Merck KGaA
Darmstadt, Germany

News Release

Your Contact
Brenda Mulligan +978-821-5345

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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

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

- **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**
- **M7824 continues to be explored in tumors and settings where addressing both mechanisms could lead to improved clinical outcomes**

Darmstadt, Germany, June 4, 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 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

Frankfurter Strasse 250
64293 Darmstadt · Germany
Hotline +49 6151 72-5000
www.emdgroup.com

Head Media Relations -62445
Spokesperson: -9591 / -7144 / -6328
Fax +49 6151 72 3138
media.relations@emdgroup.com

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 common events were skin and subcutaneous tissue disorders. Eight patients (10%) discontinued treatment due to TRAEs.

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	Lead Author	Abstract #	Presentation Date / Time (CDT)	Location
M7824				
Poster Discussion				
Results from a second-line (2L) NSCLC cohort treated with M7824 (MSB0011359C), a bifunctional fusion protein targeting PD-L1 and TGF-β	Luis G. Paz-Ares	9017	Sun, Jun 03, 11:30 a.m. – 12:45 p.m.	Arie Crown Theater
Oral Presentation				
Safety and activity of M7824, a bifunctional fusion protein targeting PD-L1 and TGF- β, in patients with HPV associated cancers	Julius Strauss	3007	Sat, Jun 02, 5:12 p.m. – 5:24 p.m.	Hall B1
Poster Session				
Selection of the recommended Phase 2 dose (RP2D) for M7824	Yulia Vugmeyster	2566	Mon, Jun 04, 8:00 a.m. – 11:30 a.m.	Hall A

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(MSB0011359C), a bifunctional fusion protein targeting TGF-β and PD-L1				
A sequential cohort study of combination immunotherapy with BN-brachyury vaccine, M7824, ALT-803 and epacadostat in metastatic castration-resistant prostate cancer (mCRPC) (QuEST1)	Jason Redman	TPS3130	Mon, Jun 04, 8:00 a.m. – 11:30 a.m.	Hall A

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 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.