Lorbrena® (lorlatinib) – Expanded indication

- On March 3, 2021, Pfizer announced the FDA approval of Lorbrena (lorlatinib), for the treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are anaplastic lymphoma kinase (ALK)-positive as detected by an FDA-approved test.
    - Previously, Lorbrena was approved for the treatment of patients with ALK-positive metastatic NSCLC whose disease has progressed on: Xalkori® (crizotinib) and at least one other ALK inhibitor for metastatic disease; or Alecensa® (alectinib) as the first ALK inhibitor therapy for metastatic disease; or Zykadia® (ceritinib) as the first ALK inhibitor therapy for metastatic disease.
    - The FDA also converted the accelerated approval for this indication to full approval.

- This approval expands the indication to include first-line treatment of patients with NSCLC.

- The approval of Lorbrena for the expanded indication was based on the CROWN study, an open-label, randomized, active-controlled trial in 296 patients with ALK-positive NSCLC who had not received prior systemic therapy for metastatic disease. Patients were randomized to receive Lorbrena or Xalkori. The major efficacy outcome measure was progression-free survival (PFS). Additional efficacy outcome measures were overall survival (OS), overall response rate (ORR), and duration of response (DOR).
    - Median PFS was not estimable for Lorbrena vs. 9.3 months for Xalkori (hazard ratio 0.28, 95% CI: 0.19, 0.41; $p < 0.0001$).
    - The ORR was 76% (95% CI: 68, 83) for Lorbrena vs. 58% (95% CI: 49, 66) for Xalkori.
    - The median DOR was not estimable (range: 0.9, 31.3) for Lorbrena vs. 11 months (range: 1.1, 27.5) for Xalkori.
    - At the data cutoff point OS data was not mature.

- The recommended dosage of Lorbrena is 100 mg orally once daily, with or without food, until disease progression or unacceptable toxicity.