadt, Germany in collaboration with leading carer organizations around the world to increase awareness and discussion about the often-overlooked needs of caregivers. The Embracing Carers™ global advisors include Caregiver Action Network, Carers Australia, Carers Canada, Carers UK, Carers Worldwide, Eurocarers, National Alliance for Caregiving, International Alliance of Carer Organizations (IACO) and Shanghai Roots & Shoots, China.

About EMD Serono, Inc.

EMD Serono - the biopharmaceutical business of Merck KGaA, Darmstadt, Germany, in the U.S. and Canada – is engaged in the discovery, research and development of medicines for patients with difficult to treat diseases. The business is committed to transforming lives by developing and delivering meaningful solutions that help address the therapeutic and support needs of individual patients. Building on a proven legacy and deep expertise in neurology, fertility and endocrinology, EMD Serono is developing potential new oncology and immuno-oncology medicines while continuing to explore potential therapeutic options for diseases such as psoriasis, lupus and multiple sclerosis. Today, the business has approximately 1,300 employees around the country with commercial, clinical and research operations based in the company's home state of Massachusetts. www.emdserono.com

About Merck KGaA, Darmstadt, Germany

Merck KGaA, Darmstadt, Germany, is a leading science and technology company in healthcare, life science and performance materials. Around 50,000 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 2016, Merck KGaA, Darmstadt, Germany, generated sales of € 15.0 billion in 66 countries.

Founded in 1668, Merck KGaA, Darmstadt, Germany, is the world's oldest pharmaceutical and chemical company. The founding family remains the majority owner of the publicly listed corporate group. 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 company operates as EMD Serono, MilliporeSigma and EMD Performance Materials.

About the International Alliance of Carer Organizations (IACO)

Incorporated in 2012, the International Alliance of Carer Organizations (IACO) serves as an

education regarding family carers on a global scale. By bringing visibility and an understanding of the growing numbers of carers worldwide, IACO facilities international collaboration by bringing together countries from around the globe that advocate for family carers.

For further information: Lisa Buffington 1 781 681 2340

conditions as set out in our Legal Statement and Privacy Policy.

This site contains information that is intended for US residents only. Canadian residents should consult the EMD Inc. website at www.emdserono.ca for information on products and services approved in Canada.

SITEMAP

LEGAL STATEMENT

PRIVACY POLICY

CONTACT US

EMD Serono and American Cancer Society Collaborate to Support Needs of Cancer Caregivers

ROCKLAND, Mass., Nov. 7, 2018 /PRNewswire/ -- Embracing Carers™, the global initiative designed to increase awareness, discussion, and action about the often-overlooked needs of caregivers, joined the American Cancer Society today to announce a collaboration that will support unpaid family caregivers who care for patients with cancer. Embracing Carers™ is an initiative of Merck KGaA, Darmstadt, Germany, which operates its biopharmaceutical business as EMD Serono in the US and Canada.

The collaboration will focus on two critical areas of need for cancer patient caregivers: the increasing responsibilities in managing medical-related tasks at home and the need for self-care to prevent burnout, depression, and isolation. Caregivers typically do not receive instruction or support for these topics, instead developing critical skills through trial and error. Caregivers also generally experience higher rates of clinical depression, premature aging, and chronic health conditions than the non-caregiving population, demonstrating the impact that the stresses associated with caregiving can have.

care, port care, maintaining sterility in bandage care, identifying signs of infection, managing pain and other treatment side effects, and medication management.

The video series will also provide advice on self-care and communication, including coping and stress management (anxiety, depression, fear of recurrence, anger), communication skills (how to ask for help, speaking with health professionals), intentional exercise, nutritious meal preparation, deep breathing and meditation, and seeking respite care.

"Across the world, countless caregivers care for loved ones with cancer every day and in every country," said Rachel Cannady, Strategic Director of Cancer Caregiver Support at the American Cancer Society. "In many situations, they do not know who to turn to – or are even aware that there are resources out there to help them. Aside from the patients themselves, their caregivers are often the only people who know everything that is going on with the patient. They link with the physician and health care team, coordinate the patient's care, and serve as the primary communicator to family, friends, and medical staff, all while trying to help their loved one live as normal a life as possible."

"Once the patient returns home from surgery or recurrent treatments, their caregivers perform at-home, medical-related tasks that they aren't trained or prepared for," Cannady continued. "This new partnership with Embracing Carers™ is a practical way to give caregivers new skills that will benefit the patient and themselves, enhancing the ability of the caregiver and the overall care of cancer patients."

"What we have seen is that the experience of caregiving is a universal one, but the specific skills that caregivers need can vary widely by illness," said Joe Horvat, Senior Vice President, Oncology for EMD Serono. "The American Cancer Society estimates that there will be more than 1.7 million new cancer cases this year alone, which means millions of affected caregivers. We hope that the video series that we are unveiling today will make a difference in the lives of those who care for people living with cancer."

"We see caregiving as one of the most substantial – and yet largely unaddressed – public health issues of our time," Horvat continued. "Caregivers are the lynchpin of the health care system, and we want to shine a light on their roles, their needs, and the fact that there is help and support out there for them. We do this by collaborating with organizations that support caregiver initiatives, driving greater visibility and awareness of caregiver challenges, supporting

The development of this video package fills a deep gap. Consultation on the video content was provided by leading experts in the field of caregiving and employees of the American Cancer Society. To watch and share the video series please visit: www.cancer.org/caregivervideos.

About Embracing Carers™

Embracing Carers™ is a global initiative led by Merck KGaA, Darmstadt, Germany, operating as EMD Serono, EMD Millipore, and EMD Performance Materials in the United States and Canada. It is a collaboration with leading caregiver organizations around the world designed to increase awareness, discussion, and action about the often-overlooked needs of caregivers. Given that caregivers need support and often do not know where to turn for help, Embracing Carers™ was created to fill that void.

About EMD Serono, Inc.

EMD Serono - the biopharmaceutical business of Merck KGaA, Darmstadt, Germany, in the U.S. and Canada – is engaged in the discovery, research and development of medicines for patients with difficult to treat diseases. The business is committed to transforming lives by developing and delivering meaningful solutions that help address the therapeutic and support needs of individual patients. Building on a proven legacy and deep expertise in neurology, fertility and endocrinology, EMD Serono is developing potential new oncology and immuno-oncology medicines while continuing to explore potential therapeutic options for diseases such as psoriasis, lupus and multiple sclerosis. Today, the business has approximately 1,300 employees around the country with commercial, clinical and research operations based in the company's home state of Massachusetts. www.emdserono.com

Your Contact

Lisa Buffington 1 781 681 2340

SOURCE EMD Serono

COMPANY

LEADERSHIP TEAM

PARTNERING

PRESS

CONTACT US

COMPLIANCE & TRANSPARENCY

THERAPEUTIC AREAS

YOUR REQUESTS

FDA Accepts File for Cladribine Tablets as Potential Treatment for Relapsing Forms of Multiple Sclerosis

ROCKLAND, Mass., July 30, 2018 /PRNewswire/ --

Cladribine tablets is an investigational oral therapy with proposed dosing of a maximum of 20 days over two years with no additional dosing required in years 3 and 4

The New Drug Application includes close to 12,000 patient years of data and up to 10 years of safety data in some patients

Cladribine tablets is approved as MAVENCLAD® in 38 countries

cladribine tablets as a potential treatment for patients with relapsing forms of multiple sclerosis (MS) has been accepted for filing by the U.S. Food and Drug Administration (FDA).

"We are delighted the FDA has accepted cladribine tablets for filing," said Belén Garijo, Member of the Executive Board and CEO Healthcare of Merck KGaA, Darmstadt, Germany. "Our goal is to offer cladribine tablets to patients and physicians in the U.S. as a new treatment paradigm for relapsing MS, and we look forward to working closely with the FDA throughout the review process."

The acceptance indicates that the FDA has found the Company's resubmission sufficiently complete to permit a substantive review. The resubmission is in response to the Complete Response Letter issued by the FDA in 2011 requesting an improved understanding of safety risks and the overall benefit-risk profile.

The NDA acceptance follows global approvals of cladribine tablets under the trade name MAVENCLAD® in 38 countries since August 2017, including the European Union (EU), Canada, Australia, Israel, Argentina, United Arab Emirates, Chile and Lebanon. Additional filings in other countries are planned for 2018.

Cladribine tablets is an investigational agent that has been studied as a short-course (a maximum of 20 days of treatment over two years) oral therapy that is thought to selectively target lymphocytes, which may be integral to the pathological process of relapsing MS.

"Most available MS therapies require continued, regular dosing of medication. A treatment approach consisting of short, infrequent oral treatment cycles may help lower the treatment burden for patients," said Thomas Leist, M.D., PhD, Director, Comprehensive Multiple Sclerosis Center at Jefferson University Hospitals. "Based on additional clinical research in recent years, we know more about the treatment course, safety, and impact of cladribine tablets across several key measures of MS, and hope it will be made available to the U.S. MS community."

The NDA acceptance includes close to 12,000 patient years of data with over 2,700 patients included in the clinical trial program, and up to 10 years of safety data in some patients. The clinical development program included data from three Phase III trials, CLARITY, CLARITY EXT and ORACLE MS, the Phase II ONWARD study and long-term follow-up data from the eight-year prospective registry, PREMIERE.

About Cladribine Tablets

Cladribine tablets is an investigational short-course oral therapy that is thought to selectively target lymphocytes which may be integral to the pathological process of relapsing MS (RMS). Cladribine tablets is currently under clinical investigation and not approved for the treatment for any use in the United States. MAVENCLAD® has received approvals for patients with highly active RMS as defined by clinical or imaging features in the European Union (EU), Israel, Argentina, United Arab Emirates, Chile and Lebanon. In December 2017, Health Canada and the Therapeutic Goods Administration (TGA) in Australia approved MAVENCLAD® for the treatment of relapsing-remitting MS (RRMS).

The clinical development program for cladribine tablets includes:

- The CLARITY (Cladribine Tablets Treating MS Orally) study: a two-year Phase III placebo-controlled study designed to evaluate the efficacy and safety of cladribine tablets as a monotherapy in patients with RRMS.
- The CLARITY extension study: a Phase III placebo-controlled study following on from the CLARITY study, which evaluated the safety and efficacy of cladribine tablets over two additional years beyond the two-year CLARITY study, according to the treatment assignment scheme for years 3 and 4.
- The ORACLE MS (Oral Cladribine in Early MS) study: a two-year Phase III placebo-controlled study designed to evaluate the efficacy and safety of cladribine tablets as a monotherapy in patients at risk of developing MS (patients who have experienced a first clinical event suggestive of MS).
- The ONWARD (Oral Cladribine Added ON to Interferon beta-1a in Patients With Active Relapsing Disease) study: a Phase II placebo-controlled study designed primarily to evaluate the safety and tolerability of adding cladribine tablets treatment to patients with

- PREMIERE (Prospective Observational Long-term Safety Registry of Multiple Sclerosis) study: a long-term follow-up safety registry of multiple sclerosis patients who participated in cladribine tablets clinical studies.

The clinical development program of cladribine tablets in MS comprises close to 12,000 patient years of data with over 2,700 patients included in the clinical trial program, and up to 10 years of follow-up in some patients.

In the two-year CLARITY study, the most commonly reported adverse event (AE) in patients treated with cladribine tablets was lymphopenia. The incidence of infections was 48.3% with cladribine tablets and 42.5% with placebo, with 99.1% and 99.0% respectively rated mild-to-moderate by investigators.

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.

EMD Serono, Inc. and Multiple Sclerosis

For more than 20 years, EMD Serono has been relentlessly focused on understanding the journey people living with MS face in order to create a meaningful, positive experience for them and the broader MS community. However, there is still much that is unknown about this complex and unpredictable disease. EMD Serono is digging deeper to advance the science and reconstruct a new understanding of MS, inside and out. We are committed to delivering solutions that improve the lives of all those affected by MS. http://www.GetCloserToMS.com

About EMD Serono, Inc.

EMD Serono - the biopharmaceutical business of Merck KGaA, Darmstadt, Germany, in the U.S. and Canada - is engaged in the discovery, research and development of medicines for patients with difficult to treat diseases. The business is committed to transforming lives by developing and delivering meaningful solutions that help address the therapeutic and support needs of individual patients. Building on a proven legacy and deep expertise in neurology, fertility and

psoriasis, lupus and multiple sclerosis. Today, the business has approximately 1,300 employees around the country with commercial, clinical and research operations based in the company's home state of Massachusetts. http://www.emdserono.com

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 http://www.emdgroup.com/subscribe to register again for your online subscription of this service as our newly introduced geo-targeting requires new links in the email. You may later change your selection or discontinue this service.

EMD Serono is the biopharmaceutical business of Merck KGaA, Darmstadt, Germany. This site contains information that is intended for residents of the United States only and is not meant to substitute for the advice provided by a medical professional. Always consult a physician if you have health concerns. Use and access of this site is subject to the terms and conditions as set out in our Legal Statement and Privacy Policy.

This site contains information that is intended for US residents only. Canadian residents should consult the EMD Inc. website at www.emdserono.ca for information on products and services approved in Canada.

SITEMAP

LEGAL STATEMENT

PRIVACY POLICY

CONTACT US

Merck KGaA, Darmstadt, Germany data at ASCO 2018 to showcase progress and further optionality of oncology pipeline

Not intended for UK-based media

Two-year safety and efficacy data in mMCC for avelumab from pivotal JAVELIN Merkel 200 trial

Early clinical activity in advanced NSCLC and HPV-associated cancers for investigational bifunctional immunotherapy, M7824

Encouraging interim analysis of Phase II data in NSCLC sub- population for investigational c-Met inhibitor, tepotinib

Record number of abstracts accepted across oncology, immuno- oncology and DNA Damage Response (DDR)

e21620, e21544; **tepotinib (c-Met kinase inhibitor)**: 9082, 9016; **M6620 (ATR inhibitor)**: 2549, e21048; **M3814 (DNA-PK)**: 2518 **M7824 (TGF-ß trap/anti- PD-L1)**: 3007, 9017, 2566; **M2698 (dual p70S6k/Akt inhibitor)**: 2584

Darmstadt, Germany, May 16, 2018 – Merck KGaA, Darmstadt, Germany, a leading science and technology company which operates its biopharmaceutical business as EMD Serono in the US and Canada, today announced new data from a number of high priority clinical development programs across its oncology portfolio to be presented at this year's American Society of Clinical Oncology Annual Meeting (ASCO), June 1-5, 2018, Chicago IL. Abstracts representing seven therapeutic agents and eight tumor types will highlight the company's position as a key emerging player in oncology.

"This year's data at ASCO demonstrate the potential of our pipeline to really deliver transformative advancements in cancer care," said Luciano Rossetti, Executive Vice President, Head of Global Research & Development at the biopharma business of Merck KGaA, Darmstadt, Germany. "With our strong commitment and focus on the areas we believe in most, Merck KGaA, Darmstadt, Germany's oncology and immuno-oncology pipeline is demonstrating significant potential in the near term with our later-stage priority programs and, in parallel, our early pipeline includes truly innovative programs that could make a real difference for patients."

New data for avelumab (BAVENCIO®), which is being jointly developed and commercialized with Pfizer, include an oral presentation on two-year results from the pivotal JAVELIN Merkel 200 trial. These long-term results include data on avelumab's duration of response and represent the first study to report long-term survival data for an immunotherapy in metastatic Merkel cell carcinoma (mMCC).

The company will also present further evidence for M7824, an investigational TGF-ß trap/anti-PD-L1 bi-functional immunotherapy fusion protein, from expansion cohorts of the ongoing M7824 Phase I clinical trial (NCT02517398) program. TGF- β, a cytokine released by cells (including tumor cells), suppresses anti-tumor immune responses through a vast number of mechanisms leading to uninhibited tumor growth and metastasis. These data include results in patients with human papillomavirus (HPV)-associated cancers (presented in collaboration with the National Cancer Institute) and data in patients with advanced non-small cell lung cancer

of 40.7% (11/27) was observed in PD-L1+ patients (≥1%), and in patients with high PD-L1 expression (80%; Ab clone 73-10 [>80% = >50% with 22C3]), the ORR was 71.4% (5/7). These data signal the potential of M7824 and provide evidence that combining a transforming growth factor-β (TGF- β) trap with the anti-PD-L1 mechanism in one molecule may generate anti-tumor activity in these patient groups with significant medical need. Treatment with M7824 was well tolerated in both studies and safety data were consistent with that observed in the overall Phase I clinical program. No new safety signals were identified.

For tepotinib**, an investigational small molecule inhibitor of the c-Met receptor tyrosine kinase, new data to be presented include promising initial results from an ongoing Phase II VISION study providing further indication for the potential of tepotinib in patients living with advanced NSCLC harboring MET exon 14 skipping mutations. Alterations of the c-Met signaling pathway are found in various cancer types and correlate with aggressive tumor behavior and poor clinical prognosis. Based on investigator assessment of data from 15 patients in the study, 60% (9/15) had a confirmed partial response (PR) and 20% (3/15) had stable disease (SD.) In addition, independent assessment of 13 patients demonstrated treatment with tepotinib led to a confirmed PR in 46.2% (6/13) and SD in 7.7% (1/13) of patients. In this study, the safety data are consistent with that observed in previous studies and confirm that treatment with tepotinib is well tolerated; no new safety signals were identified.

Tepotinib is an important part of Merck KGaA, Darmstadt, Germany's strategic focus on precision medicines and these results reinforce the company's progress in delivering treatments to those patients more likely to benefit, in order to achieve the best possible outcomes. Both M7824 and tepotinib were discovered in-house at Merck KGaA, Darmstadt, Germany.

Further pipeline updates include Phase I dose escalation data for the investigational DNA-dependent protein kinase (DNA-PK) inhibitor M3814, Phase I triplet therapy with ATR-inhibitor, M6620 +veliparib+cisplatin in advanced solid tumors, and Phase I data for M2698, a potent and selective dual inhibitor of p70S6K and AKT1/3 in the PAM pathway (PI3K/AKT/mTOR pathway). The PAM pathway regulates cell survival and growth and this pathway often displays unusual activity in many human cancers.

Data for the legacy brand ERBITUX® continue to build on Merck KGaA, Darmstadt, Germany's heritage in oncology reinforcing its role as a standard of care in RAS wild-type metastatic colorectal cancer (mCRC), the standard of care in first-line recurrent or metastatic squamous

in full.

*Avelumab is under clinical investigation for treatment of NSCLC, metastatic urothelial carcinoma (mUC), and mesothelioma, and has not been demonstrated to be safe and effective for these indications. There is no guarantee that avelumab will be approved for NSCLC, mUC, or mesothelioma by any health authority worldwide.

**Tepotinib is the recommended International Nonproprietary Name (INN) for the c-Met kinase inhibitor (MSC2156119J). Tepotinib is currently under clinical investigation and not approved for any use anywhere in the world.
Tepotinib, M7824, M3814, M2698 and M6620 are under clinical investigation and have not been proven to be safe and effective. There is no guarantee any product will be approved in the sought-after indication by any health authority worldwide.

Notes to Editors
Accepted Merck KGaA, Darmstadt, Germany-supported key abstracts slated for presentation are listed below. In addition, a number of investigator-sponsored studies have been accepted (not listed).

Avelumab: Oral Presentations

Title: Two-year efficacy and safety update from JAVELIN Merkel 200 part A: A registrational study of avelumab in metastatic Merkel cell carcinoma progressed on chemotherapy.
Lead Author: Paul Nghiem, MD, PhD
Abstract #: 9507
Presentation Date / Time (CDT): Mon, Jun 04, 10:12 AM - 10:24 AM
Location: Arie Crown Theater

Title: Avelumab (anti–PD-L1) in combination with crizotinib or lorlatinib in patients with previously treated advanced NSCLC: Phase 1b results from JAVELIN Lung 101.
Lead Author: Alice Tsang Shaw, MD, PhD
Abstract #: 9008

Avelumab: Poster Sessions

Title: Avelumab (anti–PD-L1) in patients with platinum-treated advanced NSCLC: 2.5- year follow-up from the JAVELIN Solid Tumor trial.
Lead Author: Arun Rajan, MD
Abstract #: 9090
Presentation Date / Time (CDT): Sun, Jun 03, 8:00 AM - 11:30 AM
Location: Hall A

Title: Phase 1b study of avelumab in advanced previously treated mesothelioma: long- term follow-up from JAVELIN Solid Tumor.
Lead Author: Raffit Hassan, MD
Abstract #: 8563
Presentation Date / Time (CDT): Sun, Jun 03, 8:00 AM - 11:30 AM
Location: Hall A

Title: Second-line avelumab treatment of patients (pts) with metastatic Merkel cell carcinoma (mMCC): Experience from a global expanded access program (EAP).
Lead Author: John WT Walker, MD, PhD
Abstract #: 9537
Presentation Date / Time (CDT): Mon, Jun 04, 1:15 PM - 4:45 PM
Location: Hall A

Title: Association of efficacy and adverse events of special interest of avelumab in the JAVELIN solid tumor and JAVELIN Merkel 200 trials.
Lead Author: Karen Kelly, MD, FASCO
Abstract #: 3057
Presentation Date / Time (CDT): Mon, Jun 04, 8:00 AM - 11:30 AM
Location: Hall A

Title: SPEAR-bladder (study informing treatment pathway decision in bladder cancer): First- through third-line time to treatment failure in the US.
Lead Author: Gurjyot K. Doshi, MD
Abstract #: 4544

Avelumab: Publications

Title: Avelumab in patients with previously treated metastatic melanoma: phase 1b results from the JAVELIN Solid Tumor trial
Lead Author: Keilholz U, Mehnert J, Bauer S, et al.
Abstract #: e21531

Title: Characteristics, treatment patterns and safety events From 4 cohorts of advanced or metastatic cancer patients based on healthcare claims data
Lead Author: Russo L, Esposito D, Lamy FX, et al.
Abstract #: e13603

Title: Healthcare resource use and expenditures among patients with Merkel cell carcinoma by level of comorbidity
Lead Author: Kearney M, Thokagevistk K, Boutmy E, et al.
Abstract #: e18932

Title: Projecting long-term survival for avelumab in patients with refractory Merkel cell carcinoma
Lead Author: Phatak H, Proskorovsky I, Lanitis T, et al.
Abstract #: e21623

Title: Predicting overall survival in patients (Pts) with treatment-naive metastatic Merkel cell carcinoma (mMCC) treated with avelumab
Lead Author: Bullement A, D'Angelo SP, Amin A, et al.
Abstract #: e21620

Title: A novel, open-access data commons for improved disease management in Merkel cell carcinoma patients
Lead Author: Murphy M, Sartor O, Bertagnolli M, et al.
Abstract #: e21544

M7824 (TGF β-trap/anti-PD-L1): Oral Presentation

Lead Author: Julius Strauss, MD
Abstract #: 3007
Presentation Date / Time (CDT): Sat, Jun 02, 5:12 PM - 5:24 PM
Location: Hall B1

M7824 (TGF β-trap/anti-PD-L1): Poster Discussion

Title: Results from a second- line (2L) NSCLC cohort treated with M7824 (MSB0011359C), a bifunctional fusion protein targeting TGF-β and PD-L1.
Lead Author: Luis G. Paz- Ares, MD, PhD
Abstract #: 9017
Presentation Date / Time (CDT): Sun, Jun 03, 11:30 AM - 12: 45 PM
Location: Arie Crown Theatre

M7824 (TGF β-trap/anti-PD-L1): Poster Session

Title: Selection of the recommended phase 2 dose (RP2D) for M7824 (MSB0011359C), a bifunctional fusion protein targeting TGF-β and PD-L1.
Lead Author: Yulia Vugmeyster, PhD
Abstract #: 2566
Presentation Date / Time (CDT): Mon, Jun 04, 8:00 AM - 11:30 AM
Location: Hall A

Tepotinib: Poster Discussion

Title: Tepotinib in patients with advanced non-small cell lung cancer (NSCLC) harboring MET exon 14- skipping mutations: Phase II trial.
Lead Author: Enriqueta Felip, MD
Abstract #: 9016
Presentation Date / Time (CDT): Sun, Jun 03, 11:30 AM - 12:45 PM
Location: Arie Crown Theater

Tepotinib: Poster Session

Title: Can duration of response be used as a surrogate endpoint for overall survival in advanced non-small cell lung cancer?

Presentation Date / Time (CDT): Sun, Jun 03, 8:00 AM - 11:30 AM
Location: Hall A

M2698: Poster Session

Title: Precision oncology: Results of a phase I study of M2698, a p70S6K/AKT targeted agent in patients with advanced cancer and tumor PI3K/AKT/mTOR (PAM) pathway abnormalities.
Lead Author: Apostolia Maria Tsimberidou, MD, PhD
Abstract #: 2584
Presentation Date / Time (CDT): Mon, Jun 04, 8:00 AM - 11:30 AM
Location: Hall A

M3814: Poster Discussion

Title: A phase Ia/Ib trial of the DNA-PK inhibitor M3814 in combination with radiotherapy (RT) in patients (pts) with advanced solid tumors: Dose-escalation results.
Lead Author: Baukelien Van Triest, MD, PhD
Abstract #: 2518
Presentation Date / Time (CDT): Mon, Jun 04, 3:00 PM - 4:15 PM
Location: S406

M6620: Poster Discussion

Title: Phase I trial of the triplet M6620 (formerly VX970) + veliparib + cisplatin in patients with advanced solid tumors.
Lead Author: Geraldine Helen O'Sullivan Coyne, MD, PhD
Abstract #: 2549
Presentation Date / Time (CDT): Mon, Jun 04, 8:00 AM - 11:30 AM
Location: Hall A

M6620: Publication

Title: Safety and tolerability of intravenous M6620 (VX- 970) administered with gemcitabine in subjects with advanced non-small cell lung cancer (NSCLC)
Lead Author: Plummer R, Cook N, Arkenau H-T, et al.
Abstract #: e21048

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 again for your online subscription of this service as our newly introduced geo-targeting requires new links in the email. You may later change your selection or discontinue this service.

About Avelumab

Avelumab is a human anti-programmed death ligand-1 (PD-L1) antibody. Avelumab has been shown in preclinical models to engage both the adaptive and innate immune functions. By blocking the interaction of PD-L1 with PD-1 receptors, avelumab has been shown to release the suppression of the T cell-mediated antitumor immune response in preclinical models. Avelumab has also been shown to induce NK cell-mediated direct tumor cell lysis via antibody-dependent cell- mediated cytotoxicity (ADCC) in vitro. In November 2014, Merck KGaA, Darmstadt, Germany, and Pfizer announced a strategic alliance to co-develop and co- commercialize avelumab.

Approved Indications in the US

The FDA granted accelerated approval for avelumab (BAVENCIO®) for the treatment of (i) adults and pediatric patients 12 years and older with metastatic Merkel cell carcinoma (mMCC) and (ii) patients with locally advanced or metastatic urothelial carcinoma (mUC) who have disease progression during or following platinum- containing chemotherapy, or have disease progression within 12months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy. These indications are approved under accelerated approval based on tumor response rate and duration of response. Continued approval for these indications may be contingent upon verification and description of clinical benefit in confirmatory trials.

Important Safety Information from the US FDA Approved Label

The warnings and precautions for BAVENCIO include immune-mediated adverse reactions (such as pneumonitis, hepatitis, colitis, endocrinopathies, nephritis and renal dysfunction, and other adverse reactions), infusion-related reactions and embryo-fetal toxicity.

musculoskeletal pain, diarrhea, nausea, infusion-related reaction, peripheral edema, decreased appetite/hypophagia, urinary tract infection and rash.

About Erbitux® (cetuximab)

Erbitux® is a highly active IgG1 monoclonal antibody targeting the epidermal growth factor receptor (EGFR). As a monoclonal antibody, the mode of action of Erbitux is distinct from standard non-selective chemotherapy treatments in that it specifically targets and binds to the EGFR. This binding inhibits the activation of the receptor and the subsequent signal-transduction pathway, which results in reducing both the invasion of normal tissues by tumor cells and the spread of tumors to new sites. It is also believed to inhibit the ability of tumor cells to repair the damage caused by chemotherapy and radiotherapy and to inhibit the formation of new blood vessels inside tumors, which appears to lead to an overall suppression of tumor growth. Erbitux also targets cytotoxic immune effector cells towards EGFR expressing tumor cells (antibody dependent cell-mediated cytotoxicity, ADCC).

The most commonly reported side effect with Erbitux is an acne-like skin rash. In approximately 5% of patients, hypersensitivity reactions may occur during treatment with Erbitux; about half of these reactions are severe.

Erbitux has already obtained market authorization in over 100 countries world-wide for the treatment of RAS wild-type metastatic colorectal cancer and for the treatment of squamous cell carcinoma of the head and neck (SCCHN). Merck KGaA, Darmstadt, Germany licensed the right to market Erbitux, a registered trademark of ImClone LLC, outside the U.S. and Canada from ImClone LLC, a wholly-owned subsidiary of Eli Lilly and Company, in 1998.

About M3814

M3814 is an investigational small-molecule which is thought to inhibit DNA-dependent protein kinase (DNA-PK). DNA-PK is a key enzyme for non-homologous end-joining (NHEJ), an important DNA double strand break (DSB) repair pathway. Clinical studies investigating combinations of M3814 with other commonly used DNA-damaging agents such as radiotherapy and chemotherapy are underway.

About M7824

M7824 is an investigational bifunctional immunotherapy that is designed to bring together a TGF-β trap and 'fuse' it with the anti-PD-L1 mechanism. M7824 is designed to simultaneously block the two immunosuppressive pathways – targeting both pathways aims to control tumor

About M2698

M2698 is an investigational small-molecule which is thought to inhibit p70S6K and Akt. Both targets are part of the PI3K/AKT/mTOR (PAM)pathway, which is often dysregulated in solid tumors.

About tepotinib

Tepotinib (MSC2156119J) is an investigational small-molecule inhibitor of the c-Met receptor tyrosine kinase. Alterations of the c-Met signaling pathway are found in various cancer types and it is thought to correlate with aggressive tumor behavior and poor clinical prognosis.

About M6620

M6620 (previously known as VX-970) is an investigational small-molecule thought to inhibit ataxia telangiectasia and Rad3-related protein (ATR). ATR is believed to be a key sensor for DNA damage, activating the DNA damage checkpoint and leading to cell cycle arrest. Inhibition of ATR could potentially enhance the efficacy of DNA-damaging agents, but is also being investigated as a monotherapy against tumors with high levels of replication stress induced by overexpression of oncogenes.

About Merck KGaA, Darmstadt, Germany

Merck KGaA, Darmstadt, Germany, is a leading science and technology company in healthcare, life science and performance materials. Almost 53,000 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 2017, Merck KGaA, Darmstadt, Germany, generated sales of € 15.3 billion in 66 countries.

Founded in 1668, Merck KGaA, Darmstadt, Germany, is the world's oldest pharmaceutical and chemical company. The founding family remains the majority owner of the publicly listed corporate group. 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 company operates as EMD Serono, MilliporeSigma and EMD Performance Materials.

For further information: Gangolf Schrimpf +49 6151 72 9591 Investor Relations +49 6151 72 3321

COMPANY

LEADERSHIP TEAM

PARTNERING

PRESS

CONTACT US

COMPLIANCE & TRANSPARENCY

THERAPEUTIC AREAS

YOUR REQUESTS

SITEMAP

LEGAL STATEMENT

PRIVACY POLICY

Merck KGaA, Darmstadt, Germany Presents Update on Tepotinib in Advanced Lung Cancer at ASCO 2018

Not intended for UK-based media

Data from an ongoing Phase II tepotinib study show anti-tumor clinical activity in patients with advanced non-small cell lung cancer harboring MET exon 14 skipping mutations

Patients with advanced lung cancer harboring MET exon 14 mutations currently have a poor prognosis and limited treatment options

Safety data are consistent with data previously reported, with no new safety signals identified

9017, 2566; **M2698 (dual p70S6k/Akt inhibitor):** 2584**; M6620 (ATR inhibitor):** 2549**; M3814 (DNA-PK):** 2518

Darmstadt, Germany, June 3, 2018 – Merck KGaA, Darmstadt, Germany, a leading science and technology company which operates its healthcare business in the U.S. and Canada as EMD Serono, today announced that the investigational, targeted therapy tepotinib* has shown clinical activity in an ongoing Phase II study of patients with advanced non-small cell lung cancer (NSCLC) harboring MET exon 14 skipping mutations. Data from the VISION trial will be presented during the American Society of Clinical Oncology (ASCO) 2018 Annual Meeting in Chicago, June 1-5, 2018.

"Patients living with advanced non-small cell lung cancer harboring MET exon 14 skipping mutations have limited treatment options available to them and typically face poor clinical outcomes," said investigator Enriqueta Felip, M.D., Medical Oncologist, Vall d'Hebron Institute of Oncology (VHIO). "More than half of the patients in the Phase II VISION study had an investigator-assessed confirmed response, demonstrating the potential of tepotinib and the need to further evaluate this precision medicine option."

Initial data from the Phase II VISION study of tepotinib in patients living with advanced NSCLC harboring MET exon 14 skipping mutations will be presented today at ASCO during the "Lung Cancer—Non-Small Cell Metastatic" poster discussion session, 11:30 a.m. – 12:45 p.m. CDT. Treatment with tepotinib led to a confirmed complete response (CR) or confirmed partial response (PR) in 53.6% (15/28) and stable disease (SD) in 17.9% (5/28) of patients based on investigator assessment. Based on independent assessment of updated data from 28 patients (patients with at least 2 post-baseline assessments or who discontinued for any reason), 42.9% (12/28) had a PR and 21.4% (6/28) had SD.

In this ongoing study, the safety data are consistent with that observed in previous studies; no new safety signals have been identified to date. A total of 26 out of 38 patients with data available experienced treatment-related adverse events (TRAEs), most commonly Grade 1/2 peripheral edema (13 patients) and diarrhea (10 patients). Seven patients reported Grade 3 TRAEs, including asymptomatic amylase increase (2 patients) and one instance each of: asthenia, generalized edema, aspartate aminotransferase increase, gamma-glutamyl

dizziness, and interstitial lung disease. The VISION study is continuing to enroll patients harboring MET exon 14 skipping mutations from Europe, United States and Japan.

"These data support our plans to continue with the clinical development of tepotinib in this particularly aggressive, advanced lung cancer. Patients with this form of nonsmall cell lung cancer currently have a poor prognosis and limited treatment options," said Luciano Rossetti, M.D., Executive Vice President, Global Head of Research & Development at the biopharma business of Merck KGaA, Darmstadt, Germany. "Tepotinib is an important late-stage investigational therapy and a key part of our strategic focus on innovative precision medicines."

Tepotinib, discovered in-house at Merck KGaA, Darmstadt, Germany, is an investigational inhibitor of the c-Met receptor tyrosine kinase. Alterations of the c-Met signaling pathway are found in various cancer types and correlate with aggressive tumor behavior and poor clinical prognosis. Tepotinib has been designed with the potential to improve outcomes in aggressive tumors that have a poor prognosis and harbor these specific mutations. In March, the Japanese Ministry of Health, Labour and Welfare granted SAKIGAKE 'fast-track' designation to tepotinib in patients with NSCLC harboring MET exon 14 skipping mutations.

Tepotinib Poster Session

Title: Can duration of response be used as a surrogate endpoint for overall survival in advanced nonsmall cell lung cancer?
Lead Author: Boris M Pfeiffer
Abstract #: 9082
Presentation Date / Time (CDT): Sun, Jun 03, 8:00 a.m. - 11:30 a.m.
Location: Hall A

Tepotinib Poster Discussion

Title: Tepotinib in patients with advanced nonsmall cell lung cancer (NSCLC) harboring MET exon 14-skipping mutations: Phase II trial.
Lead Author: Enriqueta Felip, M.D.
Abstract #: 9016
Presentation Date / Time (CDT): Sun, Jun 03, 11:30 a.m. - 12:45 p.m.
Location: Arie Crown Theater

immunotherapy M7824 and updates from its DNA Damage Response portfolio. Merck KGaA, Darmstadt, Germany, is committed to exploring an array of targets and taking creative scientific approaches to developing novel therapies for hard-to-treat cancers.

*Tepotinib is the recommended International Nonproprietary Name (INN) for the c-Met kinase inhibitor (MSC 2156119J). Tepotinib is currently under clinical investigation and not approved for any use anywhere in the world.

About Non-Small Cell Lung Cancer

Globally, lung cancer is the most common cause of cancer-related deaths in men and the second most common in women,[1] responsible for more deaths than colon, breast and prostate cancer combined.[2] NSCLC is the most common type of lung cancer, accounting for 80 to 85% of all lung cancers.[3] MET exon 14 skipping mutations occur in 3-4% of lung cancers.[5,6] The five-year survival rate for people diagnosed with lung cancer that has spread (metastasized) to other areas of the body is 1%.[4]

About Tepotinib

Tepotinib is an investigational, small-molecule inhibitor of the c-Met receptor tyrosine kinase discovered in-house at Merck KGaA, Darmstadt, Germany. Alterations of the c-Met signaling pathway are found in various cancer types and correlate with aggressive tumor behavior and poor clinical prognosis. Tepotinib is currently being investigated in a Phase II study in NSCLC.

About SAKIGAKE

SAKIGAKE designation is granted by the Japanese Ministry of Health, Labour and Welfare, promoting research and development in Japan and aiming at early practical application for innovative pharmaceutical products, medical devices and regenerative medicines. SAKIGAKE designation can reduce a drug's review period down from 12 months to a target of 6 months. The system's objective is to designate drugs that have the potential of prominent effectiveness against serious and life-threatening diseases in order to make them available to patients in Japan ahead of the rest of the world.

About Merck KGaA, Darmstadt, Germany

Merck KGaA, Darmstadt, Germany, is a leading science and technology company in healthcare, lifescience and performance materials. Almost 53,000 employees work to further develop

crystals for smartphones and LCD televisions. In 2017, Merck KGaA, Darmstadt, Germany, generated sales of € 15.3 billion in 66 countries.

Founded in 1668, Merck KGaA, Darmstadt, Germany, is the world's oldest pharmaceutical and chemical company. The founding family remains the majority owner of the publicly listed corporate group. 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 company operates as EMD Serono, MilliporeSigma and EMD Performance Materials.

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 again for your online subscription of this service as our newly introduced geo-targeting requires new links in the email. You may later change your selection or discontinue this service.

References

1. American Cancer Society (2015) Global facts & figures third edition. Available from: www.cancer.org/acs/groups/content/@research/documents/document/acspc-044738.pdf. Accessed February 2018

2. American Cancer Society (2017) Key statistics for lung cancer. Available from: https://www.cancer.org/cancer/non-small-cell-lung-cancer/about/key-statistics.html. Accessed February 2018.

3. American Cancer Society (2016) What is non-small cell lung cancer? Available from: https://www.cancer.org/cancer/non-small-cell-lung-cancer/about/what-is-non-small-cell-lungcancer.html. Accessed February 2018.

4. Cancer.net. Lung cancer – non-small cell: statistics. Available from: http://www.cancer.net/cancer-types/lung-cancer-non-small-cell/statistics. Accessed February 2018.

5. Lutterbach B et al. Lung cancer cell lines harboring MET gene amplification are dependent on Met for growth and survival. Cancer Res. (2007) 67(5):2081-8.

For further information: Brenda Mulligan: +1 978 821 5345

COMPANY

LEADERSHIP TEAM

PARTNERING

PRESS

CONTACT US

COMPLIANCE & TRANSPARENCY

THERAPEUTIC AREAS

YOUR REQUESTS

Merck KGaA, Darmstadt, Germany Presents Updated Clinical Results for Bifunctional Immunotherapy M7824 at ASCO 2018

ASCO Abstract #

M7824 (TGF-ß trap/anti-PD-L1): 3007, 9017, 2566, **TPS3130; Tepotinib (c-Met kinase inhibitor)**: 9082, 9016; **M2698 (dual p70S6k/Akt inhibitor)**: 2584; **M6620 (ATR inhibitor)**: 2549; **M3814 (DNA-PK)**: 2518

M7824 is an investigational immunotherapy that is designed to bring together both anti-transforming growth factor-β and anti-PD-L1 mechanisms

Data to be presented at ASCO 2018 show M7824's anti-tumor activity in patients with advanced non-small cell lung cancer and advanced human papillomavirus associated cancers

Merck KGaA, Darmstadt, Germany, a leading science and technology company which operates its healthcare business in the U.S. and Canada as EMD Serono, today announced results from expansion cohorts of the ongoing M7824 Phase I clinical trial (NCT02517398) program at the American Society of Clinical Oncology (ASCO) 2018 Annual Meeting in Chicago, June 1–5, 2018. These data include results in patients with advanced non-small cell lung cancer (NSCLC) and in human papillomavirus (HPV) associated cancers (NCT03427411), presented in collaboration with the National Cancer Institute (NCI), providing further evidence that bringing together a transforming growth factor-β (TGF-β) trap with the anti-PD-L1 mechanism may generate clinically relevant anti-tumor activity.

"M7824's dual approach to fighting cancer, which brings together a TGF-β trap with the anti-PD-L1 mechanism, complements our existing immuno-oncology portfolio," said Luciano Rossetti, M.D., Global Head of Research & Development at the biopharma business of Merck KGaA, Darmstadt, Germany. "The unique design of this fusion protein offers the potential to optimally engage the TGF-β pathway. This is one example of the creative approaches we are taking to address challenging cancers where we believe we can deliver a transformational change for patients."

In patients with second line (no prior immunotherapy) advanced NSCLC from the cohort of the ongoing Phase I clinical trial (NCT02517398), signs of clinical activity were seen across PD-L1 expression levels. At the recommended Phase II dose (1200 mg every 2 weeks), an investigator-assessed confirmed overall response rate (ORR) of 40.7% (11/27 patients) was observed in patients with PD-L1+ tumors (≥1%, Ab clone 73-10). In patients with high PD-L1+ expressing tumors (≥80%; Ab clone 73-10 [≥80% as measured with Ab clone 73-10 comparable with tumor proportion score (TPS) ≥50% with 22C3]), ORR was 71.4% (5/7 patients). A median progression-free survival (PFS) of 6.8 months was observed for PD-L1+ patients (1200 mg every 2 weeks) and the median PFS was not reached for the high PD-L1-expressing population owing to the number of patients still responding at the time of analysis. Safety data in this study were consistent with those observed in the overall M7824 Phase I clinical program. The most common treatment-related adverse events (TRAEs) were pruritus (20.0%), maculopapular rash (18.8%) and decreased appetite (12.5%). Grade 3 TRAEs were experienced by 21 patients (26.3%), Grade 4 TRAEs occurred in 2 patients (2.5%). The most

From the ongoing Phase I, open-label trial NCT03427411 (presented in collaboration with the NCI), signs of tumor burden reduction were seen in 47% (8/17 patients) of patients with advanced HPV associated cancers, including cervical, anal, or head and neck squamous cell carcinoma, enrolled in the dose escalation part of the study. The ORR was 35.3% in patients with HPV associated cancer and 41.7% (including 1 patient with response post-pseudoprogression) in patients with proven HPV-positive disease (12 patients). Safety data in this study were consistent with those observed in the broader M7824 clinical program. A total of 4 patients (23.5%) experienced Grade ≥3 TRAEs, including colitis, cystitis, gastroparesis, pleural effusion and hypokalemia (Grade 4); notably, 3 of these patients had tumor burden reduction. No other Grade 4 or 5 TRAEs were seen.

M7824 is an investigational bifunctional immunotherapy that brings together a TGF-β trap and 'fuses' it with the anti-PD-L1 mechanism. M7824 is designed to simultaneously block the two immunosuppressive pathways and control tumor growth by potentially restoring and enhancing anti-tumor responses. M7824 is an important part of a novel combination approach that seeks to harness the power of the immune system and address the tremendously complex nature of difficult-to-treat tumors such as NSCLC and HPV associated cancers. These data build on a number of recent readouts for M7824, including preliminary data in gastric cancer at the ASCO 2018 Gastrointestinal Cancers Symposium. Merck KGaA, Darmstadt, Germany, will present data from additional cohorts in hard-to-treat cancer types in the coming year.

In addition to M7824, data from a number of high-priority clinical development programs are also being presented at ASCO 2018, including tepotinib (NSCLC), M2698 (advanced tumors) and two molecules from the DNA Damage Response portfolio (advanced solid tumors).

Merck KGaA, Darmstadt, Germany, is committed to exploring an array of targets and taking creative scientific approaches to developing novel therapies for hard-to-treat cancers. With the belief that rational combination is key to the development of potential new and more efficacious treatment options, the company has a particular focus on combination treatment approaches, whether it be with chemotherapy/radiotherapy, other targeted therapies and/or immunotherapies from its own or partners' portfolios.

M7824 at ASCO

Title: Results from a second-line (2L) NSCLC cohort treated with M7824 (MSB0011359C), a bifunctional fusion protein targeting PD-L1 and TGF-β
Lead Author: Luis G. Paz-Ares
Abstract #: 9017
Presentation Date / Time (CDT): Sun, Jun 03, 11:30 a.m. – 12:45 p.m.
Location: Arie Crown Theater

Oral Presentation

Title: Safety and activity of M7824, a bifunctional fusion protein targeting PD-L1 and TGF- β, in patients with HPV associated cancers
Lead Author: Julius Strauss
Abstract #: 3007
Presentation Date / Time (CDT): Sat, Jun 02, 5:12 p.m. – 5:24 p.m.
Location: Hall B1

Poster Sessions

Title: Selection of the recommended Phase 2 dose (RP2D) for M7824 (MSB0011359C), a bifunctional fusion protein targeting TGF-β and PD-L1
Lead Author: Yulia Vugmeyster
Abstract #: 2566
Presentation Date / Time (CDT): Mon, Jun 04, 8:00 a.m. – 11:30 a.m.
Location: Hall A

Title: A sequential cohort study of combination immunotherapy with BN-brachyury vaccine, M7824, ALT-803 and epacadostat in metastatic castration-resistant prostate cancer (mCRPC) (QuEST1)
Lead Author: Jason Redman
Abstract #: TPS3130
Presentation Date / Time (CDT): Mon, Jun 04, 8:00 a.m. – 11:30 a.m.
Location: **Title**: Hall A

TGF-β trap and 'fuse' it with the anti-PD-L1 mechanism. M7824 is designed to simultaneously block the two immunosuppressive pathways – targeting both pathways aims to control tumor growth by potentially restoring and enhancing anti-tumor responses. M7824 is currently in Phase I studies for solid tumors.

About Merck KGaA, Darmstadt, Germany

Merck KGaA, Darmstadt, Germany, is a leading science and technology company in healthcare, life science and performance materials. Almost 53,000 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 2017, Merck KGaA, Darmstadt, Germany, generated sales of € 15.3 billion in 66 countries.

Founded in 1668, Merck KGaA, Darmstadt, Germany, is the world's oldest pharmaceutical and chemical company. The founding family remains the majority owner of the publicly listed corporate group. 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 company operates as EMD Serono, MilliporeSigma and EMD Performance Materials.

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 again for your online subscription of this service as our newly introduced geo-targeting requires new links in the email. You may later change your selection or discontinue this service.

For further information: Brenda Mulligan +1 978 821 5345

Merck KGaA, Darmstadt, Germany, and Pfizer Provide Update on Avelumab in Platinum-Resistant/Refractory Ovarian Cancer

Darmstadt, Germany, and New York, US, November 19, 2018 – Merck KGaA, Darmstadt, Germany, and Pfizer Inc. (NYSE: PFE) today announced that the Phase III JAVELIN Ovarian 200 trial evaluating avelumab* alone or in combination with pegylated liposomal doxorubicin (PLD), a type of chemotherapy, compared with PLD did not meet the prespecified primary endpoints of overall survival (OS) or progression-free survival (PFS) in patients with platinum-resistant or -refractory ovarian cancer. Signals were observed in the combination arm relative to PLD, and further analyses of the trial are warranted (HR for the primary PFS endpoint for avelumab + PLD vs PLD alone: 0.78 [repeated confidence interval (RCI): 0.587, 1.244; one-sided p-value: 0.0301]; HR for the primary OS endpoint for avelumab + PLD vs PLD alone: 0.89 [RCI: 0.744, 1.241; one-sided p-value: 0.2082]; HR for the primary PFS endpoint for avelumab alone vs PLD alone: 1.68 [RCI: 1.320, 2.601; one-sided p-value: >0.99]; HR for the primary OS endpoint for avelumab alone vs PLD alone: 1.14 [RCI: 0.948, 1.580; one-sided p-value: 0.8253]; objective response, a secondary endpoint: 13.3% [95% CI 8.8, 19.0] for avelumab + PLD; 3.7% [95% CI 1.5, 7.5] for avelumab alone; and 4.2% [95% CI 1.8, 8.1] for PLD alone). No new safety signals were observed for avelumab alone or in combination, and the safety profile for

shared with the scientific community.

"JAVELIN Ovarian 200 enrolled a high proportion of patients with aggressive, refractory disease that had no response to prior platinum-based chemotherapy, a population known to have disease that is challenging to treat; as such, this group of patients is typically not included in Phase III ovarian cancer trials," said Chris Boshoff, M.D., Ph.D., Senior Vice President and Head of Immuno-Oncology, Early Development and Translational Oncology, Pfizer Global Product Development. "We initiated the JAVELIN Ovarian 200 trial as the first Phase III study of a checkpoint inhibitor in the platinum-resistant or -refractory setting recognizing these patients have the most pressing need for new treatment options. The results speak to the significant challenges these women face."

"Although OS and PFS did not reach statistical significance, study results indicate potential clinical activity of the combination of avelumab and chemotherapy which will be analyzed further," said Luciano Rossetti, M.D., Executive Vice President, Global Head of Research & Development at the Biopharma business of Merck KGaA, Darmstadt, Germany, which in the US and Canada operates as EMD Serono. "We thank the patients, their families and the investigators who participated in the JAVELIN Ovarian 200 trial, and wish to underscore that the alliance remains committed to driving advances in ovarian cancer, a commitment that includes two ongoing Phase III trials in previously untreated patients testing avelumab in combination with chemotherapy and, separately, one in combination with chemotherapy followed by maintenance treatment of avelumab in combination with a PARP inhibitor."

"Effective management of platinum-resistant or -refractory ovarian cancer remains the biggest unmet medical need facing women with recurrent ovarian cancer today. The current treatment options have only limited and short-lived efficacy for the majority of women, as evidenced by an average life expectancy that does not exceed one year for this group," said Eric Pujade-Lauraine, M.D., Ph.D., head of the Women Cancers and Clinical Research Department at Hôpitaux Universitaires Paris Centre, site Hôtel-Dieu. "As a researcher and clinician, I know how important it is to continue to improve the outlook for women with advanced ovarian cancer and look forward to the results of more trials exploring the role of avelumab in delaying recurrence in platinum-sensitive patients and earlier lines of therapy."

Four out of five patients with ovarian cancer are diagnosed at advanced stages. The disease often has no symptoms early on, when it is much more treatable.[1] Approximately 70% of

of ovarian cancer patients have platinum-resistant or -refractory disease, and eventually almost all patients will become platinum-resistant.[3-6]

JAVELIN Ovarian 200 is a Phase III, multicenter, randomized study investigating the efficacy and safety of avelumab alone or in combination with PLD versus PLD alone in 566 women with ovarian cancer that is resistant or refractory to platinum chemotherapy. The primary objectives were to demonstrate superior OS or PFS for one or both avelumab-based treatment regimens compared with PLD.

In addition to JAVELIN Ovarian 200, the avelumab ovarian cancer clinical development program includes several ongoing clinical trials investigating avelumab in combination with other therapies. JAVELIN Ovarian 100 is an open-label, international, multicenter, randomized Phase III study of avelumab in combination with and/or as follow-on (maintenance) treatment to platinum-based chemotherapy in previously untreated patients with locally advanced or metastatic (Stage III or Stage IV) epithelial ovarian cancer. JAVELIN Ovarian 100 is the first Phase III study to evaluate the addition of an immunotherapy to the standard of care in frontline treatment for this aggressive disease. JAVELIN Ovarian PARP 100 is a randomized, open-label, multicenter Phase III study of avelumab plus chemotherapy followed by maintenance therapy of avelumab in combination with a PARP inhibitor or chemotherapy followed by maintenance therapy with a PARP inhibitor, in patients with previously untreated advanced ovarian cancer. Avelumab is also undergoing investigation in combination with other therapies for gynecologic cancers.

*Avelumab is under clinical investigation for treatment of ovarian cancer and has not been demonstrated to be safe and effective for this indication. There is no guarantee that avelumab will be approved for ovarian cancer by any health authority worldwide.

About the JAVELIN Clinical Trial Program

The clinical development program for avelumab, known as JAVELIN, involves at least 30 clinical programs and more than 9,000 patients evaluated across more than 15 different tumor types. In addition to ovarian cancer, these tumor types include breast, gastric/gastro-esophageal junction and head and neck cancers, melanoma, mesothelioma, Merkel cell carcinoma, non-small cell lung cancer, renal cell carcinoma and urothelial carcinoma.

disease is generally advanced when it is diagnosed, as it often has few to no symptoms at the early stages. This makes it difficult to detect until the disease has progressed. Symptoms can be vague or non-specific, making it easy to confuse with less serious non-cancerous conditions. The five-year survival rate ranges from approximately 30% to 50%, but for those with metastatic disease, it drops to less than 20%.[7,8]

About Avelumab

Avelumab is a human anti-programmed death ligand-1 (PD-L1) antibody. Avelumab has been shown in preclinical models to engage both the adaptive and innate immune functions. By blocking the interaction of PD-L1 with PD-1 receptors, avelumab has been shown to release the suppression of the T cell-mediated antitumor immune response in preclinical models.[9-11] Avelumab has also been shown to induce NK cell-mediated direct tumor cell lysis via antibody-dependent cell-mediated cytotoxicity (ADCC) *in vitro*.[11-13] In November 2014, Merck KGaA, Darmstadt, Germany, and Pfizer announced a strategic alliance to co-develop and co-commercialize avelumab.

Approved Indications

In the US, the FDA granted accelerated approval for avelumab (BAVENCIO®) for the treatment of (i) adults and pediatric patients 12 years and older with metastatic Merkel cell carcinoma (mMCC) and (ii) patients with locally advanced or metastatic urothelial carcinoma (mUC) who have disease progression during or following platinum-containing chemotherapy, or have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy. These indications are approved under accelerated approval based on tumor response rate and duration of response. Continued approval for these indications may be contingent upon verification and description of clinical benefit in confirmatory trials.

Avelumab is currently approved for patients with MCC in more than 35 countries globally, with the majority of these approvals in a broad indication that is not limited to a specific line of treatment.

Important Safety Information from the US FDA Approved Label

BAVENCIO can cause **immune-mediated pneumonitis**, including fatal cases. Monitor patients for signs and symptoms of pneumonitis, and evaluate suspected cases with radiographic imaging. Administer corticosteroids for Grade 2 or greater pneumonitis. Withhold BAVENCIO for moderate (Grade 2) and permanently discontinue for severe (Grade 3), life-threatening (Grade

with Grade 3.

BAVENCIO can cause **immune-mediated hepatitis**, including fatal cases. Monitor patients for abnormal liver tests prior to and periodically during treatment. Administer corticosteroids for Grade 2 or greater hepatitis. Withhold BAVENCIO for moderate (Grade 2) immune-mediated hepatitis until resolution and permanently discontinue for severe (Grade 3) or life-threatening (Grade 4) immune-mediated hepatitis. Immune-mediated hepatitis was reported in 0.9% (16/1738) of patients, including two (0.1%) patients with Grade 5, and 11 (0.6%) with Grade 3.

BAVENCIO can cause **immune-mediated colitis**. Monitor patients for signs and symptoms of colitis. Administer corticosteroids for Grade 2 or greater colitis. Withhold BAVENCIO until resolution for moderate or severe (Grade 2 or 3) colitis, and permanently discontinue for life-threatening (Grade 4) or recurrent (Grade 3) colitis upon reinitiation of BAVENCIO. Immune-mediated colitis occurred in 1.5% (26/1738) of patients, including seven (0.4%) with Grade 3.

BAVENCIO can cause **immune-mediated endocrinopathies**, including adrenal insufficiency, thyroid disorders, and type 1 diabetes mellitus.

Monitor patients for signs and symptoms of **adrenal insufficiency** during and after treatment, and administer corticosteroids as appropriate. Withhold BAVENCIO for severe (Grade 3) or life-threatening (Grade 4) adrenal insufficiency. Adrenal insufficiency was reported in 0.5% (8/1738) of patients, including one (0.1%) with Grade 3.

Thyroid disorders can occur at any time during treatment. Monitor patients for changes in thyroid function at the start of treatment, periodically during treatment, and as indicated based on clinical evaluation. Manage hypothyroidism with hormone replacement therapy and hyperthyroidism with medical management. Withhold BAVENCIO for severe (Grade 3) or life-threatening (Grade 4) thyroid disorders. Thyroid disorders, including hypothyroidism, hyperthyroidism, and thyroiditis, were reported in 6% (98/1738) of patients, including three (0.2%) with Grade 3.

Type 1 diabetes mellitus including diabetic ketoacidosis: Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Withhold BAVENCIO and administer antihyperglycemics or insulin in patients with severe or life-threatening (Grade ≥ 3) hyperglycemia, and resume treatment when metabolic control is achieved. Type 1

BAVENCIO can cause **immune-mediated nephritis and renal dysfunction**. Monitor patients for elevated serum creatinine prior to and periodically during treatment. Administer corticosteroids for Grade 2 or greater nephritis. Withhold BAVENCIO for moderate (Grade 2) or severe (Grade 3) nephritis until resolution to Grade 1 or lower. Permanently discontinue BAVENCIO for life-threatening (Grade 4) nephritis. Immune-mediated nephritis occurred in 0.1% (1/1738) of patients.

BAVENCIO can result in **other severe and fatal immune-mediated adverse reactions** involving any organ system during treatment or after treatment discontinuation. For suspected immune-mediated adverse reactions, evaluate to confirm or rule out an immune-mediated adverse reaction and to exclude other causes. Depending on the severity of the adverse reaction, withhold or permanently discontinue BAVENCIO, administer high-dose corticosteroids, and initiate hormone replacement therapy, if appropriate. Resume BAVENCIO when the immune-mediated adverse reaction remains at Grade 1 or lower following a corticosteroid taper. Permanently discontinue BAVENCIO for any severe (Grade 3) immune-mediated adverse reaction that recurs and for any life-threatening (Grade 4) immune-mediated adverse reaction. The following clinically significant immune-mediated adverse reactions occurred in less than 1% of 1738 patients treated with BAVENCIO: myocarditis with fatal cases, myositis, psoriasis, arthritis, exfoliative dermatitis, erythema multiforme, pemphigoid, hypopituitarism, uveitis, Guillain-Barré syndrome, and systemic inflammatory response.

BAVENCIO can cause severe (Grade 3) or life-threatening (Grade 4) **infusion-related reactions**. Patients should be premedicated with an antihistamine and acetaminophen prior to the first 4 infusions and for subsequent doses based upon clinical judgment and presence/severity of prior infusion reactions. Monitor patients for signs and symptoms of infusion-related reactions, including pyrexia, chills, flushing, hypotension, dyspnea, wheezing, back pain, abdominal pain, and urticaria. Interrupt or slow the rate of infusion for mild (Grade 1) or moderate (Grade 2) infusion-related reactions. Permanently discontinue BAVENCIO for severe (Grade 3) or life-threatening (Grade 4) infusion-related reactions. Infusion-related reactions occurred in 25% (439/1738) of patients, including three (0.2%) patients with Grade 4 and nine (0.5%) with Grade 3.

BAVENCIO can cause **fetal harm** when administered to a pregnant woman. Advise patients of the potential risk to a fetus including the risk of fetal death. Advise females of childbearing

human milk. Advise a lactating woman **not to breastfeed** during treatment and for at least 1 month after the last dose of BAVENCIO due to the potential for serious adverse reactions in breastfed infants.

The most common adverse reactions (all grades, ≥ 20%) in patients with **metastatic Merkel cell carcinoma (MCC)** were fatigue (50%), musculoskeletal pain (32%), diarrhea (23%), nausea (22%), infusion-related reaction (22%), rash (22%), decreased appetite (20%), and peripheral edema (20%).

Selected treatment-emergent laboratory abnormalities (all grades, ≥ 20%) in patients with **metastatic MCC** were lymphopenia (49%), anemia (35%), increased aspartate aminotransferase (34%), thrombocytopenia (27%), and increased alanine aminotransferase (20%).

The most common adverse reactions (all grades, ≥ 20%) in patients with **locally advanced or metastatic urothelial carcinoma (UC)** were fatigue (41%), infusion-related reaction (30%), musculoskeletal pain (25%), nausea (24%), decreased appetite/hypophagia (21%), and urinary tract infection (21%).

Selected laboratory abnormalities (Grades 3-4, ≥ 3%) in patients with **locally advanced or metastatic UC** were hyponatremia (16%), increased gamma-glutamyltransferase (12%), lymphopenia (11%), hyperglycemia (9%), increased alkaline phosphatase (7%), anemia (6%), increased lipase (6%), hyperkalemia (3%), and increased aspartate aminotransferase (3%).

Please see full US Prescribing Information and Medication Guide available at http://www.BAVENCIO.com.

Alliance between Merck KGaA, Darmstadt, Germany, and Pfizer Inc., New York, US
Immuno-oncology is a top priority for Merck KGaA, Darmstadt, Germany, and Pfizer. The global strategic alliance between Merck KGaA, Darmstadt, Germany, and Pfizer enables the companies to benefit from each other's strengths and capabilities and further explore the therapeutic potential of avelumab, an anti-PD-L1 antibody initially discovered and developed by Merck KGaA, Darmstadt, Germany. The immuno-oncology alliance is jointly developing and commercializing avelumab and advancing Pfizer's PD-1 antibody. The alliance is focused on developing high-priority international clinical programs to investigate avelumab as a monotherapy as well as combination regimens, and is striving to find new ways to treat cancer.

www.emdgroup.com/subscribe to register online, change your selection or discontinue this service.

About Merck KGaA, Darmstadt, Germany

Merck KGaA, Darmstadt, Germany, the vibrant science and technology company, operates across healthcare, life science and performance materials. Around 53,000 employees work to make a positive difference to millions of people's lives every day by creating more joyful and sustainable ways to live. From advancing gene editing technologies and discovering unique ways to treat the most challenging diseases, to enabling the intelligence of devices – the company is everywhere. In 2017, Merck KGaA, Darmstadt, Germany, generated sales of € 15.3 billion in 66 countries.

The company holds the global rights to the name and trademark "Merck" internationally. The only exceptions are the United States and Canada, where the company's business sectors operate as EMD Serono in healthcare, MilliporeSigma in life science, and EMD Performance Materials. Since its founding 1666, scientific exploration and responsible entrepreneurship have been key to the company's technological and scientific advances. To this day, the founding family remains the majority owner of the publicly listed company.

Pfizer Inc.: Working together for a healthier world®

At Pfizer, we apply science and our global resources to bring therapies to people that extend and significantly improve their lives. We strive to set the standard for quality, safety and value in the discovery, development and manufacture of health care products. Our global portfolio includes medicines and vaccines as well as many of the world's best-known consumer health care products. Every day, Pfizer colleagues work across developed and emerging markets to advance wellness, prevention, treatments and cures that challenge the most feared diseases of our time. Consistent with our responsibility as one of the world's premier innovative biopharmaceutical companies, we collaborate with health care providers, governments and local communities to support and expand access to reliable, affordable health care around the world. For more than 150 years, we have worked to make a difference for all who rely on us. We routinely post information that may be important to investors on our website at www.pfizer.com. In addition, to learn more, please visit us on www.pfizer.com and follow us on Twitter at @Pfizer and @Pfizer_News, LinkedIn, YouTube and like us on Facebook at Facebook.com/Pfizer.

obligation to update forward-looking statements contained in this release as the result of new information or future events or developments.

This release contains forward-looking information about avelumab, including clinical trials evaluating avelumab for the treatment of ovarian cancer, the alliance between Merck KGaA, Darmstadt, Germany, and Pfizer involving anti-PD-L1 and anti-PD-1 therapies, and clinical development plans, including their potential benefits, that involves substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Risks and uncertainties include, among other things, uncertainties regarding the commercial success of avelumab; the uncertainties inherent in research and development, including the ability to meet anticipated clinical study commencement and completion dates and regulatory submission dates, as well as the possibility of unfavorable study results, including unfavorable new clinical data and additional analyses of existing clinical data; risks associated with interim data; the risk that clinical trial data are subject to differing interpretations, and, even when we view data as sufficient to support the safety and/or effectiveness of a product candidate, regulatory authorities may not share our views and may require additional data or may deny approval altogether; whether regulatory authorities will be satisfied with the design of and results from our clinical studies; whether and when any drug applications may be filed for avelumab in any jurisdictions or for any potential indications for avelumab, combination therapies or other product candidates; whether and when regulatory authorities in any jurisdictions where applications are pending or may be submitted for avelumab, combination therapies or other product candidates may approve any such applications, which will depend on the assessment by such regulatory authorities of the benefit-risk profile suggested by the totality of the efficacy and safety information submitted; decisions by regulatory authorities regarding labeling and other matters that could affect the availability or commercial potential of avelumab, combination therapies or other product candidates; and competitive developments.

A further description of risks and uncertainties can be found in Pfizer’s Annual Report on Form 10-K for the fiscal year ended December 31, 2017, and in its subsequent reports on Form 10-Q, including in the sections thereof captioned “Risk Factors” and “Forward-Looking Information and Factors That May Affect Future Results”, as well as in its subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and Exchange Commission and available at www.sec.gov and www.pfizer.com.

1. American Cancer Society. Facts and figures 2018. Special section: ovarian cancer. Available at: https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2018/cancer-facts-and-figures-special-section-ovarian-cancer-2018.pdf. Accessed November 2018.
2. Ledermann, JA, Raja FA, Fotopoulou C, et al. Newly diagnosed and relapsed epithelial ovarian carcinoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol.* 2013; 24 (Supplement 6): vi24–vi32, doi:10.1093/annonc/mdt333.
3. Christie EL, Bowtell DD. Acquired chemotherapy resistance in ovarian cancer. *Ann Oncol*. 2017; 28 (Supplement 8):viii13-viii15.
4. Cooke SL, Brenton JD. Evolution of platinum resistance in high-grade serous ovarian cancer. *Lancet Oncol*. 2011; 12(12):1169-1174.
5. Tomao F, Marchetti C, Romito A, et al. Overcoming platinum resistance in ovarian cancer treatment: from clinical practice to emerging chemical therapies. *Expert Opin Pharmacother*. 2017;18(14):1443-1455.
6. Committee on the State of the Science in Ovarian Cancer Research; Board on Health Care Services; Institute of Medicine; National Academies of Sciences, Engineering, and Medicine. Washington (DC): National Academies Press (US); 2016 Apr 25.
7. World Cancer Research Fund / American Institute for Cancer Research. Continuous Update Project. Available at: https://www.wcrf.org/dietandcancer/cancer-trends/worldwide-cancer-data. Accessed November 2018.
8. American Cancer Society. Survival Rates for Ovarian Cancer, by Stage. Available at: https://www.cancer.org/cancer/ovarian-cancer/detection-diagnosis-staging/survival-rates.html. Accessed November 2018
9. Dolan DE, Gupta S. PD-1 pathway inhibitors: changing the landscape of cancer immunotherapy. *Cancer Control*. 2014;21(3):231-237.
10. Dahan R, Sega E, Engelhardt J, et al. FcγRs modulate the anti-tumor activity of antibodies targeting the PD-1/PD-L1 axis. *Cancer Cell*. 2015;28(3):285-295.
11. Boyerinas B, Jochems C, Fantini M, et al. Antibody-dependent cellular cytotoxicity activity of a novel anti-PD-L1 antibody avelumab (MSB0010718C) on human tumor cells. *Cancer Immunol Res*. 2015;3(10):1148-1157.
12. Kohrt HE, Houot R, Marabelle A, et al. Combination strategies to enhance antitumor ADCC. *Immunotherapy*. 2012;4(5):511-527.
13. Hamilton G, Rath B. Avelumab: combining immune checkpoint inhibition and antibody-dependent cytotoxicity. *Expert Opin Biol Ther*. 2017;17(4):515-523.

COMPANY

LEADERSHIP TEAM

PARTNERING

PRESS

CONTACT US

COMPLIANCE & TRANSPARENCY

THERAPEUTIC AREAS

YOUR REQUESTS

New Efficacy and Safety Data on MS Portfolio to be Presented at ECTRIMS 2018

EXPLORE MORE

- **Late-breaking Phase II primary endpoint data for investigational therapy evobrutinib, the first oral BTK inhibitor to show clinical proof-of-concept in RMS**
- **Up to 10 years of patient experience provides further insight into the benefit-risk profile of investigational cladribine tablets**
- **Late-breaking data from multi-sponsored European IFNβ Pregnancy Registry highlight Rebif safety outcomes during pregnancy**
- **A total of 23 abstracts for cladribine tablets, Rebif and evobrutinib will be presented at ECTRIMS 2018**

ROCKLAND, Mass, October 8, 2018 – EMD Serono, the biopharmaceutical business of Merck KGaA, Darmstadt, Germany, in the U.S. and Canada, today announced that it will present data from approved and investigational multiple sclerosis (MS) treatments from its neurology and immunology portfolio at the 34th Congress of the European Committee for Treatment and Research In Multiple Sclerosis (ECTRIMS), taking place from 10–12 October 2018, in Berlin, Germany. EMD Serono will present 23 abstracts, including new safety and efficacy data on investigational cladribine tablets, Rebif® (interferon beta-1a) and investigational therapy evobrutinib, a highly-specific, oral Bruton's Tyrosine Kinase (BTK) inhibitor.

Key cladribine tablets data will include:

Registry (up to 10-years of follow-up).

- An overview of the first six months of real-world evidence safety data on cladribine tablets.
- Results from a post hoc analysis of the CLARITY study will characterize relapse severity and frequency in relapsing-remitting MS (RRMS) patients in cladribine tablets versus placebo.
- New data from post hoc analyses to support the duration of effect of cladribine tablets across patient subgroups of different ages and with different disease activity status (in Years 3 and 4 post-treatment) will be presented.

Key late-breaking data presentations include:

- Results of primary 24-week MRI endpoint analysis, along with a description of interim key secondary and safety analysis from a Phase II study of investigational BTK-inhibitor evobrutinib in patients with relapsing MS. The late-breaking oral presentation will highlight the first evidence of clinical activity of a BTK-inhibitor in a non-oncology indication.
- Presentation highlighting pregnancy and infant outcomes with multiple IFNβ therapies, including Rebif®, from the European IFNβ pregnancy registry and Nordic health registers.

"We are proud to be presenting new data across our Neurology and Immunology franchise during ECTRIMS 2018," said Luciano Rossetti, Head of Global R&D for EMD Serono. "As we continue to enhance our understanding of the benefit-risk profile of cladribine tablets and the use of Rebif, we are also excited by the presentation of the first clinical data for a BTK inhibitor (evobrutinib) in an MS patient population."

Additional EMD Serono activities at ECTRIMS 2018:

- Results of the EMD Serono-sponsored 'MS in the 21st Century International Unmet Needs Survey' will show that MS patients have substantially different perceptions of the current unmet needs in MS compared with healthcare professionals (HCPs).
- Following on from the #MSInsideOut campaign launch on World MS Day earlier in the year, EMD Serono will be premiering the MS Inside Out Documentary film executively produced by Shift.ms during an event on October 11. At the event, EMD Serono will shine a light on the untold stories of MS, as well as revealing the findings and key results from a new global MS carers survey conducted in collaboration between leading international carer organizations IACO (International Alliance of Carer Organization) and Eurocarers. The data presented at ECTRIMS will further demonstrate the need for a deeper understanding of those affected by MS and their carer.
- EMD Serono will also be announcing the annual Grant for Multiple Sclerosis Innovation (GMSI) Award winners in Berlin. First launched at ECTRIMS 2012, the GMSI Award supports the advancement of science and medical research in the field of MS and provides a grant of up to €1,000,000 per year to one or more selected research projects.

Below are a selection of abstracts that have been accepted for presentation at ECTRIMS 2018:

Cladribine Tablets Presentations

Title	Authors	Abstract No.	Presentation Date/ Time/Session
An exploratory analysis of the efficacy of Cladribine Tablets 3.5mg/kg in patients with relapsing multiple sclerosis stratified according to age above and below 45 years in the CLARITY study	Giovannoni G, Rammohan K, Cook S, Soelberg-Sorensen P, Vermersch P, Keller B, Verdun di Cantogno E	A-0950-0028-00859	Session Title: Poster Session 3 Session Date: 12.10.2018 Presenting Time: 12:15-14:15 h
Sustained efficacy in relapsing remitting multiple sclerosis following switch to placebo treatment from Cladribine Tablets in patients with high disease activity at baseline	Vermersch P, Giovannoni G, Soelberg-Sorensen P, Keller B, Jack D	A-0950-0028-00886	Session Title: Poster Session 1 Session Date: 10.10.2018 Presenting Time: 17:00-19:00 h
CLARITY: An analysis of severity and frequency of relapses in patients with relapsing-remitting multiple sclerosis treated	Schippling S, Sormani M P, De Stefano N, Giovannoni G, Galazka A, Keller B, Alexandri N	A-0950-0028-01315	Session Title: Poster Session 1 Session Date: 10.10.2018 Presenting Time: 17:00-19:00 h

Lymphopenia rates in CLARITY/CLARITY Extension are unrelated to disease activity at baseline	Cook S, Giovannoni G, Vermersch P, Soelberg-Sorensen P, Keller B, Jack D	A-0950-0028-00836	Session Title: Poster Session 2 Session Date: 11.10.2018 Presenting Time: 17:15-19:15 h
Updated safety analysis of Cladribine Tablets in the treatment of patients with multiple sclerosis	Cook S, Giovannoni G, Leist T, Syed S, Nolting A, Schick R	A-0950-0028-00889	Session Title: Poster Session 2 Session Date: 11.10.2018 Presenting Time: 17:15-19:15 h
Durability of NEDA-3 status in patients with relapsing multiple sclerosis receiving Cladribine Tablets: CLARITY Extension	Giovannoni G, Keller B, Jack D	A-0950-0028-01763	Session Title: Poster Session 2 Session Date: 11.10.2018 Presenting Time: 17:15-19:15 h
ADA genetic variants influence central inflammation and clinical characteristics in MS: implications for cladribine treatment	Stampanoni Bassi M, Buttari F, Simonelli I, Sica F, Furlan R, Marfia G A, Salvetti M, Uccelli A, Matarese G, Visconti A, Centonze D	A-0950-0028-01895	Poster Session 1 10 October 2018 Presenting Time: 17:00-19:00 h
Neuroblastoma cell line and lymphocytes talk for	Ruggieri M, Mastrapasqua M,	A-0950-0028-	ePoster

inflammation pathways in Multiple Sclerosis (MS): an "in vitro" study	A, Paolicelli D, Visconti A, Trojano M on behalf of MSRUN group		
Dissection of the distinct susceptibility of hematopoietic precursors and immune cells to cladribine	Carlini F, Ivaldi F, Kerlero de Rosbo N, Boschert U , Visconti A, Uccelli A	A-0950-0028-01855	ePoster
Gene expression profiles of proteins involved in Cladribine metabolism and their possible correlation with Epstein-Barr virus variants	Mechelli R, Manfrè G, Pellicciari G, Reniè R, Romano C, Ristori G, Visconti A, Salvetti M on behalf of MSRUN group	A-0950-0032-01730	Poster Session 3 12 October 2018 Presenting Time: 12:15-14:15 h
A Systematic Review of Real-world Adherence and Persistence of Daily Oral Disease-Modifying Drugs (Dimethyl Fumarate, Fingolimod, and Teriflunomide) in Multiple Sclerosis	Edwards NC, Edwards RA, Dellarole A, Grosso M, Phillips A	TBC	Poster Session 3 12 October 2018 Presenting Time: 12:15-14:15 h

Rebif® (interferon beta-1a) Presentations

Title	Authors	Abstract No.	Presentation Date/ Time/Session

Subcutaneous Interferon beta-1a, 10-Year Results from the United Kingdom Multiple Sclerosis Risk Sharing Scheme	Harty G, Wong S L, Gillett A, Davies A	A-0950-0030-00894	Session 2 Session Date: 11.10.2018 Presenting Time: 17:15-19:15 h
Rapid reduction of lesion accumulation in specific white matter tracts as assessed by lesion mapping in RR-MS patients treated with IFN beta-1a	De Stefano N, Giorgio A, Gentile G, Stromillo M L, Visconti A, Battaglini M	A-0950-0023-02002	ePoster
Dynamics of pseudo-atrophy in RRMS patients treated with Interferon beta-1a as assessed by monthly brain MRI	De Stefano N, Giorgio A, Gentile G, Stromillo M L, Visconti A, Sormani M P, Battaglini M	A-0950-0023-02027	Session Title: Poster Session 2 Session Date: 11.10.2018 Presenting Time: 17:15-19:15 h
A Real-World Comparison of Infections and Lymphocyte Counts among Relapsing-Remitting Multiple Sclerosis Patients 50 years or older treated with Subcutaneous Interferon-Beta 1a or Dimethyl Fumarate Session	Hayward B, Cardoso S, Grosso M, Ansari S, Napoli S	A-0950-0031-02072	Title: Poster Session 1 Session Date: 10.10.2018 Presenting Time: 17:00-19:00 h
Value of the MoCA test	K. Charest, A.	A-0950-	ePoster

patients without subjective cognitive complaints	Duquette, I. Rouleau		

Rebif® (interferon beta-1a) Late-breaker Presentation

Pregnancy and Infant Outcomes with Interferon Beta: Data from the European Interferon Beta Pregnancy Registry and Population Based Registries in Finland and Sweden	Hellwig K, Geissbuehler Y, Sabidó M, Popescu C, Adamo A, Klinger J, Huppke P, Ornoy A, Korhonen P, Myhr K-M, Montgomery S , Burkill S on behalf of the European Interferon Beta Pregnancy Study Group	A-0950-0000-02658	Session Title: Poster Session 3 Session Date: Friday, 12 October 2018 Presenting Time: 12.15 – 14.15 h

Evobrutinib (Bruton's Tyrosine Kinase Inhibitor) Presentations

Title	Authors	Abstract No.	Presentation Date/ Time/Session
Safety, Tolerability, Pharmacokinetics and Concentration-QT Analysis of the Novel BTK Inhibitor Evobrutinib (M2951) in Healthy Volunteers	Becker A, Martin E, Ona V, Mitchell DY, Willmer J, Johne A	A-0950-0028-01166	Session Title: Poster Session 1 Session Date: 10.10.2018 Presenting Time: 17:00-19:00 h

BTK Inhibition Prevents Inflammatory Macrophage Differentiation: A Potential Role in MS	Grenningloh R, Haselmeyer P, Bender, A, Bruttger J	A-0950-0028-01194	Session 1 Session Date: 10.10.2018 Presenting Time: 17:00-19:00 h
Inhibition of Bruton's Tyrosine Kinase Selectively Prevents Antigen-Activation of B Cells and Ameliorates B Cell-Mediated Experimental Autoimmune Encephalomyelitis	Torke S, Grenningloh R, Boschert U, Weber MS	A-0950-0028-01220	Session Title: Poster Session 1 Session Date: 10.10.2018 Presenting Time: 17:00-19:00 h
Evobrutinib (Bruton's Tyrosine Kinase Inhibitor) Late-breaker Presentation			
Primary analysis of a randomised, placebo-controlled, phase 2 study of the Bruton's tyrosine kinase inhibitor evobrutinib (M2951) in patients with relapsing multiple sclerosis	Montalban X, Arnold DL, Weber MS, Staikov I, Piasecka-Stryczynska K, Willmer J, Martin E, Dangond F, Wolinsky JS	A-0950-0000-02722	Scientific Session 17: Late Breaking News Scientific Session, Hall A Session Date: 12.10.2018 Presenting Time: 14:39-14:51 h

Additional EMD Serono-sponsored Presentations

Title	Authors	Abstract No.	Presentation Date/ Time/Session

perceptions on multiple sclerosis management and care – where do their priorities differ? Results from a qualitative survey.	behalf of MS in the 21st Century Steering Group, and Contango E V	01926	Session Date: 12.10.2018 Presenting Time: 12:15-14:15 h
MS in the 21st Century mapping study identifying the global educational offerings for multiple sclerosis patients	Rieckmann P, Langdon D on behalf of MS in the 21st Century Steering Group, and Contango E V	AA-0950-0034-01860	ePoster

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 again for your online subscription of this service as our newly introduced geo-targeting requires new links in the email. You may later change your selection or discontinue this service.

About Cladribine Tablets
Cladribine tablets is an investigational short-course oral therapy that is thought to selectively target lymphocytes which may be integral to the pathological process of relapsing MS (RMS). Cladribine tablets is currently under clinical investigation and not approved for the treatment for any use in the United States. MAVENCLAD® has received approvals for patients with highly active RMS as defined by clinical or imaging features in the European Union (EU), Israel, Argentina, United Arab Emirates, Chile and Lebanon. In December 2017, Health Canada and the Therapeutic Goods Administration (TGA) in Australia approved MAVENCLAD® for the treatment of relapsing-remitting MS (RRMS).

The clinical development program for cladribine tablets includes:

- The CLARITY (Cladribine Tablets Treating MS Orally) study: a two-year Phase III placebo-controlled study designed to evaluate the efficacy and safety of cladribine tablets as a monotherapy in patients with RRMS.
- The CLARITY extension study: a Phase III placebo-controlled study following on from the CLARITY study, which evaluated the safety and efficacy of cladribine tablets over two additional years beyond the two-year CLARITY study, according to the treatment assignment scheme for years 3 and 4.

monotherapy in patients at risk of developing MS (patients who have experienced a first clinical event suggestive of MS).

- The ONWARD (Oral Cladribine Added ON to Interferon beta-1a in Patients With Active Relapsing Disease) study: a Phase II placebo-controlled study designed primarily to evaluate the safety and tolerability of adding cladribine tablets treatment to patients with relapsing forms of MS, who have experienced breakthrough disease while on established interferon-beta therapy.
- PREMIERE (Prospective Observational Long-term Safety Registry of Multiple Sclerosis) study: a long-term follow-up safety registry of multiple sclerosis patients who participated in cladribine tablets clinical studies.

The clinical development program of cladribine tablets in MS comprises close to 12,000 patient years of data with over 2,700 patients included in the clinical trial program, and up to 10 years of follow-up in some patients.

In the two-year CLARITY study, the most commonly reported adverse event (AE) in patients treated with cladribine tablets was lymphopenia. The incidence of infections was 48.3% with cladribine tablets and 42.5% with placebo, with 99.1% and 99.0% respectively rated mild-to-moderate by investigators.

About Evobrutinib
Evobrutinib (M2951) is in clinical development to investigate its potential as a treatment for multiple sclerosis (MS), rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). 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 Rebif® (interferon beta-1a)
Rebif (interferon beta-1a) is used to treat relapsing forms of MS to decrease the frequency of relapses and delay the occurrence of some of the physical disability that is common in people with MS. The efficacy and safety of Rebif in controlled clinical trials beyond 2-years has not been established.

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.

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.

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.

There are no adequate and well-controlled studies in pregnant women. Rebif should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Rebif full prescribing information is available at http://www.emdserono.com/ms.country.us/en/images/Rebif_PI_tcm115_140051.pdf?Version=

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.

EMD Serono, Inc. and Multiple Sclerosis
For more than 20 years, EMD Serono has been relentlessly focused on understanding the journey people living with MS face in order to create a meaningful, positive experience for them

solutions that improve the lives of all those affected by MS. www.GetCloserToMS.com

About EMD Serono, Inc.
EMD Serono - the biopharmaceutical business of Merck KGaA, Darmstadt, Germany, in the U.S. and Canada – is engaged in the discovery, research and development of medicines for patients with difficult to treat diseases. The business is committed to transforming lives by developing and delivering meaningful solutions that help address the therapeutic and support needs of individual patients. Building on a proven legacy and deep expertise in neurology, fertility and endocrinology, EMD Serono is developing potential new oncology and immuno-oncology medicines while continuing to explore potential therapeutic options for diseases such as psoriasis, lupus and multiple sclerosis. Today, the business has approximately 1,300 employees around the country with commercial, clinical and research operations based in the company's home state of Massachusetts. www.emdserono.com

EMD Serono is the biopharmaceutical business of Merck KGaA, Darmstadt, Germany. This site contains information that is intended for residents of the United States only and is not meant to substitute for the advice provided by a medical professional. Always consult a physician if you have health concerns. Use and access of this site is subject to the terms and conditions as set out in our Legal Statement and Privacy Policy.

This site contains information that is intended for US residents only. Canadian residents should consult the EMD Inc. website at www.emdserono.ca for information on products and services approved in Canada.

SITEMAP

LEGAL STATEMENT

PRIVACY POLICY

CONTACT US

Notification of Stolen Fertility Drugs: Gonal-f® RFF Redi-ject® and Gonal-f® Multi-Dose

EMD Serono, Inc. of Rockland, Massachusetts is working with the U.S. Food and Drug Administration (FDA), Office of Criminal Investigations (OCI), the Italian Medicines Agency (AIFA), and other law enforcement officials to recover cases of select lots of prescription Gonal-f® RFF Redi-ject® (follitropin alfa injection) and Gonal-f® Multi-Dose (follitropin alfa for injection), which are injectable fertility medications that are stored refrigerated and room temperature, respectively. On May 17, 2018, a delivery truck containing the products was hijacked near Bari, Italy, while en route for shipment to the United States. This product's trademark has been registered with U.S. Customs, who have been alerted to the possibility of illicit shipments into the U.S.

The stolen truck contained 16,457 packages of Gonal-f® RFF Redi-ject® and Gonal-f® Multi-Dose. All of the lot numbers associated with the product stolen are exclusive to this specific shipment. Lot numbers of the stolen products are listed in Table 1 below. The lot numbers can be found on the flap of each box, below the tamper-proof seal and next to the 2D barcode.

NAME	NDC	LOT	EXPIRATION	DOSAGE FORM
Gonal-f® RFF Redi-ject® 450 IU (0.75 mL)	44087-1116-1	BA049137	5/31/2019	Liquid for injection
Gonal-f® Multi-Dose 1050 IU	44087-9070-1	BA049037	9/30/2019	Vial powder with diluent for injection
Gonal-f® Multi-Dose 450 IU	44087-9030-1	BA049143	2/29/2020	Vial powder with diluent for injection
Gonal-f® Multi-Dose 450 IU	44087-9030-1	BA049040	9/30/2019	Vial powder with diluent for injection

These lot numbers are not valid for the United States and therefore should be deemed suspect product.

Anyone who may be in possession of these lots should NOT use them and should report the suspect product to EMD Serono by calling 1-888-398-4567 or email us at us.customerservice@emdserono.com. Anyone who has information regarding this incident, or has received suspicious or unsolicited offers for Gonal-f® RFF Redi-ject® and Gonal-f® Multi-Dose after the date of the theft, should contact the U.S. Food and Drug Administration (FDA) Office of Criminal Investigations at 1-800-551-3989 or to visit the OCI Web Site.

EMD Serono recommends that consumers always inspect the product and label for signs of tampering or contamination prior to use. Gonal-f® RFF Redi-ject® and Gonal-f® Multi-Dose are packaged in "tamper-evident" cartons, meaning that if the package has been opened, it will be evident to the consumer. Consumers can also use EMD Serono's Check My Meds™ app to

at us.customerservice@emdserono.com. This information should also be reported to FDA's MedWatch Safety Information and Adverse Event Reporting Program.

EMD Serono advises customers and consumers to always purchase product only from licensed distributors and pharmacies to ensure that the product has not deviated from the authorized supply chain (which excludes online pharmacies). For consumer inquiries about a specific product, please call EMD Serono at 1-888-398-4567 or email us at us.customerservice@emdserono.com.

Pharmacies, other healthcare professionals and patients who may be in possession of these lots should NOT use them. If these lots are accidentally used, healthcare professionals and patients are encouraged to report such use, and any adverse events, side effects, or product quality problems related to such use to the FDA's MedWatch Safety Information and Adverse Event Reporting Program:

- Complete and submit the report online
- Download form or call 1-800-332-1088 to request a reporting form, then complete and return to the address on the pre-addressed form, or submit by fax to 1-800-FDA-0178

All Gonal-f® RFF Redi-ject® and Gonal-f® Multi-Dose products with lot numbers other than those listed in the table above meet the standards of quality for distribution and use by patients.

EMD Serono has taken quick and appropriate actions to ensure the safety of its products and will continue to work closely with law enforcement, the FDA, the AIFA, and distribution partners to maintain the integrity of the supply chain.

EMD Serono is the biopharmaceutical business of Merck KGaA, Darmstadt, Germany. This site contains information that is intended for residents of the United States only and is not meant to substitute for the advice provided by a medical professional. Always consult a physician if you have health concerns. Use and access of this site is subject to the terms and conditions as set out in our Legal Statement and Privacy Policy.

This site contains information that is intended for US residents only. Canadian residents should consult the EMD Inc. website at www.emdserono.ca for information on products and services approved in Canada.

Positive Late-Breaking Phase II Data Evaluating Investigational Oral Therapy, Evobrutinib in RMS

- **First Bruton's Tyrosine Kinase inhibitor (BTKi) demonstrating clinical proof-of-concept in relapsing multiple sclerosis (RMS)**
- **Study met primary endpoint demonstrating significant reduction in Gd+ enhancing T1 lesions on MRI with evobrutinib versus placebo**
- **Clinically meaningful decrease in annual relapse rates observed**

ROCKLAND, Mass, October 12, 2018 – EMD Serono, the biopharmaceutical business of Merck KGaA, Darmstadt, Germany, in the U.S. and Canada, today announced the 24-week results of the double-blind, randomized, placebo-controlled, 48-week, Phase II study of evobrutinib in patients with relapsing multiple sclerosis (RMS) at the 34th Congress of the European Committee for Treatment and Research In Multiple Sclerosis (ECTRIMS) in Berlin, Germany. In this study, dimethyl fumarate (240mg BID) represented an open-label reference arm, and there were no formal statistical comparisons between dimethyl fumarate and evobrutinib or placebo. The study met its primary endpoint, with evobrutinib 75mg QD (once-daily) and 75mg BID

is a highly-specific, oral Bruton's Tyrosine Kinase (BTK) inhibitor and the first BTK inhibitor to show clinical proof-of-concept in relapsing MS.

"We are among the first to evaluate a BTK inhibitor for chronic autoimmune diseases, and we continue to be highly encouraged by the results we've seen in patients with relapsing MS thus far," said Luciano Rossetti, Global Head of Research & Development at EMD Serono. "Evobrutinib was discovered in-house and is an example of the innovation coming from our own labs. We have a long history of delivering innovative solutions with the aim of advancing MS care, and look forward to further exploring the potential of evobrutinib in future clinical trials."

Ninety-one percent of randomized patients (244 of 267) completed 24 weeks of treatment. Mean (SD) total T1 Gd+ lesions (weeks 12-24) was 3.85 (5.44), 4.06 (8.02), 1.69 (4.69) and 1.15 (3.70) in the placebo, evobrutinib 25mg QD, 75mg QD and 75mg BID groups, respectively. Compared to placebo, T1 Gd+ lesions per scan were significantly reduced with evobrutinib 75mg QD (lesion rate ratio [RR]=0.30; p=0.0015) and 75mg BID (RR=0.44; p=0.0313), but not 25mg QD (RR=1.45; p=0.295), with evidence of a dose-response relationship (trend test p=0.0011).

"The results of this study highlight the potential of BTK inhibitors as an oral disease-modifying treatment for relapsing MS," said Dr. Xavier Montalban, Professor of Medicine and Department Division Director, Neurology, at the University of Toronto and Director of the MS Centre at St. Michael's Hospital. "These findings suggest that the dual mechanism of action of evobrutinib, which impacts pathogenic adaptive and innate immune cells in multiple sclerosis, could translate into clinical efficacy."

Evobrutinib also led to clinically relevant decreases in annualized relapse rate (ARR). A reduction in ARR was seen with evobrutinib 75mg QD (0.13; p=0.09) and 75mg BID (0.08; p=0.06) versus placebo (0.37), with evidence of a dose-response relationship (trend test p=0.01).

An additional secondary endpoint examined the total number of T2 lesions as assessed by MRI. Mean (SD) new or enlarging T2 lesions (weeks 12-24) was 5.96 (6.99), 6.52 (11.57), 3.41 (10.75) and 2.19 (4.72) in the placebo, evobrutinib 25mg QD, 75mg QD and 75mg BID groups, respectively. Compared to placebo, new or enlarging T2 lesions per scan were significantly reduced with evobrutinib 75mg BID (RR=0.42; p=0.019).

treatment-related TEAEs (>5%) included increased ALT, AST and lipase in the 75 mg BID group; these events were reversible and asymptomatic. The percentage of shifts from Grade 0 to Grade 3 or greater in ALT were 1.9%, 5.7%, 2.1% and 6.1% in the the placebo, evobrutinib 25mg QD, 75mg QD and 75mg BID groups, respectively.

The results, which include the dimethyl fumarate (240mg BID) reference arm, are being presented in a late-breaking oral presentation, "Primary Analysis of a Randomised, Placebo-Controlled, Phase II Study of the Bruton's Tyrosine Kinase Inhibitor Evobrutinib (M2951) in Patients with Relapsing Multiple Sclerosis" at ECTRIMS 2018 in Berlin, Germany, on October 12, 2018 at 2:15pm CET. A recording of the session will be available after the congress on onlinelibrary.ectrims-congress.eu.

The Company presented three additional posters on evobrutinib and a total of 23 abstracts from its MS portfolio at ECTRIMS, underscoring the company's rich legacy in advancing MS treatment and ongoing commitment to future therapies.

For more information about the data presented at ECTRIMS, please visit https://www.ectrims-congress.eu/2018.html.

About Evobrutinib

Evobrutinib (M2951) is in clinical development to investigate its potential as a treatment for multiple sclerosis (MS), rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). 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

About the Evobrutinib Multiple Sclerosis Phase II Study

This double-blind, placebo-controlled, 48-week, Phase II study evaluates the safety and efficacy of evobrutinib in patients aged 18–65 years with relapsing-remitting multiple sclerosis (RRMS) or secondary progressive multiple sclerosis (SPMS) with superimposed relapses. Patients were randomized to evobrutinib 25mg QD, 75mg QD, 75mg BID, PBO or open-label dimethyl fumarate (240mg BID; reference arm). The primary endpoint was the sum of T1 Gd+ lesions at weeks 12, 16, 20, and 24. Key secondary endpoints included annualised relapse rate (ARR) at week 24 and safety. Primary analysis (evobrutinib groups versus PBO) was planned when all patients reached 24 weeks of treatment or prematurely discontinued. For more information about the study, visit ClinicalTrials.gov.

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.

EMD Serono, Inc. and Multiple Sclerosis

For more than 20 years, EMD Serono has been relentlessly focused on understanding the journey people living with MS face in order to create a meaningful, positive experience for them and the broader MS community. However, there is still much that is unknown about this complex and unpredictable disease. EMD Serono is digging deeper to advance the science and reconstruct a new understanding of MS, inside and out. We are committed to delivering solutions that improve the lives of all those affected by MS. www.GetCloserToMS.com

About EMD Serono, Inc.

EMD Serono - the biopharmaceutical business of Merck KGaA, Darmstadt, Germany, in the U.S. and Canada – is engaged in the discovery, research and development of medicines for patients with difficult to treat diseases. The business is committed to transforming lives by developing and delivering meaningful solutions that help address the therapeutic and support needs of individual patients. Building on a proven legacy and deep expertise in neurology, fertility and endocrinology, EMD Serono is developing potential new oncology and immuno-oncology medicines while continuing to explore potential therapeutic options for diseases such as

home state of Massachusetts. www.emdserono.com

For further information: Alice McGrail 1-781-681-2886

Two-Year Update of Pivotal JAVELIN Merkel 200 Trial Shows Continued Durable Responses with BAVENCIO® (avelumab)

ASCO Abstract #
Avelumab: 9507, 9537

Two-year follow-up data on meaningful durable responses, overall survival (OS) and progression-free survival (PFS) to be presented in patients with metastatic Merkel cell carcinoma (mMCC), a rare and aggressive type of skin cancer

Chicago, Illinois, June 4, 2018 – Merck KGaA, Darmstadt, Germany, which operates its biopharmaceutical business as EMD Serono in the US and Canada, and Pfizer Inc. (NYSE: PFE) today announced that updated efficacy and safety data from the pivotal JAVELIN Merkel 200 trial of BAVENCIO® (avelumab) in patients with metastatic Merkel cell carcinoma (mMCC), will be presented as an oral abstract session at the 54th American Society of Clinical Oncology

meaningful durable responses and stable rates of progression-free survival (PFS) and overall survival (OS) from previous analyses in patients who responded to this treatment. Clinical activity was observed across all patient subgroups, irrespective of PD-L1 expression in tumor tissue or Merkel cell polyomavirus status. The safety profile for BAVENCIO in this trial has not changed with longer follow-up and remains consistent with that observed in the overall JAVELIN clinical development program.

"These efficacy and safety results build upon the data that supported our FDA approval," said Luciano Rossetti, M.D., Executive Vice President, Global Head of Research & Development at the Biopharma business of Merck KGaA, Darmstadt, Germany. "Alongside our other data at ASCO, this two-year analysis is a significant advance in our understanding of the utility of BAVENCIO in MCC patients."

In JAVELIN Merkel 200 – an open-label, single-arm Phase II study – patients with histologically confirmed mMCC whose disease had progressed on or after chemotherapy administrated for distant metastatic disease received BAVENCIO 10 mg/kg intravenously every two weeks until disease progression or unacceptable toxicity. Eighty-eight patients were followed for a median of 29.2 months (range 24.8–38.1 months). The confirmed overall response rate (ORR) of 33% (95% confidence interval [CI] 23.3–43.8; complete response in 11.4%) remained unchanged from previous analyses reported at both one year and 18 months. Responses remained ongoing in 19 of 29 patients who responded to treatment, including 12 patients whose duration of response exceeded two years. Durable responses led to stable rates of PFS (29% at 12 months, 29% at 18 months and 26% at 24 months). Median OS was 12.6 months (95% CI 7.5–17.1) and the two-year OS rate was 36% (50% at 12 months and 39% at 18 months). With a minimum follow-up of two years, no new safety signals were identified for BAVENCIO and was consistent with prior reports. Sixty-seven patients (76.1%) had a treatment-related adverse event (TRAE), 10 patients (11.4%) had a Grade 3 or less TRAE and 20 patients (22.7%) had an immune-related adverse event. No treatment-related deaths occurred.

"These results represent a key milestone for patients with mMCC, as chemotherapy has historically been the only treatment option for this devastating disease," said Chris Boshoff, M.D., Ph.D., Senior Vice President and Head of Immuno-Oncology, Early Development and Translational Oncology, Pfizer Global Product Development. "These data, alongside the additional real-world data which are also being presented at ASCO, strengthen our confidence in BAVENCIO as a treatment option for this rare and aggressive skin cancer."

program for BAVENCIO as a second-line treatment for patients with mMCC will be presented. These data will be presented during a poster session on Monday, June 4 from 1:15–4:45 p.m. CDT.

The alliance's JAVELIN clinical development program involves at least 30 clinical programs, including seven Phase III trials, and nearly 8,300 patients across more than 15 tumor types.

BAVENCIO® (avelumab) was first approved in the US in 2017 by the US Food and Drug Administration (FDA) for the treatment of adults and pediatric patients 12 years and older with metastatic Merkel cell carcinoma (mMCC). In addition to the FDA accelerated approval in mMCC, avelumab is also approved in the US under accelerated approval for the treatment of patients with locally advanced or metastatic urothelial carcinoma (UC) who have disease progression during or following platinum-containing chemotherapy, or who have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy. These indications are approved under accelerated approval based on tumor response rate and duration of response. Continued approval for these indications may be contingent upon verification and description of clinical benefit in confirmatory trials.

About JAVELIN Merkel 200

JAVELIN Merkel 200 is an international, multicenter, open-label, single-arm Phase II study of BAVENCIO conducted in 88 patients with metastatic MCC. Patients in this study were generally elderly (median age was 72.5 years, range 33–88 years) and pre-treated, with at least one line of chemotherapy (one [59.1%], two [29.5%] or three or more [11.4%] previous treatments). Patients received BAVENCIO 10 mg/kg intravenously once every two weeks. The protocol-defined analysis set for efficacy and safety consisted of all patients who received at least one dose of study treatment. The cut-off date for the planned primary analysis was six months after start of study treatment of the last patient. The primary endpoint of the study was confirmed best overall response according to RECIST v1.1 and assessed by an independent review committee. Secondary endpoints were duration of response, PFS, OS, response status by RECIST at six and 12 months, safety and tolerability, pharmacokinetics, and immunogenicity of BAVENCIO.

About Avelumab

blocking the interaction of PD-L1 with PD-1 receptors, avelumab has been shown to release the suppression of the T cell-mediated antitumor immune response in preclinical models.2-4 Avelumab has also been shown to induce NK cell-mediated direct tumor cell lysis via antibody-dependent cell-mediated cytotoxicity (ADCC) in vitro.4-6 In November 2014, Merck KGaA, Darmstadt, Germany, and Pfizer announced a strategic alliance to co-develop and co-commercialize avelumab.

Approved Indications in the US

The FDA granted accelerated approval for avelumab (BAVENCIO®) for the treatment of (i) adults and pediatric patients 12 years and older with metastatic Merkel cell carcinoma (mMCC) and (ii) patients with locally advanced or metastatic urothelial carcinoma (mUC) who have disease progression during or following platinum-containing chemotherapy, or have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy. These indications are approved under accelerated approval based on tumor response rate and duration of response. Continued approval for these indications may be contingent upon verification and description of clinical benefit in confirmatory trials.

Important Safety Information from the US FDA Approval Label

BAVENCIO can cause **immune-mediated pneumonitis**, including fatal cases. Monitor patients for signs and symptoms of pneumonitis, and evaluate suspected cases with radiographic imaging. Administer corticosteroids for Grade 2 or greater pneumonitis. Withhold BAVENCIO for moderate (Grade 2) and permanently discontinue for severe (Grade 3), life-threatening (Grade 4), or recurrent moderate (Grade 2) pneumonitis. Pneumonitis occurred in 1.2% (21/1738) of patients, including one (0.1%) patient with Grade 5, one (0.1%) with Grade 4, and five (0.3%) with Grade 3.

BAVENCIO can cause **immune-mediated hepatitis**, including fatal cases. Monitor patients for abnormal liver tests prior to and periodically during treatment. Administer corticosteroids for Grade 2 or greater hepatitis. Withhold BAVENCIO for moderate (Grade 2) immune-mediated hepatitis until resolution and permanently discontinue for severe (Grade 3) or life-threatening

3.

BAVENCIO can cause **immune-mediated colitis**. Monitor patients for signs and symptoms of colitis. Administer corticosteroids for Grade 2 or greater colitis. Withhold BAVENCIO until resolution for moderate or severe (Grade 2 or 3) colitis, and permanently discontinue for life-threatening (Grade 4) or recurrent (Grade 3) colitis upon reinitiation of BAVENCIO. Immune-mediated colitis occurred in 1.5% (26/1738) of patients, including seven (0.4%) with Grade 3.

BAVENCIO can cause **immune-mediated endocrinopathies**, including adrenal insufficiency, thyroid disorders, and type 1 diabetes mellitus.

Monitor patients for signs and symptoms of **adrenal insufficiency** during and after treatment, and administer corticosteroids as appropriate. Withhold BAVENCIO for severe (Grade 3) or life-threatening (Grade 4) adrenal insufficiency. Adrenal insufficiency was reported in 0.5% (8/1738) of patients, including one (0.1%) with Grade 3.

Thyroid disorders can occur at any time during treatment. Monitor patients for changes in thyroid function at the start of treatment, periodically during treatment, and as indicated based on clinical evaluation. Manage hypothyroidism with hormone replacement therapy and hyperthyroidism with medical management. Withhold BAVENCIO for severe (Grade 3) or life-threatening (Grade 4) thyroid disorders. Thyroid disorders, including hypothyroidism, hyperthyroidism, and thyroiditis, were reported in 6% (98/1738) of patients, including three (0.2%) with Grade 3.

Type 1 diabetes mellitus including diabetic ketoacidosis: Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Withhold BAVENCIO and administer antihyperglycemics or insulin in patients with severe or life-threatening (Grade ≥ 3) hyperglycemia, and resume treatment when metabolic control is achieved. Type 1 diabetes mellitus without an alternative etiology occurred in 0.1% (2/1738) of patients, including two cases of Grade 3 hyperglycemia.

BAVENCIO can cause **immune-mediated nephritis and renal dysfunction**. Monitor patients for elevated serum creatinine prior to and periodically during treatment. Administer corticosteroids for Grade 2 or greater nephritis. Withhold BAVENCIO for moderate (Grade 2) or severe (Grade 3) nephritis until resolution to Grade 1 or lower. Permanently discontinue

BAVENCIO can result in **other severe and fatal immune-mediated adverse reactions** involving any organ system during treatment or after treatment discontinuation. For suspected immune-mediated adverse reactions, evaluate to confirm or rule out an immune-mediated adverse reaction and to exclude other causes. Depending on the severity of the adverse reaction, withhold or permanently discontinue BAVENCIO, administer high-dose corticosteroids, and initiate hormone replacement therapy, if appropriate. Resume BAVENCIO when the immune-mediated adverse reaction remains at Grade 1 or lower following a corticosteroid taper. Permanently discontinue BAVENCIO for any severe (Grade 3) immune-mediated adverse reaction that recurs and for any life-threatening (Grade 4) immune-mediated adverse reaction. The following clinically significant immune-mediated adverse reactions occurred in less than 1% of 1,738 patients treated with BAVENCIO: myocarditis with fatal cases, myositis, psoriasis, arthritis, exfoliative dermatitis, erythema multiforme, pemphigoid, hypopituitarism, uveitis, Guillain-Barré syndrome, and systemic inflammatory response.

BAVENCIO can cause severe (Grade 3) or life-threatening (Grade 4) **infusion-related reactions**. Patients should be premedicated with an antihistamine and acetaminophen prior to the first 4 infusions and for subsequent doses based upon clinical judgment and presence/severity of prior infusion reactions. Monitor patients for signs and symptoms of infusion-related reactions, including pyrexia, chills, flushing, hypotension, dyspnea, wheezing, back pain, abdominal pain, and urticaria. Interrupt or slow the rate of infusion for mild (Grade 1) or moderate (Grade 2) infusion-related reactions. Permanently discontinue BAVENCIO for severe (Grade 3) or life-threatening (Grade 4) infusion-related reactions. Infusion-related reactions occurred in 25% (439/1738) of patients, including three (0.2%) patients with Grade 4 and nine (0.5%) with Grade 3.

BAVENCIO can cause **fetal harm** when administered to a pregnant woman. Advise patients of the potential risk to a fetus including the risk of fetal death. Advise females of childbearing potential to use effective contraception during treatment with BAVENCIO and for at least 1 month after the last dose of BAVENCIO. It is not known whether BAVENCIO is excreted in human milk. Advise a lactating woman **not to breastfeed** during treatment and for at least 1 month after the last dose of BAVENCIO due to the potential for serious adverse reactions in breastfed infants.

(23%), nausea (22%), infusion-related reaction (22%), rash (22%), decreased appetite (20%), and peripheral edema (20%).

Selected treatment-emergent laboratory abnormalities (all grades, ≥ 20%) in patients with metastatic MCC were lymphopenia (49%), anemia (35%), increased aspartate aminotransferase (34%), thrombocytopenia (27%), and increased alanine aminotransferase (20%).

The most common adverse reactions (all grades, ≥ 20%) **in patients with locally advanced or metastatic urothelial carcinoma (UC)** were fatigue (41%), infusion-related reaction (30%), musculoskeletal pain (25%), nausea (24%), decreased appetite/hypophagia (21%), and urinary tract infection (21%).

Selected laboratory abnormalities (Grades 3-4, ≥ 3%) in patients **with locally advanced or metastatic UC** were hyponatremia (16%), increased gamma-glutamyltransferase (12%), lymphopenia (11%), hyperglycemia (9%), increased alkaline phosphatase (7%), anemia (6%), increased lipase (6%), hyperkalemia (3%), and increased aspartate aminotransferase (3%).

Please see full US Prescribing Information and Medication Guide available at www.BAVENCIO.com.

Alliance between Merck KGaA, Darmstadt, Germany, and Pfizer Inc., New York, US

Immuno-oncology is a top priority for Merck KGaA, Darmstadt, Germany, and Pfizer. The global strategic alliance between Merck KGaA, Darmstadt, Germany, and Pfizer enables the companies to benefit from each other's strengths and capabilities and further explore the therapeutic potential of avelumab, an anti-PD-L1 antibody initially discovered and developed by Merck KGaA, Darmstadt, Germany. The immuno-oncology alliance is jointly developing and commercializing avelumab and advancing Pfizer's PD-1 antibody. The alliance is focused on developing high-priority international clinical programs to investigate avelumab, as a monotherapy, as well as combination regimens, and is striving to find new ways to treat cancer.

All Merck KGaA, Darmstadt, Germany, Press Releases are distributed by e-mail at the same time they become available on the Merck KGaA, Darmstadt, Germany, Website. Please go to

About Merck KGaA, Darmstadt, Germany

Merck KGaA, Darmstadt, Germany, is a leading science and technology company in healthcare, life science and performance materials. More than 53,000 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 2017, Merck KGaA, Darmstadt, Germany, generated sales of € 15.3 billion in 66 countries.

Founded in 1668, Merck KGaA, Darmstadt, Germany, is the world's oldest pharmaceutical and chemical company. The founding family remains the majority owner of the publicly listed corporate group. Merck KGaA, Darmstadt, Germany holds the global rights to the "Merck" name and brand except in the United States and Canada, where the company operates as EMD Serono, MilliporeSigma and EMD Performance Materials.

About EMD Serono, Inc.

EMD Serono is the biopharmaceutical business of Merck KGaA, Darmstadt, Germany – a leading science and technology company – in the US and Canada focused exclusively on specialty care. For more than 40 years, the business has integrated cutting-edge science, innovative products and industry-leading patient support and access programs. EMD Serono has deep expertise in neurology, fertility and endocrinology, as well as a robust pipeline of potential therapies in oncology, immuno-oncology and immunology as R&D focus areas. Today, the business has 1,200 employees around the country with commercial, clinical and research operations based in the company's home state of Massachusetts.

www.emdserono.com

Pfizer Inc.: Working together for a healthier world®

At Pfizer, we apply science and our global resources to bring therapies to people that extend and significantly improve their lives. We strive to set the standard for quality, safety and value in the discovery, development and manufacture of health care products. Our global portfolio includes medicines and vaccines as well as many of the world's best-known consumer health care products. Every day, Pfizer colleagues work across developed and emerging markets to

biopharmaceutical companies, we collaborate with health care providers, governments and local communities to support and expand access to reliable, affordable health care around the world. For more than 150 years, we have worked to make a difference for all who rely on us. We routinely post information that may be important to investors on our website at www.pfizer.com. In addition, to learn more, please visit us at www.pfizer.com and follow us on Twitter at @Pfizer and @Pfizer_News, LinkedIn, YouTube and like us on Facebook at Facebook.com/Pfizer.

Pfizer Disclosure Notice

The information contained in this release is as of June 4, 2018. Pfizer assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments.

This release contains forward-looking information about avelumab, the Merck KGaA, Darmstadt, Germany-Pfizer Alliance involving anti-PD-L1 and anti-PD-1 therapies, and clinical development plans, including their potential benefits, that involves substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Risks and uncertainties include, among other things, uncertainties regarding the commercial success of avelumab; the uncertainties inherent in research and development, including the ability to meet anticipated clinical study commencement and completion dates and regulatory submission dates, as well as the possibility of unfavorable study results, including unfavorable new clinical data and additional analyses of existing clinical data; risks associated with interim data; the risk that clinical trial data are subject to differing interpretations, and, even when we view data as sufficient to support the safety and/or effectiveness of a product candidate, regulatory authorities may not share our views and may require additional data or may deny approval altogether; whether regulatory authorities will be satisfied with the design of and results from our clinical studies; whether and when any drug applications may be filed in any jurisdictions for potential indications for avelumab, combination therapies or other product candidates; whether and when regulatory authorities in any jurisdictions where applications are pending or may be submitted for avelumab, combination therapies or other product candidates may approve any such applications, which will depend on the assessment by such regulatory authorities of the benefit-risk profile suggested by the totality of the efficacy and safety information submitted; decisions by regulatory authorities

A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2016, and in its subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information and Factors That May Affect Future Results", as well as in its subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and Exchange Commission and available at www.sec.gov and www.pfizer.com.

References

1. Nghiem P. Two-year efficacy and safety update from JAVELIN Merkel 200 part A: a phase 2 study of avelumab in metastatic Merkel cell carcinoma progressed on chemotherapy. Abstract 9507. To be presented at ASCO 2018, June 1-4, 2018. Chicago, IL.

2. Dolan DE, Gupta S. PD-1 pathway inhibitors: changing the landscape of cancer immunotherapy. Cancer Control 2014;21(3):231–7.

3. Dahan R, Sega E, Engelhardt J, et al. FcγRs modulate the anti-tumor activity of antibodies targeting the PD-1/PD-L1 axis. Cancer Cell 2015;28(3):285–95.

4. Boyerinas B, Jochems C, Fantini M, et al. Antibody-dependent cellular cytotoxicity activity of a novel anti-PD-L1 antibody avelumab (MSB0010718C) on human tumor cells. Cancer Immunol Res 2015;3(10):1148-57.

5. Kohrt HE, Houot R, Marabelle A, et al. Combination strategies to enhance antitumor ADCC. Immunotherapy 2012;4(5):511–27.

6. Hamilton G, Rath B. Avelumab: combining immune checkpoint inhibition and antibody-dependent cytotoxicity. Expert Opin Biol Ther 2017;17(4):515–23.

Up to 10-Years of Follow-up Data Reaffirm Safety Profile of Investigational Cladribine Tablets

EXPLORE MORE

- **Real-world evidence and longer clinical trial follow-up show no increased incidence of serious adverse events**
- **Additional post-hoc data analyses support sustained efficacy of cladribine tablets in patients with relapsing MS with high disease activity**

ROCKLAND, Mass, October 10, 2018 – EMD Serono, the biopharmaceutical business of Merck KGaA, Darmstadt, Germany, in the U.S. and Canada, today announced the presentation of new data for cladribine tablets at the 34th Congress of the European Committee for Treatment and Research In Multiple Sclerosis (ECTRIMS) in Berlin, Germany. The data presented at ECTRIMS 2018 build on the existing real-world and clinical evidence around the safety and efficacy of cladribine tablets and reaffirm the benefit-risk profile of the oral treatment, which is taken for a maximum of 20 days over two years.

treatment emergent adverse event (TEAE) profile associated with cladribine tablets in patients with relapsing MS (RMS) was confirmed, with no new safety findings. The integrated analysis is based on patients followed for up to 10 years[1] (923 patients received cladribine tablets 3.5 mg/kg; 641 patients received placebo). As part of this analysis, an overview of the post-approval safety data from the EU approval on August 2017 to July 2018 also showed no new safety or tolerability signals for cladribine tablets.

Adjusted adverse events incidences per 100 patient-years (Adj-AE per 100PY) for those experiencing ≥1 serious TEAE were 3.88 for cladribine tablets and 3.24 for placebo in the two-year update, versus 4.00 for cladribine tablets and 3.57 for placebo reported previously. In addition to serious TEAE, Adj-AE per 100PY were also analyzed for serious lymphopenia, serious infection and infestations, serious herpes zoster, serious neoplasm, benign, malignant and unspecified. Results showed no new adverse events for cladribine tablets have been seen since the first approval in Europe last year. A total of 47 adverse drug reactions were reported from post-approval sources, none of which were new safety findings.

"In my opinion, we are entering an era of immune reconstitution therapy (IRT) in MS, where therapy is intermittently administered but which has an effect on the disease that lasts much longer than the period of dosing," said Prof. Gavin Giovannoni, a lead investigator in the CLARITY studies and Chair of Neurology, Barts and The London School of Medicine and Dentistry. "The new data presented suggest cladribine tablets delivers sustained efficacy well beyond the dosing regimen with no new safety signals found in the long-term."

Post hoc analyses of CLARITY EXT show that following 20 days of treatment with cladribine tablets 3.5 mg/kg in Years 1 and 2, annual NEDA-3 status was sustained in patients treated with cladribine tablets 3.5 mg/kg or placebo up to the end of Year 4[2]. There is also an analysis of EDSS, and clinical and MRI outcomes in patients with high disease activity.

A further *post hoc* analysis of CLARITY data indicated that the relapse and MRI efficacy of cladribine tablets does not appear to be impacted by age, consistent with previous similar analyses[3]. Data from this study showed that qualifying relapses were reduced in RMS patients aged below and above 45. With regards to MRI measures, the data showed that the number of cumulative new T1 Gd+ and active T2 lesions at Week 96 was reduced with cladribine tablets compared to placebo in both age groups[3].

R&D for EMD Serono. “With more and more patients able to access cladribine tablets globally, it becomes increasingly important for us to invest in scientific research that helps to clarify how patients may benefit from our therapies.”

---

[1]Cook S et al. Updated safety analysis of Cladribine Tablets in the treatment of patients with multiple sclerosis. Presentation at ECTRIMS 2018

[2]Vermersch P et al. Sustained efficacy in relapsing remitting multiple sclerosis following switch to placebo treatment from Cladribine Tablets in patients with high disease activity at baseline. Presentation at ECTRIMS 2018

[3]Giovannoni G et al. An exploratory analysis of the efficacy of Cladribine Tablets 3.5mg/kg in patients with relapsing multiple sclerosis stratified according to age above and below 45 years in the CLARITY study. Presentation at ECTRIMS 2018

About Cladribine Tablets
Cladribine tablets is an investigational short-course oral therapy that is thought to selectively target lymphocytes which may be integral to the pathological process of relapsing MS (RMS). Cladribine tablets is currently under clinical investigation and not approved for the treatment for any use in the United States. MAVENCLAD® has received approvals for patients with highly active RMS as defined by clinical or imaging features in the European Union (EU), Israel, Argentina, United Arab Emirates, Chile and Lebanon. MAVENCLAD is also approved in Canada and Australia.

The clinical development program for cladribine tablets includes:

- The CLARITY (Cladribine Tablets Treating MS Orally) study: a two-year Phase III placebo-controlled study designed to evaluate the efficacy and safety of cladribine tablets as a monotherapy in patients with RRMS.
- The CLARITY extension study: a Phase III placebo-controlled study following on from the CLARITY study, which evaluated the safety and efficacy of cladribine tablets over two additional years beyond the two-year CLARITY study, according to the treatment assignment scheme for years 3 and 4.
- The ORACLE MS (Oral Cladribine in Early MS) study: a two-year Phase III placebo-controlled study designed to evaluate the efficacy and safety of cladribine tablets as a monotherapy in patients at risk of developing MS (patients who have experienced a first clinical event suggestive of MS).

evaluate the safety and tolerability of adding cladribine tablets treatment to patients with relapsing forms of MS, who have experienced breakthrough disease while on established interferon-beta therapy.

- PREMIERE (Prospective Observational Long-term Safety Registry of Multiple Sclerosis) study: a long-term follow-up safety registry of multiple sclerosis patients who participated in cladribine tablets clinical studies.

The clinical development program of cladribine tablets in MS comprises close to 12,000 patient years of data with over 2,700 patients included in the clinical trial program, and up to 10 years of follow-up in some patients.

In the two-year CLARITY study, the most commonly reported adverse event (AE) in patients treated with cladribine tablets was lymphopenia. The incidence of infections was 48.3% with cladribine tablets and 42.5% with placebo, with 99.1% and 99.0% respectively rated mild-to-moderate by investigators.

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.

EMD Serono, Inc. and Multiple Sclerosis
For more than 20 years, EMD Serono has been relentlessly focused on understanding the journey people living with MS face in order to create a meaningful, positive experience for them and the broader MS community. However, there is still much that is unknown about this complex and unpredictable disease. EMD Serono is digging deeper to advance the science and reconstruct a new understanding of MS, inside and out. We are committed to delivering solutions that improve the lives of all those affected by MS. www.GetCloserToMS.com

About EMD Serono, Inc.
EMD Serono - the biopharmaceutical business of Merck KGaA, Darmstadt, Germany, in the U.S. and Canada – is engaged in the discovery, research and development of medicines for patients with difficult to treat diseases. The business is committed to transforming lives by developing and delivering meaningful solutions that help address the therapeutic and support needs of individual patients. Building on a proven legacy and deep expertise in neurology, fertility and endocrinology, EMD Serono is developing potential new oncology and immuno-oncology medicines while continuing to explore potential therapeutic options for diseases such as psoriasis, lupus and multiple sclerosis. Today, the business has approximately 1,300 employees around the country with commercial, clinical and research operations based in the company's home state of Massachusetts. www.emdserono.com

For further information: Alice McGrail 1-781-681-2886

COMPANY

LEADERSHIP TEAM

PARTNERING

PRESS

CONTACT US

COMPLIANCE & TRANSPARENCY

THERAPEUTIC AREAS

YOUR REQUESTS