## Opdivo® (nivolumab), Cabometyx® (cabozantinib) – Expanded indication

- On January 21, 2021, Bristol Myers Squibb and Exelixis announced the FDA approval of Opdivo (nivolumab) plus Cabometyx (cabozantinib), for the first-line treatment of patients with advanced renal cell carcinoma (RCC).
    - Opdivo was previously approved, in combination with ipilimumab, for the first-line treatment of patients with intermediate or poor risk advanced RCC and as a single agent for treatment of patients with advanced RCC who have received prior anti-angiogenic therapy.
    - Cabometyx was previously approved as a single agent for treatment of patients with advanced RCC.

- Opdivo is also approved for unresectable or metastatic melanoma; adjuvant treatment of melanoma; metastatic non-small cell lung cancer; malignant pleural mesothelioma; classical Hodgkin lymphoma; squamous cell carcinoma of the head and neck; urothelial carcinoma; microsatellite instability-high or mismatch repair deficient metastatic colorectal cancer; hepatocellular carcinoma (HCC); and esophageal squamous cell carcinoma.

- Cabometyx is also approved for HCC.

- The approval of Opdivo and Cabometyx for the expanded indication was based on CHECKMATE-9ER, a randomized, open-label study in patients with previously untreated advanced RCC. Patients were randomized to Opdivo plus Cabometyx or Sutent® (sunitinib). Treatment continued until disease progression or unacceptable toxicity. The major efficacy outcome measure was progression-free survival (PFS). Additional efficacy outcome measures were overall survival (OS) and objective response rate (ORR).
    - Median PFS was 16.6 months with Opdivo plus Cabometyx vs. 8.3 months with Sutent (hazard ratio [HR] 0.51, 95% CI: 0.41, 0.64; $p < 0.0001$).
    - Median OS was not reached with Opdivo plus Cabometyx or Sutent (HR 0.60; 95% CI: 0.40, 0.89; $p = 0.0010$).
    - The confirmed ORR was 55.7% and 27.1% for the Opdivo plus Cabometyx and Sutent arms, respectively ($p < 0.0001$).

- The most common adverse reactions with Opdivo plus Cabometyx combination therapy were diarrhea, fatigue, hepatotoxicity, palmarplantar erythrodysaesthesia syndrome, stomatitis, rash, hypertension, hypothyroidism, musculoskeletal pain, decreased appetite, nausea, dysgeusia, abdominal pain, cough, and upper respiratory tract infection.

- The recommended dose of Opdivo, when used in combination with Cabometyx for advanced RCC, is 240 mg intravenous (IV) infusion every 2 weeks or 480 mg IV infusion every 4 weeks. Opdivo should be administered until disease progression, unacceptable toxicity, or up to 2 years. The dose of Cabometyx, when used in combination with Opdivo, is 40 mg orally once daily until disease progression or unacceptable toxicity.

- Refer to the Opdivo and Cabometyx drug labels for dosing for their other uses and indications