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BAVENCIO Pivotal Phase III JAVELIN Bladder 100 Results Published in The New England Journal of Medicine

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Not intended for UK-based media

Rockland, MA and New York, US, September 18, 2020 – EMD Serono, the biopharmaceutical business of Merck KGaA, Darmstadt, Germany in the US and Canada, and Pfizer Inc. (NYSE: PFE) today announced the publication of detailed results from the Phase III JAVELIN Bladder 100 study online ahead of print in *The New England Journal of Medicine*. These results were published simultaneously with additional analyses being presented at the European Society for Medical Oncology (ESMO) Virtual Congress 2020 and describe the efficacy of BAVENCIO® (avelumab) as a first-line maintenance treatment across various subgroups of patients with locally advanced or metastatic urothelial carcinoma (UC) and highlight exploratory biomarkers as well as patient-reported outcomes. In June, the US Food and Drug Administration (FDA) approved BAVENCIO for the maintenance treatment of patients with locally advanced or metastatic UC that has not progressed with first-line platinum-containing chemotherapy based on the JAVELIN Bladder 100 results.

In the JAVELIN Bladder 100 study, BAVENCIO plus best supportive care (BSC) significantly extended overall survival (OS) compared with BSC alone in the two primary populations of all randomized patients and patients whose tumors were PD-L1+, and significantly more patients who received BAVENCIO as first-line maintenance were alive at one year.[1] The clinical benefits of BAVENCIO were seen across a range of patient populations.[1,2]

“These data, which supported the recent FDA approval and updates to NCCN and ESMO guidelines, establish that BAVENCIO first-line maintenance treatment could fundamentally change clinical practice for the treatment of patients with locally advanced or metastatic urothelial carcinoma,” said Thomas Powles, MBBS, MRCP, MD, Professor of Genitourinary Oncology, Lead for Solid Tumour Research at Barts Cancer Institute, Queen Mary University of London, and Director of Barts Cancer Centre, London, UK. “It is notable that the longer overall survival with BAVENCIO maintenance therapy was observed across all pre-specified subgroups examined and that this prolonged overall survival was gained without a detrimental impact on patients’ quality of life.”

Primary Analysis
In the JAVELIN Bladder 100 study, OS was significantly longer with BAVENCIO plus BSC compared to BSC alone in the primary population of all randomized patients (n=700) whose disease had not progressed on first-line platinum-containing chemotherapy:

- Median OS was 21.4 months (95% CI, 18.9 to 26.1) vs 14.3 months (95% CI, 12.9 to 17.9), respectively (HR 0.69; 95% CI, 0.56 to 0.86; P<0.001).[1]
- At one year, 71.3% of patients (95% CI, 66.0% to 76.0%) in the BAVENCIO arm were alive vs 58.4% (95% CI, 52.7% to 63.7%) of patients who received BSC alone.[1]

In the other primary population of patients with PD-L1+ tumors (n=358):

- OS was also significantly longer with BAVENCIO plus BSC vs BSC alone (HR 0.56; 95% CI, 0.40 to 0.79; P<0.001).[1]
- At one year, 79.1% (95% CI, 72.1% to 84.5%) of patients who received BAVENCIO were alive vs 60.4% (95% CI, 52.0% to 67.7%) in the BSC arm.

All endpoints were measured from the time of randomization, after completion of four to six cycles of chemotherapy.

Subgroup Analysis
Results of an exploratory subgroup analysis show that consistent results were observed with the JAVELIN Bladder regimen of BAVENCIO first-line maintenance across pre-specified subgroups, including best response to first-line chemotherapy, type of chemotherapy regimen, site of baseline metastasis, and other baseline factors.[1] In particular, hazard ratios for OS based on response to first-line chemotherapy were as follows:

- 0.69 for complete or partial response
- 0.70 for stable disease

With regard to first-line chemotherapy regimen, hazard ratios were as follows:

- 0.69 with gemcitabine plus cisplatin
- 0.66 with gemcitabine plus carboplatin

Further detail from the subgroup analysis were presented in an on-demand mini oral session at the meeting (Presentation #704MO). Additional data evaluating the association between clinical outcomes and exploratory biomarkers will be presented in the Proffered Paper 1 - GU, non prostate session on Saturday, September 19 (Presentation #699O), and patient-reported outcomes are featured in an on-demand e-poster display (Presentation #745P).

Safety
No new safety signals were identified in the JAVELIN Bladder 100 study, and the safety profile was consistent with previous studies of BAVENCIO monotherapy.[1] Treatment-related adverse events of grade 3 or higher occurred in 57 patients (16.6%) treated with BAVENCIO plus BSC; no grade 3 or higher treatment-related events occurred in the control arm.[1] No grade 4 or fatal immune-related adverse events occurred.[1] Investigators attributed two patient deaths in the BAVENCIO plus BSC arm (0.6%), due to sepsis and ischemic stroke, to study treatment toxicity.[1]

About JAVELIN Bladder 100
JAVELIN Bladder 100 (NCT02603432) is a Phase III, multicenter, multinational, randomized, open-label, parallel-arm study investigating first-line maintenance treatment with BAVENCIO plus BSC versus BSC alone in patients with locally advanced or metastatic UC. The primary endpoint was OS in the two primary populations of all patients and patients with PD-L1+ tumors defined by the Ventana SP263 assay. Secondary endpoints included progression-free survival, anti-tumor activity, safety, pharmacokinetics, immunogenicity, predictive biomarkers and patient-reported outcomes in the co-primary populations. All primary and secondary endpoints are measured from the time of randomization.

About Urothelial Carcinoma
Bladder cancer is the tenth most common cancer worldwide.[4] In 2018, there were over half a million new cases of bladder cancer diagnosed, with around 200,000 deaths from the disease globally.[4] In the US, an estimated 80,470 cases of bladder cancer were diagnosed in 2019, with around 12,500 locally advanced or metastatic cases presented annually.[5,6] UC, which accounts for about 90% of all bladder cancers,[7] becomes harder to treat as it

advances, spreading through the layers of the bladder wall.[8] Only 25% to 55% of patients receive any second-line therapy after first-line chemotherapy.[9-14] In the US and EU5 markets, approximately 40% to 50% of patients receive an immune checkpoint inhibitor in second-line therapy.[3] For patients with advanced UC, the five-year survival rate is 5%.[5]

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.[15-17] In November 2014, Merck KGaA, Darmstadt, Germany and Pfizer announced a strategic alliance to co-develop and co-commercialize BAVENCIO.

BAVENCIO Approved Indications
BAVENCIO® (avelumab) is indicated in the US for the maintenance treatment of patients with locally advanced or metastatic urothelial carcinoma (UC) that has not progressed with first-line platinum-containing chemotherapy. BAVENCIO is also indicated for the treatment of patients with locally advanced or metastatic UC 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.

BAVENCIO 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 adults and pediatric patients 12 years and older with metastatic Merkel cell carcinoma (MCC). This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval may be contingent upon verification and description of clinical benefit in confirmatory trials.

BAVENCIO is currently approved for patients with MCC in 50 countries globally, with the majority of these approvals in a broad indication that is not limited to a specific line of treatment.

BAVENCIO 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% of patients, including one (0.1%) patient with fatal, one (0.1%) with Grade 4, and five (0.3%) with Grade 3.

BAVENCIO can cause **hepatotoxicity and 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 occurred with BAVENCIO as a single agent in 0.9% of patients, including two (0.1%) patients with fatal, and 11 (0.6%) with Grade 3.

- BAVENCIO in combination with axitinib can cause **hepatotoxicity** with higher than expected frequencies of Grade 3 and 4 alanine aminotransferase (ALT) and aspartate aminotransferase (AST) elevation. Consider more frequent monitoring of liver enzymes as compared to when the drugs are used as monotherapy. Withhold BAVENCIO and axitinib for moderate (Grade 2) hepatotoxicity and permanently discontinue the combination for severe or life-threatening (Grade 3 or 4) hepatotoxicity. Administer

corticosteroids as needed. In patients treated with BAVENCIO in combination with axitinib, Grades 3 and 4 increased ALT and AST occurred in 9% and 7% of patients, respectively, and immune-mediated hepatitis occurred in 7% of patients, including 4.9% with Grade 3 or 4.

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 until resolution. Permanently discontinue for life-threatening (Grade 4) or recurrent (Grade 3) colitis upon reinitiation of BAVENCIO. Immune-mediated colitis occurred in 1.5% 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% 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 control 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% 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% 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% 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 as a single agent or in 489 patients who received BAVENCIO in combination with axitinib: myocarditis including fatal cases, pancreatitis including fatal cases, myositis, psoriasis, arthritis, exfoliative dermatitis, erythema multiforme, pemphigoid, hypopituitarism, uveitis, Guillain-Barré syndrome, and systemic inflammatory response.

BAVENCIO can cause severe or life-threatening **infusion-related reactions**. Premedicate patients with an antihistamine and acetaminophen prior to the first 4 infusions. 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% of patients, including three (0.2%) patients with Grade 4 and nine (0.5%) with Grade 3.

BAVENCIO in combination with axitinib can cause **major adverse cardiovascular events (MACE)** including severe and fatal events. Consider baseline and periodic evaluations of left ventricular ejection fraction. Monitor for signs and symptoms of cardiovascular events. Optimize management of cardiovascular risk factors, such as hypertension, diabetes, or dyslipidemia. Discontinue BAVENCIO and axitinib for Grade 3-4 cardiovascular events. MACE occurred in 7% of patients with advanced RCC treated with BAVENCIO in combination with axitinib compared to 3.4% treated with sunitinib. These events included death due to cardiac events (1.4%), Grade 3-4 myocardial infarction (2.8%), and Grade 3-4 congestive heart failure (1.8%).

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%).

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%).

A fatal adverse reaction (sepsis) occurred in one (0.3%) patient with locally advanced or metastatic urothelial carcinoma (UC) receiving BAVENCIO plus best supportive care (BSC) as first-line maintenance treatment. In patients with previously treated locally advanced or metastatic UC, fourteen patients (6%) who were treated with BAVENCIO experienced either pneumonitis, respiratory failure, sepsis/urosepsis, cerebrovascular accident, or gastrointestinal adverse events, which led to death.

The most common adverse reactions (all grades, ?20%) in patients with locally advanced or metastatic UC receiving BAVENCIO plus BSC (vs BSC alone) as first-line maintenance treatment were fatigue (35% vs 13%), musculoskeletal pain (24% vs 15%), urinary tract infection (20% vs 11%), and rash (20% vs 2.3%). In patients with previously treated locally advanced or metastatic UC receiving BAVENCIO, the most common adverse reactions (all grades, ?20%) were fatigue, infusion-related reaction, musculoskeletal pain, nausea, decreased appetite, and urinary tract infection.

Selected laboratory abnormalities (all grades, ?20%) in patients with locally advanced or metastatic UC receiving BAVENCIO plus BSC (vs BSC alone) as first-line maintenance treatment were blood triglycerides increased (34% vs 28%), alkaline phosphate increased (30% vs 20%), blood sodium decreased (28% vs 20%), lipase increased (25% vs 16%), aspartate aminotransferase (AST) increased (24% vs 12%), blood potassium increased (24% vs 16%), alanine aminotransferase (ALT) increased (24% vs 12%), blood cholesterol increased (22% vs 16%), serum amylase increased (21% vs 12%), hemoglobin decreased (28% vs 18%), and white blood cell decreased (20% vs 10%).

Fatal adverse reactions occurred in 1.8% of patients with advanced renal cell carcinoma (RCC) receiving BAVENCIO in combination with axitinib. These included sudden cardiac death (1.2%), stroke (0.2%), myocarditis (0.2%), and necrotizing pancreatitis (0.2%).

The most common adverse reactions (all grades, ?20%) in patients with advanced RCC receiving BAVENCIO in combination with axitinib (vs sunitinib) were diarrhea (62% vs 48%), fatigue (53% vs 54%), hypertension (50% vs 36%), musculoskeletal pain (40% vs 33%), nausea (34% vs 39%), mucositis (34% vs 35%), palmar-plantar erythrodysesthesia (33% vs 34%), dysphonia (31% vs 3.2%), decreased appetite (26% vs 29%), hypothyroidism (25% vs 14%), rash (25% vs 16%), hepatotoxicity (24% vs 18%), cough (23% vs 19%), dyspnea (23% vs 16%), abdominal pain (22% vs 19%), and headache (21% vs 16%).

Selected laboratory abnormalities (all grades, ?20%) worsening from baseline in patients with advanced RCC receiving BAVENCIO in combination with axitinib (vs sunitinib) were blood triglycerides increased (71% vs 48%), blood creatinine increased (62% vs 68%), blood cholesterol increased (57% vs 22%), alanine aminotransferase increased (ALT) (50% vs 46%), aspartate aminotransferase increased (AST) (47% vs 57%), blood sodium decreased (38% vs 37%), lipase increased (37% vs 25%), blood potassium increased (35% vs 28%), platelet count decreased (27% vs 80%), blood bilirubin increased (21% vs 23%), and hemoglobin decreased (21% vs 65%).

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

About Merck KGaA, Darmstadt, Germany-Pfizer Alliance
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 BAVENCIO, an anti-PD-L1 antibody initially discovered and developed by Merck KGaA, Darmstadt, Germany. The immuno-oncology alliance is jointly developing and commercializing BAVENCIO. The alliance is focused on developing high-priority international clinical programs to investigate BAVENCIO as a monotherapy as well as combination regimens, and is striving to find new ways to treat cancer.

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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 MS. Today, the business has approximately 1,500 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, a leading science and technology company, operates across healthcare, life science and performance materials. Around 57,000 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 2019, Merck KGaA, Darmstadt, Germany, generated sales of € 16.2 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 business sectors of Merck KGaA, Darmstadt, Germany operate as EMD Serono in healthcare, MilliporeSigma in life science, and EMD Performance Materials. Since its founding 1668, 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.: Breakthroughs that change patients’ lives
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, including innovative medicines and vaccines. 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.

Pfizer Disclosure Notice –
The information contained in this release is as of September 18, 2020. 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 an indication for first-line maintenance therapy for BAVENCIO for the treatment of patients with locally advanced or metastatic urothelial carcinoma, the alliance between Merck KGaA, Darmstadt, Germany and Pfizer involving BAVENCIO 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 endpoints, commencement and/or completion dates for our clinical trials, regulatory submission dates, regulatory approval dates and/or launch dates, as well as the possibility of unfavorable new clinical data and further analyses of existing
clinical data; risks associated with interim data; the risk that clinical trial data are subject to differing interpretations and assessments by regulatory authorities; 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 other jurisdictions for BAVENCIO for first-line maintenance therapy for locally advanced or metastatic urothelial carcinoma in any jurisdictions or for any other potential indications for BAVENCIO or combination therapies in any jurisdictions; whether and when regulatory authorities in any jurisdictions where any applications are pending or may be submitted for BAVENCIO or combination therapies, including BAVENCIO for locally advanced or metastatic urothelial carcinoma may approve any such applications, which will depend on myriad factors, including making a determination as to whether the product’s benefits outweigh its known risks and determination of the product’s efficacy, and, if approved, whether they will be commercially successful; decisions by regulatory authorities impacting labeling, manufacturing processes, safety and/or other matters that

could affect the availability or commercial potential of BAVENCIO, including BAVENCIO for locally advanced or metastatic urothelial carcinoma; the impact of COVID-19 on our business, operations and financial results; 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, 2019, 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.

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