## Beqvez™ (fidanacogene elaparvovec-dzkt) – New orphan drug approval

- On April 26, 2024, Pfizer announced the FDA approval of Beqvez (fidanacogene elaparvovec-dzkt), for the treatment of adults with moderate to severe hemophilia B (congenital factor IX deficiency) who:
  - Currently use factor IX prophylaxis therapy, or
  - Have current or historical life-threatening hemorrhage, or
  - Have repeated, serious spontaneous bleeding episodes, and,
  - Do not have neutralizing antibodies to adeno-associated virus serotype Rh74var (AAVRh74var) capsid as detected by an FDA-approved test.

- Hemophilia is a rare genetic bleeding disorder that prevents normal blood clotting because of a deficiency in clotting factor IX. People with hemophilia are at risk for excessive and recurrent spontaneous and/or post-traumatic bleeding, which can be life-threatening, particularly in those with severe hemophilia.

- Beqvez is the second gene therapy approved for hemophilia B. CSL Behring's Heivmgenix® (etranacogene dezaparvovec-drlb) was approved in November 2022.

- The efficacy of Beqvez was established in an ongoing, prospective, open-label, single-arm, study in 45 adult male patients with moderately severe to severe hemophilia B. All patients completed a prospective lead-in study of at least six months for baseline data collection while they received routine factor IX prophylaxis in the usual care setting before entering the clinical study. Patients then received a single intravenous (IV) infusion of Beqvez. The main efficacy outcome was a non-inferiority (NI) test of annualized bleeding rate (ABR) during the efficacy evaluation period (EEP), week 12 to data cutoff following Beqvez treatment, compared with baseline ABR during the lead-in period.
  - The model derived mean ABR was 4.5 bleeds/year (95% CI: 1.9, 7.2) during the baseline period and 2.5 bleeds/year (95% CI: 1.0, 3.9) during post-Beqvez EEP, resulting in a difference between the mean post-Beqvez EEP ABR and the baseline ABR of -2.1 bleeds/year (95% CI: -4.8, 0.7). The upper bound of the 95% CI in the difference was less than 3.0 bleeds/year, meeting the NI study success criterion.
  - Six out of 45 patients (13%) resumed routine factor IX prophylaxis after Beqvez treatment, starting from 0.4 years to 1.7 years after Beqvez infusion.

- Warnings and precautions for Beqvez include hepatotoxicity, infusion-reactions, malignancy, and monitoring laboratory tests.

- The most common adverse reaction (≥ 5%) with Beqvez use was an increase in transaminases.

- The recommended dose of Beqvez is a single-dose IV infusion of $5 \times 10^{11}$ vector genomes per kg (vg/kg) of body weight.
  - Refer to the Beqvez drug label for complete dosing and administration recommendations.

- Beqvez will be priced at $3.5 million for a one-time dose.

- Pfizer's launch plans for Beqvez are pending. Beqvez will be available as a suspension for IV infusion with each mL containing $1 \times 10^{13}$ vg.