May 15, 2019

Merck Data at ASCO 2019 Showcase Multiple Innovative Molecules with Potential to Impact Unmet Needs in Cancer Care

- New biomarker analyses for BAVENCIO® (avelumab) in combination with axitinib in first-line renal cell carcinoma (RCC)
- Data presented across several modalities and mechanisms showcase the scientific innovation and diversity of the company’s pipeline, which includes bintrafusp alfa‡ (M7824) and tepotinib†

Darmstadt, Germany, May 15, 2019 – Merck, a leading science and technology company, today announced that data across several modalities and mechanisms targeting difficult-to-treat cancers will be presented at the 2019 American Society of Clinical Oncology (ASCO) Annual Meeting, May 31–June 4, Chicago, IL, US. New data will be presented for BAVENCIO® (avelumab) and ERBITUX® (cetuximab), including rational combinations with chemotherapy, radiation therapy and other targeted agents to try to identify new ways to improve patient outcomes. This includes an oral presentation of data defining biomarkers that differentiate therapy-specific outcomes in patients with advanced renal cell carcinoma (RCC), and who have been treated first-line with BAVENCIO® (avelumab) in combination with axitinib. Abstracts also showcase the scientific innovation and diversity of Merck’s...
pipeline, with results from a number of high-priority clinical development programs, including tepotinib†, bintrafusp alfa‡ (M7824) and the company’s comprehensive DNA Damage Response (DDR) portfolio.

“At this year’s ASCO meeting we continue to demonstrate the breadth and depth of our oncology and immuno-oncology portfolio. We will present examples of the latest precision medicine and biomarker research and some of the most exciting mechanisms being investigated today, including tepotinib and our first-in-class bifunctional fusion protein immunotherapy, bintrafusp alfa,” said Luciano Rossetti, Global Head of Research & Development for the Biopharma business of Merck. “Merck’s oncology pipeline has significant promise in the near term through our late-stage priority programs, and our early pipeline includes several potentially groundbreaking modalities. We look forward to sharing the latest science with the global oncology community.”

For BAVENCIO® (avelumab), Merck will share data from five studies across tumor types including Merkel cell carcinoma, RCC, hepatocellular carcinoma and urothelial carcinoma. This includes an oral presentation of biomarker analyses of baseline tumor samples from the Phase III JAVELIN Renal 101 trial in previously untreated patients with advanced RCC. The trial indicated that PD-L1 expression (≥1% immune cells) was associated with the longest progression-free survival (PFS) in the avelumab plus axitinib arm and the shortest PFS in the sunitinib arm (HR, 0.63; 95% CI, 0.49, 0.81). An analysis of relevant gene expression signatures (GES) indicated that in the avelumab plus axitinib arm, PFS was enhanced in immune GES–positive patients vs those in the negative group (HR, 0.63; 95% CI, 0.46, 0.86; 2-sided p=0.004), and vs those in an independent dataset (JAVELIN Renal 100; Choueiri, Lancet Oncol, 2018) (HR, 0.46; 95% CI, 0.20, 1.05; 2-sided p=0.064). The combination demonstrated a safety and tolerability profile consistent with the known safety profiles of each drug alone. The most common adverse reactions (≥20%) were diarrhea, fatigue, hypertension, musculoskeletal pain, nausea, mucositis, palmar-planter erythrodysesthesia, dysphonia, decreased appetite, hypothyroidism, rash, hepatotoxicity, cough, dyspnea, abdominal pain, and headache. Serious adverse reactions occurred in 35% of patients receiving BAVENCIO® (avelumab) in combination with axitinib. The incidence of major adverse
cardiovascular events (MACE) was higher with BAVENCIO® (avelumab) in combination with axitinib vs sunitinib.

ERBITUX® (cetuximab) data from a retrospective analysis of overall survival (OS) by subsequent therapy in patients with RAS wild-type metastatic colorectal cancer from the Phase III EPIC study will be presented, to evaluate the effect of post-study therapies (with ERBITUX®, without ERBITUX®, or no subsequent therapy) on OS.

A number of the molecules to be featured were discovered in-house at Merck. This includes tepotinib, an oral MET inhibitor designed to inhibit the oncogenic MET receptor signaling caused by MET (gene) alterations, and bintrafusp alfa, a bifunctional fusion protein designed to simultaneously target two immuno-suppressive pathways. Merck’s partnership with GSK to jointly develop and commercialize bintrafusp alfa, announced in February 2019, is part of the company’s strategic approach to oncology R&D. Together, Merck and GSK aim to rapidly and efficiently progress this molecule, which represents a potential step change in the treatment of cancer.

For tepotinib, promising updated results from the ongoing Phase II VISION study in 85 patients with non-small cell lung cancer (NSCLC) with MET exon 14 skipping mutations (identified by liquid biopsy [LBx] or tumor biopsy [TBx]) will be shared. Results show an overall response rate (ORR) of 51.4% for LBx patients (independent review committee [IRC]-assessed) or 63.9% (investigator-assessed). The ORR for TBx patients was 41.5% (IRC-assessed) or 58.5% (investigator-assessed). Median duration of response was 9.8 (IRC-assessed) or 17.1 months (investigator-assessed) for LBx patients and 12.4 (IRC-assessed) or 14.3 months (investigator-assessed) for TBx patients. Any grade treatment-related adverse events (TRAEs) reported by ≥10% of 69 patients evaluable for safety were peripheral edema (47.8%), diarrhea (18.8%), nausea (15.9%) and asthenia (10.1%). No Grade 4 or 5 TRAEs were observed. TRAEs led to permanent discontinuation in two (2.9%) patients (one interstitial lung disease, one diarrhea and nausea). These data continue to mature, and an updated data cut from the VISION study will be given as an oral presentation at the ASCO meeting on Monday, June 3.
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For bintrafusp alfa, a trial-in-progress poster will be shared on the open-label study of bintrafusp alfa vs pembrolizumab as a first-line treatment in patients with PD-L1-expressing advanced NSCLC.

Merck takes a personalized approach to R&D, and precision medicine has long been a priority. Abstracts being presented at ASCO also include biomarker research programs that aim to help identify the patients most likely to benefit from specific treatments so they can achieve the best possible medical outcomes.

*The combination of BAVENCIO and axitinib is approved for the first-line treatment of advanced RCC only in the United States. There is no guarantee that avelumab in combination with axitinib will be approved for RCC by any other health authority worldwide.

†Tepotinib is the recommended International Nonproprietary Name (INN) for the MET kinase inhibitor (MSC21561191). Tepotinib is currently under clinical investigation and not approved for any use anywhere in the world.

‡Bintrafusp alfa is the proposed International Nonproprietary Name (INN) for the bifunctional immunotherapy M7824. Bintrafusp alfa is currently under clinical investigation and not approved for any use anywhere in the world.

Notes to Editors

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

<table>
<thead>
<tr>
<th>Title</th>
<th>Lead Author</th>
<th>Abstract #</th>
<th>Presentation Date / Time (CDT)</th>
<th>Location</th>
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</thead>
<tbody>
<tr>
<td>BAVENCIO® (avelumab)</td>
<td></td>
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<tr>
<td>Oral Session</td>
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<tr>
<td>Biomarker analyses from JAVELIN Renal 101: avelumab + axitinib (A+Ax) vs sunitinib (S) in advanced renal cell carcinoma (aRCC)</td>
<td>T.K. Choueiri</td>
<td>101</td>
<td>Sat, Jun 1, 8:00 AM – 9:30 AM (8:12 AM – 8:24 AM lecture time)</td>
<td>Hall D1</td>
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<tr>
<td>Poster Sessions</td>
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<td>5-factor prognostic model for survival of patients with metastatic urothelial carcinoma receiving 3 different post-platinum PD-L1 inhibitors</td>
<td>G. Sonpavde</td>
<td>4552</td>
<td>Mon, Jun 3, 1:15 PM – 4:15 PM</td>
<td>Hall A</td>
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<tr>
<td>First-line avelumab + axitinib in patients with advanced hepatocellular carcinoma: results from a phase 1b trial (VEGF Liver 100)</td>
<td>M. Kudo</td>
<td>4072</td>
<td>Mon, Jun 3, 8:00 AM – 11:00 AM</td>
<td>Hall A</td>
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### Integrative molecular analysis of metastatic Merkel cell carcinoma to identify predictive biomarkers of response to avelumab

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<tr>
<td>Integrate molecular analysis of metastatic Merkel cell carcinoma to identify predictive biomarkers of response to avelumab</td>
<td>S. Georges</td>
<td>9569</td>
<td>Mon, Jun 3, 1:15 PM – 4:15 PM</td>
<td>Hall A</td>
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### Bintrafusp Alfa Poster Session

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<tbody>
<tr>
<td>Randomized open-label study of M7824 vs pembrolizumab as first-line (1L) treatment in patients with PD-L1 expressing advanced non-small cell lung cancer (NSCLC)</td>
<td>L. Paz-Ares</td>
<td>TPS9114</td>
<td>Sun, Jun 2, 8:00 AM – 11:00 AM</td>
<td>Hall A</td>
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### Discovery Poster Session

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<tr>
<td>Understanding contribution and independence of multiple biomarkers for predicting response to atezolizumab</td>
<td>P.K. Shah</td>
<td>2567</td>
<td>Sat, Jun 1, 8:00 AM – 11:00 AM</td>
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### ERBITUX® (cetuximab) Poster Session

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<tr>
<td>Retrospective Analysis of Overall Survival (OS) by Subsequent Therapy in Patients With RAS-Wild-type (wt) Metastatic Colorectal Cancer (mCRC) Receiving Cetuximab ± Irinotecan</td>
<td>A. Sobrero</td>
<td>3580</td>
<td>Mon, Jun 3, 8:00 AM – 11:00 AM</td>
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### Tepotinib Oral Session

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<tr>
<td>Phase II study of tepotinib in NSCLC patients with METex14 mutations</td>
<td>P.K. Paik</td>
<td>9005</td>
<td>Mon, Jun 3, 8:00 AM – 11:00 AM (9:24 AM – 9:36 AM lecture time)</td>
<td>Hall B1</td>
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**About Tepotinib**

Tepotinib, discovered in-house at Merck, is an investigational oral MET inhibitor that is designed to inhibit the oncogenic MET receptor signaling caused by MET (gene) alterations, including both MET exon 14 skipping mutations and MET amplifications, or MET protein overexpression. It has been designed to have a highly selective mechanism of action, with the potential to improve outcomes in aggressive tumors that have a poor prognosis and harbor these specific alterations.

Tepotinib is currently being investigated in NSCLC and Merck is actively assessing the potential of investigating tepotinib in combination with novel therapies and other tumor indications.

**About Bintrafusp Alfa (M7824)**

Bintrafusp alfa is an investigational bifunctional immunotherapy that is designed to combine a TGF-β trap with the anti-PD-L1 mechanism in one fusion protein. Bintrafusp alfa 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. Bintrafusp alfa is currently in Phase I studies for solid tumors, as well as a randomized Phase II trial.
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to investigate bintrafusp alfa 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 bintrafusp alfa versus pembrolizumab as a monotherapy treatment.

To date, nearly 700 patients have been treated with bintrafusp alfa across more than 10 tumor types in Phase I studies. Encouraging data from the ongoing Phase I studies indicates bintrafusp alfa's potential safety and clinical anti-tumor activity across multiple types of difficult-to-treat cancers, including advanced NSCLC, human papillomavirus-associated cancers, biliary tract cancer and gastric cancer. In addition, in pre-clinical studies bintrafusp alfa demonstrated superior anti-tumor activity, compared with anti-PD-L1 alone or with anti-PD-L1 and TGF-β trap when co-administered. In total, eight high-priority immuno-oncology clinical development studies are ongoing or expected to commence in 2019, including studies in non-small cell lung and biliary tract cancers.

About BAVENCIO® (avelumab)
BAVENCIO is a human anti-programmed death ligand-1 (PD-L1) antibody. BAVENCIO 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, BAVENCIO has been shown to release the suppression of the T cell-mediated antitumor immune response in preclinical models.1-3 BAVENCIO 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 and Pfizer announced a strategic alliance to co-develop and co-commercialize BAVENCIO.

The clinical development program for avelumab, known as JAVELIN, involves at least 30 clinical programs and about 10,000 patients evaluated across more than 15 different tumor types. These tumor types include RCC, gastric/gastro-esophageal junction cancer, head and neck cancer, Merkel cell carcinoma, non-small cell lung cancer, and urothelial carcinoma.

BAVENCIO Approved Indications
In September 2017, the European Commission granted conditional marketing authorization for BAVENCIO as a monotherapy for the treatment of adult patients with metastatic Merkel cell carcinoma (MCC). BAVENCIO is currently approved for patients with MCC in more than 45 countries globally, with the majority of these approvals in a broad indication that is not limited to a specific line of treatment.

BAVENCIO® (avelumab) in combination with axitinib is indicated in the US for the first-line treatment of patients with advanced renal cell carcinoma (RCC).

In the US, 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
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and duration of response. Continued approval for these indications may be contingent upon verification and description of clinical benefit in confirmatory trials.

BAVENCIO Safety Profile from the EU Summary of Product Characteristics (SmPC)
The special warnings and precautions for use for BAVENCIO include infusion-related reactions and immune-related adverse reactions (such as pneumonitis, hepatitis, colitis, endocrinopathies, nephritis and renal dysfunction, and other adverse reactions).

The SmPC list of the most common adverse reactions in patients with solid tumors includes fatigue, nausea, diarrhea, decreased appetite, constipation, infusion-related reactions, and weight loss and vomiting.

Axitinib Important Safety Information from the US FDA Approved Label
In the study of advanced RCC after failure of one prior systemic therapy, the warnings and precautions for axitinib include hypertension, including hypertensive crisis, arterial and venous thrombotic events, hemorrhagic events, cardiac failure, gastrointestinal perforation and fistula, hypothyroidism, wound healing complications, reversible posterior leukoencephalopathy syndrome (RPLS), proteinuria, liver enzyme elevation, hepatic impairment, and fetal harm during pregnancy.

Common adverse events (reported in at least 20% of patients) in patients receiving axitinib were diarrhea, hypertension, fatigue, decreased appetite, nausea, dysphonia, hand-foot syndrome, weight decreased, vomiting, asthenia, and constipation.

About ERBITUX® (cetuximab)
Erbitux® is an 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. Based on in vitro evidence, Erbitux® also targets cytotoxic immune effector cells towards EGFR-expressing tumor cells (antibody-dependent cell-mediated cytotoxicity [ADCC]).

Very commonly reported side effects with Erbitux® include acne-like skin rash, mild to moderate infusion-related reactions and hypomagnesemia.

Erbitux® has already obtained market authorization in 114 countries worldwide for the treatment of RAS wild-type metastatic colorectal cancer and for the treatment of squamous cell carcinoma of the head and neck. Merck licensed the right to market
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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

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About Merck
Merck, a leading science and technology company, operates across healthcare, life science and performance materials. Around 52,000 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 – Merck is everywhere. In 2018, Merck generated sales of €14.8 billion in 66 countries.

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