Qfitlia™ (fitusiran) – New orphan drug approval

- On March 28, 2025, the FDA announced the approval of Sanofi's Qfitlia (fitusiran), for **routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adult and pediatric patients aged 12 years and older with hemophilia A or B with or without factor VIII or IX inhibitors**.

- Hemophilia A and hemophilia B are genetic bleeding disorders caused by a dysfunction or deficiency of coagulation factor VIII or IX, respectively.

- Qfitlia is a **first-in-class antithrombin-directed small interfering ribonucleic acid**. It reduces the amount of antithrombin, leading to an increase in thrombin, an enzyme critical for blood clotting.

- The efficacy of Qfitlia was established in two randomized, open-label studies in a total of 177 adult and pediatric male patients with either hemophilia A or hemophilia B. In one study (ATLAS-INH), patients had inhibitory antibodies to factor VIII or IX and previously received on-demand treatment with "bypassing agents" for bleeding. In the second study (ATLAS-A/B), patients did not have inhibitory antibodies and previously received on-demand treatment with clotting factor concentrates. In both studies, patients received either a fixed dose of Qfitlia monthly or their usual on-demand treatment (bypassing agents or clotting factor concentrates) as needed for 9 months. The primary endpoint was the estimated annualized bleeding rate.

    - The fixed dose of Qfitlia is not approved because it led to excessive clotting in some patients.
    - Patients from both studies subsequently entered a long-term extension study in which they received an adjustable dose of Qfitlia based on periodic measurements of antithrombin activity. This antithrombin-based dosing regimen is the approved dosage regimen. Efficacy of Qfitlia using the antithrombin-based dosing regimen was established by comparing patients on this dosing regimen of Qfitlia during the long-term extension study to the on-demand control data from the two randomized studies.

- **In the patients with inhibitors** who received the antithrombin-based dosing regimen of Qfitlia, **there was a 73% reduction in estimated annualized bleeding rat**e compared to those who received on-demand treatment with bypassing agents. **In participants without inhibitors** who received the antithrombin-based dosing regimen of Qfitlia, **there was a 71% reduction in estimated annualized bleeding rate** compared to those who received on-demand treatment with clotting factor concentrates.

- Qfitlia carries a boxed warning for thrombotic events and acute and recurrent gallbladder disease.

- An additional warning and precaution for Qfitlia is hepatotoxicity.

- The most common adverse reactions (> 10%) with Qfitlia use were viral infection, nasopharyngitis, and bacterial infection.

- The recommended starting dose of Qfitlia is **50 mg once subcutaneously every two months**. The dose and/or dosing interval should be adjusted, if needed, to maintain antithrombin activity between 15% to 35%. Refer to the drug label for complete dose modification instructions.

    - Qfitlia is intended for use under the guidance of a healthcare provider. Proper training should be provided to patients and/or caregivers on the preparation and administration of

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Qfitlia prior to use. **A patient may self-inject Qfitlia, or the patient's caregiver may administer Qfitlia.**
  - In pediatric patients 12 to 17 years of age, it is recommended that Qfitlia be administered by or under the supervision of an adult.
  - Monitor antithrombin activity using an FDA-cleared test. Information on FDA-cleared tests for antithrombin activity is available at http://www.fda.gov/CompanionDiagnostics.

- Sanofi's launch plans for Qfitlia are pending. Qfitlia will be available as a 50 mg/0.5 mL single-dose prefilled pen and a 20 mg/0.2 mL single-dose vial.