Vyndaqel® (tafamidis meglumine) and Vyndamax™ (tafamidis) – New orphan drug approvals

- On May 6, 2019, the FDA announced the approval of Pfizer's Vyndaqel (tafamidis meglumine) and Vyndamax (tafamidis), for the treatment of the cardiomyopathy of wild type or hereditary transthyretin-mediated amyloidosis (ATTR-CM) in adults to reduce cardiovascular mortality and cardiovascular-related hospitalization.

- ATTR-CM is a rare, life-threatening disease characterized by the buildup of abnormal deposits of misfolded protein called amyloid in the heart and is defined by restrictive cardiomyopathy and progressive heart failure. It is estimated that the prevalence of ATTR-CM is approximately 100,000 people in the U.S however only 1 to 2% of those patients are diagnosed today.

- Vyndaqel and Vyndamax are the first FDA-approved treatments for ATTR-CM. Vyndaqel and Vyndamax have the same active moiety (tafamidis); however, Vyndamax was developed for patient convenience.

    — Tafamidis selectively binds to transthyretin, stabilizing the tetramer of the transthyretin transport protein and slowing the formation of amyloid that causes ATTR-CM.

- The efficacy of Vyndaqel was established in a double-blind study in 441 patients with wild type or hereditary ATTR-CM. Patients were randomized to receive Vyndaqel 20 mg, Vyndaqel 80 mg (administered as four 20-mg Vyndaqel capsules), or matching placebo once daily for 30 months. The primary endpoint was all-cause mortality and frequency of cardiovascular-related hospitalizations.

    — The primary analysis demonstrated a significant reduction ($p = 0.0006$) in all-cause mortality and frequency of cardiovascular-related hospitalizations in the pooled Vyndaqel groups vs. placebo. The percentage of patients alive at month 30 was 70.5% and 57.1% for the pooled Vyndaqel and placebo groups, respectively. The mean number of cardiovascular-related hospitalizations (per patient per year) among those alive at month 30 was 0.297 and 0.455 for Vyndaqel and placebo, respectively.
    — Individual components of the primary analysis also demonstrated a relative reduction in the risk of all-cause mortality and frequency of cardiovascular-related hospitalization of 30% ($p = 0.026$) and 32% ($p < 0.0001$), respectively, with Vyndaqel vs. placebo.

- The frequency of adverse events in patients treated with Vyndaqel was similar to that with placebo.

- The recommended dosage is either Vyndaqel 80 mg (four 20-mg tafamidis meglumine capsules) orally once daily or Vyndamax 61 mg (one 61-mg tafamidis capsule) orally once daily. Vyndamax and Vyndaqel are not substitutable on a per mg basis.

- Vyndaqel will be priced at $225,000 per year.

- Pfizer's launch plans for Vyndaqel and Vyndamax are pending. Vyndaqel will be available as a 20 mg capsule and Vyndamax will be available as a 61 mg capsule.