In Phase 2 and 1b Renal Cell Carcinoma Trials, Investigational PD-1 Immune Checkpoint Inhibitor Nivolumab Showed Antitumor Activity as a Single Agent and in Combination Regimen with Yervoy® (ipilimumab)

- In the Phase 2 dose-ranging trial, overall response rates for nivolumab as a single agent ranged from 20-22% and one-year survival rates ranged from 63-72% in patients who received prior anti-angiogenic treatment (CheckMate -010)

- In the Phase 1b trial, overall response rates for the investigational combination regimen of nivolumab and Yervoy ranged from 43-48% and 24-week progression free survival rates ranged from 64-65% in previously treated and treatment-naïve patients (CheckMate -016)

- The types of treatment-related serious adverse events were consistent with those in other nivolumab trials, with higher frequency for the combination regimen in CheckMate -016 (18%) than nivolumab as a single agent in CheckMate -010 (7.2%)

(PRINCETON, NJ, May 14, 2014) – Bristol-Myers Squibb Company (NYSE: BMY) today announced results from a Phase 2 and a Phase 1b study of its investigational PD-1 immune checkpoint inhibitor nivolumab in patients with advanced or metastatic renal cell carcinoma (RCC), commonly known as kidney cancer. In the Phase 2 CheckMate -010 trial (n=168), which evaluated three doses of nivolumab as a single agent in patients with previously treated RCC, the overall response rate (ORR) for nivolumab as a single agent ranged from 20-22% with a one-year survival rate that ranged from 63-72% in patients who received prior anti-angiogenic treatment. In the Phase 1b CheckMate -016 trial, which evaluated the safety and tolerability of nivolumab at different doses and schedules as part of a regimen with other agents, ORR for the investigational combination regimen of nivolumab and Yervoy (ipilimumab) (n=44) ranged from 43-48% with a 24-week progression free survival (PFS) rate that ranged from 64-65% in previously treated and treatment-naïve patients. The data will be presented at the 50th Annual Meeting of the American Society of Clinical Oncology (ASCO) taking place in Chicago May 30-June 3.

“There continues to be a significant unmet medical need in patients with renal cell carcinoma across all lines of therapy,” said Michael Giordano, senior vice president, Head of Development, Oncology & Immunosciences. “Results from the Phase 2 CheckMate -010 trial together with the first reported data combining two immune checkpoint inhibitors in renal cell carcinoma from CheckMate -016 offer important new insights into the potential of nivolumab as a single agent and as part of a combination regimen with Yervoy in the treatment of patients diagnosed with this disease.”
Results from Phase 2 Single-Agent Study in Previously-Treated Patients (CheckMate -010)

CheckMate -010 is a Phase 2 dose ranging study (n=168) evaluating the safety and antitumor activity of nivolumab as a single agent in patients with advanced or metastatic RCC who have been previously treated with anti-angiogenic therapy (≥1 agent targeting the VEGF pathway; ≤3 prior systemic therapies). Patients were randomized (blinded 1:1:1) to nivolumab 0.3, 2 or 10 mg/kg, and received an intravenous infusion every three weeks until progression, toxicity or withdrawal of consent. The primary objective was to evaluate the dose response relationship measured by progression-free survival (PFS); secondary objectives included overall survival (OS), objective response rate (ORR) and safety.

Results, including those shown below, will be presented as an oral session at ASCO on May 31 at 3 p.m. CDT (Abstract #5009). No dose relationship for PFS was seen in this study. These results support the ongoing evaluation of nivolumab as a single agent in the Phase 3 study of patients diagnosed with RCC who have been previously treated (CheckMate -025).

Key Nivolumab Monotherapy Efficacy and Safety Results in Previously Treated RCC Patients

<table>
<thead>
<tr>
<th>Dose Level</th>
<th>ORR, n (%)</th>
<th>Median PFS, months (80% CI)</th>
<th>Median OS, months (80% CI)</th>
<th>OS rate 12-month (%)</th>
<th>Treatment-related SAEs, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.3 mg/kg</td>
<td>12 (20)</td>
<td>2.7 (1.9, 3.0)</td>
<td>18.2 (16.2, 24.0)</td>
<td>63%</td>
<td>2 (3.4)</td>
</tr>
<tr>
<td>2 mg/kg</td>
<td>12 (22)</td>
<td>4.0 (2.8, 4.2)</td>
<td>25.5 (19.8 - 28.8)</td>
<td>72%</td>
<td>6 (11)</td>
</tr>
<tr>
<td>10 mg/kg</td>
<td>11 (20)</td>
<td>4.2 (2.8, 5.5)</td>
<td>24.7 (15.3 - 26.0)</td>
<td>70%</td>
<td>4 (7.4)</td>
</tr>
</tbody>
</table>

*Safety analysis included 59 treated pts; CI= confidence interval;

Related severe adverse events (AEs) occurred in 7.2% of patients across all doses. For 0.3, 2.0 and 10 mg/kg, 1 (2%), 6 (11%) and 4 (7%) patients, respectively, had treatment-related AEs that led to discontinuation. There was no grade 3-4 pneumonitis.

“Results from the Phase 2 CheckMate -010 trial support findings from the Phase 1b Study -003 and provide additional data on the antitumor activity of nivolumab in patients with renal cell carcinoma,” said Robert Motzer, M.D., Memorial Sloan Kettering Cancer Center, New York, NY. “These data are encouraging as we seek to identify new treatments for patients, particularly those who progress following treatment with anti-angiogenic therapy, as these patients have limited options.”
Results from Phase 1b Study of Combination Regimen in Previously Treated and Treatment-Naïve Patients (CheckMate -016)

CheckMate -016 is a multi-arm Phase 1b trial evaluating the safety and tolerability of nivolumab at different doses and schedules as part of a regimen with other agents, including as part of a combination regimen with Yervoy, in both previously treated and treatment-naïve patients with RCC. In the arm evaluating the combination regimen of nivolumab and Yervoy (n=44), patients were randomized to receive nivolumab 3 mg/kg + Yervoy 1 mg/kg or nivolumab 1 mg/kg + Yervoy 3 mg/kg, by intravenous infusion every three weeks for four doses, followed by nivolumab 3 mg/kg by intravenous infusion every two weeks until progression or toxicity. Most patients in this arm (n=34) had prior systemic therapy. The primary objective was to assess safety and tolerability, and the secondary objective was to assess antitumor activity.

Data from this cohort, including those shown below, will be featured as an oral presentation at ASCO on June 2 at 9:45 a.m. CDT (Abstract #4504). The results showed encouraging antitumor activity in both dose cohorts, with most responses ongoing, and support the company’s plans to initiate a Phase 3 trial evaluating the combination regimen of nivolumab and Yervoy as a potential treatment option in treatment-naïve patients by the end of 2014.

Key Efficacy and Safety Results in Previously Treated and Treatment-Naïve RCC Patients

<table>
<thead>
<tr>
<th></th>
<th>nivo 3 mg/kg + Yervoy 1 mg/kg</th>
<th>nivo 1 mg/kg + Yervoy 3 mg/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=21</td>
<td>N=23</td>
</tr>
<tr>
<td>ORR, n (%)</td>
<td>9 (43)</td>
<td>11 (48)</td>
</tr>
<tr>
<td>SD, n (%) [duration, wks]</td>
<td>5 (24)</td>
<td>8 (35)</td>
</tr>
<tr>
<td>Median DOR (wks)</td>
<td>31+ (28 - NR)</td>
<td>NR (12 - NR)</td>
</tr>
<tr>
<td>Median PFS (wks)</td>
<td>37 (6.0 - NR)</td>
<td>38 (18 - NR)</td>
</tr>
<tr>
<td>PFS rate 24-weeks (%)</td>
<td>65%</td>
<td>64%</td>
</tr>
</tbody>
</table>

NR = Not Reached

Related SAEs occurred in 18% for all regimens. The most common SAEs were elevated ALT and diarrhea (6.8% each). Eight patients discontinued due to any-grade related AEs. No grade 3-4 pneumonitis was seen.

Data from additional cohorts of CheckMate -016, including in combination with sunitinib or pazopanib in previously treated patients, will also be presented at ASCO (Abstract #5010).
About Renal Cell Carcinoma

In 2012, an estimated 338,000 cases of kidney cancer were diagnosed worldwide, accounting for more than two percent of all cancer diagnoses. The most common type of kidney cancer is RCC, accounting for about nine out of 10 kidney cancers. RCC – also referred to as renal cell cancer or renal cell adenocarcinoma – starts in the lining of small tubes in the kidney. Typically, RCC forms as a single tumor but more than one tumor may grow in one or both kidneys. When RCC spreads to other organs (metastasizes) it is much harder to treat. In the United States, Stage I kidney cancer, has a five-year survival rate of 81 percent and Stage IV kidney cancer has a five-year survival rate of eight percent.

About Bristol-Myers Squibb Immuno-OncoLOGY Trials in Renal Cell Carcinoma

Bristol-Myers Squibb is committed to the research and development of immuno-oncology as an innovative approach to treating RCC and has a broad development program evaluating its approved and investigational immunotherapies – either as single agents or as part of a regimen - across lines of therapy and biomarker expression. There is an ongoing Phase 3 trial evaluating nivolumab as a single agent vs. everolimus in patients who have been previously treated with an anti-angiogenic therapy (CheckMate -025). Additionally, the company plans to initiate a Phase 3 trial evaluating the investigational combination regimen of nivolumab and Yervoy in treatment-naive patients by the end of 2014.

About Nivolumab and Yervoy

Cancer cells may exploit “regulatory” pathways, such as checkpoint pathways, to hide from the immune system and shield the tumor from immune attack. Nivolumab and Yervoy are both monoclonal antibodies and immune checkpoint inhibitors, but target different receptors for distinct T-cell checkpoint pathways.

Nivolumab is an investigational, fully-human PD-1 immune checkpoint inhibitor that binds to the checkpoint receptor PD-1 (programmed death-1) expressed on activated T-cells. We are investigating whether by blocking this pathway, nivolumab would enable the immune system to resume its ability to recognize, attack and destroy cancer cells.

Bristol-Myers Squibb has a broad, global development program to study nivolumab in multiple tumor types consisting of more than 35 trials – as monotherapy or in combination with other therapies – in which more than 7,000 patients have been enrolled worldwide. Among these are several potentially registrational trials in non-small cell lung cancer, melanoma, RCC, head and neck cancer,
glioblastoma and non-Hodgkin lymphoma. In 2013, the FDA granted Fast Track designation for nivolumab in NSCLC, melanoma and RCC.

Yervoy, which is a recombinant, human monoclonal antibody, blocks the cytotoxic T-lymphocyte antigen-4 (CTLA-4). CTLA-4 is a negative regulator of T-cell activation. Ipilimumab binds to CTLA-4 and blocks the interaction of CTLA-4 with its ligands, CD80/CD86. Blockade of CTLA-4 has been shown to augment T-cell activation and proliferation. The mechanism of action of ipilimumab’s effect in patients with melanoma is indirect through T-cell mediated anti-tumor immune responses. On March 25, 2011, the FDA approved Yervoy 3 mg/kg monotherapy for patients with unresectable or metastatic melanoma. Yervoy is now approved in more than 40 countries.

YERVOY® (ipilimumab) INDICATION & IMPORTANT SAFETY INFORMATION

YERVOY (ipilimumab) is indicated for the treatment of unresectable or metastatic melanoma.

Important Safety Information

WARNING: IMMUNE-MEDIATED ADVERSE REACTIONS

YERVOY can result in severe and fatal immune-mediated adverse reactions due to T-cell activation and proliferation. These immune-mediated reactions may involve any organ system; however, the most common severe immune-mediated adverse reactions are enterocolitis, hepatitis, dermatitis (including toxic epidermal necrolysis), neuropathy, and endocrinopathy. The majority of these immune-mediated reactions initially manifested during treatment; however, a minority occurred weeks to months after discontinuation of YERVOY.

Assess patients for signs and symptoms of enterocolitis, dermatitis, neuropathy, and endocrinopathy and evaluate clinical chemistries including liver function tests (LFTs) and thyroid function tests at baseline and before each dose.

Permanently discontinue YERVOY for any of the following:

- Persistent moderate adverse reactions or inability to reduce corticosteroid dose to 7.5 mg prednisone or equivalent per day
- Failure to complete full treatment course within 16 weeks from administration of first dose
- Severe or life-threatening adverse reactions, including any of the following:
Colitis with abdominal pain, fever, ileus, or peritoneal signs; increase in stool frequency (≥7 over baseline), stool incontinence, need for intravenous hydration for >24 hours, gastrointestinal hemorrhage, and gastrointestinal perforation

- AST or ALT >5 × the upper limit of normal (ULN) or total bilirubin >3 × the ULN

- Stevens-Johnson syndrome, toxic epidermal necrolysis, or rash complicated by full-thickness dermal ulceration or necrotic, bullous, or hemorrhagic manifestations

- Severe motor or sensory neuropathy, Guillain-Barré syndrome, or myasthenia gravis

- Severe immune-mediated reactions involving any organ system

- Immune-mediated ocular disease which is unresponsive to topical immunosuppressive therapy

**Immune-mediated Enterocolitis:**

- In the pivotal Phase 3 study in YERVOY-treated patients, severe, life-threatening, or fatal (diarrhea of ≥7 stools above baseline, fever, ileus, peritoneal signs; Grade 3-5) immune-mediated enterocolitis occurred in 34 (7%) and moderate (diarrhea with up to 6 stools above baseline, abdominal pain, mucus or blood in stool; Grade 2) enterocolitis occurred in 28 (5%) patients

- Across all YERVOY-treated patients (n=511), 5 (1%) developed intestinal perforation, 4 (0.8%) died as a result of complications, and 26 (5%) were hospitalized for severe enterocolitis

- Infliximab was administered to 5 of 62 (8%) patients with moderate, severe, or life-threatening immune-mediated enterocolitis following inadequate response to corticosteroids

- Monitor patients for signs and symptoms of enterocolitis (such as diarrhea, abdominal pain, mucus or blood in stool, with or without fever) and of bowel perforation (such as peritoneal signs and ileus). In symptomatic patients, rule out infectious etiologies and consider endoscopic evaluation for persistent or severe symptoms

- Permanently discontinue YERVOY in patients with severe enterocolitis and initiate systemic corticosteroids (1-2 mg/kg/day of prednisone or equivalent). Upon improvement to ≤Grade 1, initiate corticosteroid taper and continue over at least 1 month. In clinical trials, rapid corticosteroid tapering resulted in recurrence or worsening symptoms of enterocolitis in some patients
Withhold YERVOY for moderate enterocolitis; administer anti-diarrheal treatment and, if persistent for >1 week, initiate systemic corticosteroids (0.5 mg/kg/day prednisone or equivalent)

Immune-mediated Hepatitis:

- In the pivotal Phase 3 study in YERVOY-treated patients, severe, life-threatening, or fatal hepatotoxicity (AST or ALT elevations >5x the ULN or total bilirubin elevations >3x the ULN; Grade 3–5) occurred in 8 (2%) patients, with fatal hepatic failure in 0.2% and hospitalization in 0.4%
- 13 (2.5%) additional YERVOY-treated patients experienced moderate hepatotoxicity manifested by LFT abnormalities (AST or ALT elevations >2.5x but ≤5x the ULN or total bilirubin elevation >1.5x but ≤3x the ULN; Grade 2)
- Monitor LFTs (hepatic transaminase and bilirubin levels) and assess patients for signs and symptoms of hepatotoxicity before each dose of YERVOY. In patients with hepatotoxicity, rule out infectious or malignant causes and increase frequency of LFT monitoring until resolution
- Permanently discontinue YERVOY in patients with Grade 3-5 hepatotoxicity and administer systemic corticosteroids (1-2 mg/kg/day of prednisone or equivalent). When LFTs show sustained improvement or return to baseline, initiate corticosteroid tapering and continue over 1 month. Across the clinical development program for YERVOY, mycophenolate treatment has been administered in patients with persistent severe hepatitis despite high-dose corticosteroids
- Withhold YERVOY in patients with Grade 2 hepatotoxicity
- In a dose-finding trial, Grade 3 increases in transaminases with or without concomitant increases in total bilirubin occurred in 6 of 10 patients who received concurrent YERVOY (3 mg/kg) and vemurafenib (960 mg BID or 720 mg BID)

Immune-mediated Dermatitis:

- In the pivotal Phase 3 study in YERVOY-treated patients, severe, life-threatening, or fatal immune-mediated dermatitis (e.g., Stevens-Johnson syndrome, toxic epidermal necrolysis, or rash complicated by full thickness dermal ulceration, or necrotic, bullous, or hemorrhagic manifestations; Grade 3–5) occurred in 13 (2.5%) patients
  - 1 (0.2%) patient died as a result of toxic epidermal necrolysis
o 1 additional patient required hospitalization for severe dermatitis

- There were 63 (12%) YERVOY-treated patients with moderate (Grade 2) dermatitis
- Monitor patients for signs and symptoms of dermatitis such as rash and pruritus. Unless an alternate etiology has been identified, signs or symptoms of dermatitis should be considered immune-mediated
- Permanently discontinue YERVOY in patients with severe, life-threatening, or fatal immune-mediated dermatitis (Grade 3-5). Administer systemic corticosteroids (1-2 mg/kg/day of prednisone or equivalent). When dermatitis is controlled, corticosteroid tapering should occur over a period of at least 1 month. Withhold YERVOY in patients with moderate to severe signs and symptoms
- Treat mild to moderate dermatitis (e.g., localized rash and pruritus) symptomatically. Administer topical or systemic corticosteroids if there is no improvement within 1 week

**Immune-mediated Neuropathies:**
- In the pivotal Phase 3 study in YERVOY-treated patients, 1 case of fatal Guillain-Barré syndrome and 1 case of severe (Grade 3) peripheral motor neuropathy were reported
- Across the clinical development program of YERVOY, myasthenia gravis and additional cases of Guillain-Barré syndrome have been reported
- Monitor for symptoms of motor or sensory neuropathy such as unilateral or bilateral weakness, sensory alterations, or paresthesia. Permanently discontinue YERVOY in patients with severe neuropathy (interfering with daily activities) such as Guillain-Barré–like syndromes
- Institute medical intervention as appropriate for management of severe neuropathy. Consider initiation of systemic corticosteroids (1-2 mg/kg/day of prednisone or equivalent) for severe neuropathies. Withhold YERVOY in patients with moderate neuropathy (not interfering with daily activities)

**Immune-mediated Endocrinopathies:**
- In the pivotal Phase 3 study in YERVOY-treated patients, severe to life-threatening immune-mediated endocrinopathies (requiring hospitalization, urgent medical intervention, or interfering with activities of daily living; Grade 3-4) occurred in 9 (1.8%) patients
  - All 9 patients had hypopituitarism, and some had additional concomitant endocrinopathies such as adrenal insufficiency, hypogonadism, and hypothyroidism
6 of the 9 patients were hospitalized for severe endocrinopathies

- Moderate endocrinopathy (requiring hormone replacement or medical intervention; Grade 2) occurred in 12 (2.3%) YERVOY-treated patients and consisted of hypothyroidism, adrenal insufficiency, hypopituitarism, and 1 case each of hyperthyroidism and Cushing’s syndrome
- Median time to onset of moderate to severe immune-mediated endocrinopathy was 11 weeks and ranged up to 19.3 weeks after the initiation of YERVOY
- Monitor patients for clinical signs and symptoms of hypophysitis, adrenal insufficiency (including adrenal crisis), and hyper- or hypothyroidism
  - Patients may present with fatigue, headache, mental status changes, abdominal pain, unusual bowel habits, and hypotension, or nonspecific symptoms which may resemble other causes such as brain metastasis or underlying disease. Unless an alternate etiology has been identified, signs or symptoms should be considered immune-mediated
  - Monitor thyroid function tests and clinical chemistries at the start of treatment, before each dose, and as clinically indicated based on symptoms. In a limited number of patients, hypophysitis was diagnosed by imaging studies through enlargement of the pituitary gland
- Withhold YERVOY in symptomatic patients. Initiate systemic corticosteroids (1-2 mg/kg/day of prednisone or equivalent) and initiate appropriate hormone replacement therapy. Long-term hormone replacement therapy may be necessary

Other Immune-mediated Adverse Reactions, Including Ocular Manifestations:

- In the pivotal Phase 3 study in YERVOY-treated patients, clinically significant immune-mediated adverse reactions seen in <1% were: nephritis, pneumonitis, meningitis, pericarditis, uveitis, iritis, and hemolytic anemia
- Across the clinical development program for YERVOY, likely immune-mediated adverse reactions also reported with <1% incidence were: myocarditis, angiopathy, temporal arteritis, vasculitis, polymyalgia rheumatica, conjunctivitis, blepharitis, episcleritis, scleritis, leukocytoclastic vasculitis, erythema multiforme, psoriasis, pancreatitis, arthritis, autoimmune thyroiditis, sarcoidosis, neurosensory hypoacusis, autoimmune central neuropathy (encephalitis), myositis, polymyositis, and ocular myositis
Permanently discontinue YERVOY for clinically significant or severe immune-mediated adverse reactions. Initiate systemic corticosteroids (1-2 mg/kg/day of prednisone or equivalent) for severe immune-mediated adverse reactions.

Administer corticosteroid eye drops for uveitis, iritis, or episcleritis. Permanently discontinue YERVOY for immune-mediated ocular disease unresponsive to local immunosuppressive therapy.

**Pregnancy & Nursing:**

- YERVOY is classified as pregnancy category C. There are no adequate and well-controlled studies of YERVOY in pregnant women. Use YERVOY during pregnancy only if the potential benefit justifies the potential risk to the fetus.
- Human IgG1 is known to cross the placental barrier and YERVOY is an IgG1; therefore, YERVOY has the potential to be transmitted from the mother to the developing fetus.
- It is not known whether YERVOY is secreted in human milk. Because many drugs are secreted in human milk and because of the potential for serious adverse reactions in nursing infants from YERVOY, a decision should be made whether to discontinue nursing or to discontinue YERVOY.

**Common Adverse Reactions:**

- The most common adverse reactions (≥5%) in patients who received YERVOY at 3 mg/kg were fatigue (41%), diarrhea (32%), pruritus (31%), rash (29%), and colitis (8%).

Please see Full Prescribing Information, including Boxed WARNING regarding immune-mediated adverse reactions, available at [www.bms.com](http://www.bms.com).

YERVOY® is a registered trademark of Bristol-Myers Squibb Company.

**Immuno-Oncology at Bristol-Myers Squibb**

Surgery, radiation, cytotoxic or targeted therapies have represented the mainstay of cancer treatment over the last several decades, but long-term survival and a positive quality of life have remained elusive for many patients with advanced disease. To address this unmet medical need, Bristol-Myers Squibb is leading advances in a rapidly evolving field of cancer research and treatment known as immuno-oncology, which involves agents whose primary mechanism is to work directly with the body’s immune system to fight cancer. This includes conducting research on the potential of combining immuno-oncology agents that target different and complementary pathways in the treatment of cancer.
Bristol-Myers Squibb is committed to advancing the science of immuno-oncology, with the goal of changing survival expectations and the way patients live with cancer.

About the Bristol-Myers Squibb and Ono Pharmaceutical Partnership

Through a collaboration agreement with Ono Pharmaceutical in 2011, Bristol-Myers Squibb expanded its territorial rights to develop and commercialize nivolumab (BMS-936558/ONO-4538) globally except in Japan, Korea and Taiwan where Ono has retained all rights to the compound.

About Bristol-Myers Squibb

Bristol-Myers Squibb is a global biopharmaceutical company whose mission is to discover, develop and deliver innovative medicines that help patients prevail over serious diseases. For more information, please visit www.bms.com or follow us on Twitter at http://twitter.com/bmsnews.

Bristol-Myers Squibb Forward-Looking Statement

This press release contains “forward-looking statements” as that term is defined in the Private Securities Litigation Reform Act of 1995 regarding product development. Such forward-looking statements are based on current expectations and involve inherent risks and uncertainties, including factors that could delay, divert or change any of them, and could cause actual outcomes and results to differ materially from current expectations. No forward-looking statement can be guaranteed. Among other risks, there can be no guarantee that nivolumab will receive regulatory approval, that the combination use of nivolumab and Yervoy will receive regulatory approval, or that, if approved, they will become commercially successful. Forward-looking statements in this press release should be evaluated together with the many uncertainties that affect Bristol-Myers Squibb’s business, particularly those identified in the cautionary factors discussion in Bristol-Myers Squibb’s Annual Report on Form 10-K for the year ended December 31, 2013, in our Quarterly Reports on Form 10-Q and our Current Reports on Form 8-K. Bristol-Myers Squibb undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise.

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