Retevmo™ (selpercatinib) – New orphan drug approval

- On May 8, 2020, the FDA announced the approval of Eli Lilly's Retevmo (selpercatinib), for the treatment of:

  - Adult patients with metastatic *RET* fusion-positive non-small cell lung cancer (NSCLC)
  - Adult and pediatric patients 12 years of age and older with advanced or metastatic *RET*-mutant medullary thyroid cancer (MTC) who require systemic therapy
  - Adult and pediatric patients 12 years of age and older with advanced or metastatic *RET* fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate).
  - These indications were approved under accelerated approval based on overall response rate and duration of response. Continued approval for these indications may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

- Retevmo is a selective and potent RET kinase inhibitor. It is the first therapy approved specifically for cancer patients with the *RET* gene alterations.

  - Genomic alterations in the RET kinase, which include fusions and activating point mutations, lead to overactive RET signaling and uncontrolled cell growth.

- The efficacy of Retevmo was evaluated in a single-arm, multi-cohort study in patients with *RET*-driven cancers. The study included both treatment-naive patients and heavily pretreated patients with a variety of advanced solid tumors including *RET* fusion-positive NSCLC, *RET*-mutant MTC, and *RET* fusion-positive thyroid cancer. Major efficacy outcomes were objective response rate (ORR) and duration of response (DOR).

	***RET* fusion-positive NSCLC**		***RET*-mutant MTC**		***RET* fusion-positive thyroid cancers**	
	Treatment naïve (n = 39)	**Treatment-experienced (n = 105)**	**CAB/VAN-naïve (n = 88)**	**CAB-VAN-experienced (n = 55)**	**Treatment naïve (n = 8)**	**Treatment-experienced (n = 19)**
ORR (95% CI)	85 (70, 94)	64 (54, 73)	73 (62, 82)	69 (55, 81)	100 (63, 100)	79 (54, 94)
Median DOR, months (95% CI)	NE (12, NE)	17.5 (12, NE)	22.0 (NE, NE)	NE (19.1, NE)	NE (NE, NE)	18.4 (7.6, NE)

Abbreviations: NE = not estimable; CAB = cabozantinib; VAN = vandetanib

- Warnings and precautions for Retevmo include hepatotoxicity, hypertension, QT interval prolongation, hemorrhagic events, hypersensitivity, risk of impaired wound healing, and embryo-fetal toxicity.

- The most common adverse reactions (≥ 25%) with Retevmo use were increased aspartate aminotransferase (AST), increased alanine aminotransferase (ALT), increased glucose, decreased leukocytes, decreased albumin, decreased calcium, dry mouth, diarrhea, increased creatinine, increased alkaline phosphatase, hypertension, fatigue, edema, decreased platelets, increased total cholesterol, rash, decreased sodium, and constipation.

- The recommended dosage of Retevmo is 120 mg in patients less than 50 kg and 160 mg in patients 50 kg or greater. Retevmo is taken orally twice daily (approximately every 12 hours) until disease progression or unacceptable toxicity.

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    - Patients should be selected for treatment based on the presence of a *RET* gene fusion (NSCLC or thyroid) or specific *RET* gene mutation (MTC).

- Eli Lilly plans to launch Retevmo within one week of approval. Retevmo will be available as a 40 mg and 80 mg capsule.