Ensacove™ (ensartinib) – New drug approval

- On December 18, 2024, the FDA announced the approval of Xcovery's Ensacove (ensartinib), for the treatment of adult patients with **anaplastic lymphoma kinase (ALK)-positive locally advanced or metastatic non-small cell lung cancer (NSCLC)** who have not previously received an ALK-inhibitor.

- Ensacove is a kinase inhibitor of ALK and inhibits other kinases including MET and ROS1.

- The efficacy of Ensacove was established in eXALT3, an open-label, randomized, active-controlled study in adult patients with locally advanced or metastatic ALK-positive NSCLC. Patients were randomized to receive Ensacove or Xalkori® (crizotinib) (another kinase inhibitor) until disease progression or unacceptable toxicity. The main outcome measure was progression-free survival (PFS).

    - Median PFS was 25.8 months with Ensacove vs. 12.7 months with Xalkori (hazard ratio 0.56, 95% CI: 0.40, 0.79; p = 0.0007).
    - At the time of the primary PFS analysis, overall survival results were immature. At the time of final analysis of overall survival, there was no statistically significant difference (p = 0.4570) between Ensacove and Xalkori. Median OS was 63.2 months in the Ensacove arm and 55.7 months in the Xalkori arm (hazard ratio 0.88, 95% CI: 0.63, 1.23).

- Warnings and precautions for Ensacove include interstitial lung disease (ILD)/pneumonitis; hepatotoxicity; dermatologic adverse reactions; bradycardia; hyperglycemia; visual disturbances; increased creatine phosphokinase; hyperuricemia; embryo-fetal toxicity; and FD&C Yellow No. 5 (tartrazine).

- The most common adverse reactions (≥ 20%) with Ensacove use were rash, musculoskeletal pain, constipation, pruritus, cough, nausea, edema, vomiting, fatigue, and pyrexia.

- The most common Grade 3-4 laboratory abnormality (≥ 2%) with Ensacove use were increased uric acid, decreased lymphocytes, increased alanine aminotransferase, decreased phosphate, increased gamma glutamyl transferase, increased magnesium, increased amylase, decreased sodium, increased glucose, decreased hemoglobin, increased bilirubin, decreased potassium, and increased creatine phosphokinase.

- The recommended dose of Ensacove is **25 mg orally once daily**, with or without food, until disease progression or unacceptable toxicity.

    - Patients should be selected for treatment of locally advanced or metastatic NSCLC based on the presence of **ALK rearrangement(s) in tumor specimens**. An FDA-approved test to detect ALK rearrangements for selecting patients for treatment with Ensacove is not currently available.

- Xcovery's launch plans for Ensacove are pending. Ensacove will be available as a 25 mg and 100 mg capsule.