Ibtrozi™ (taletrectinib) – New orphan drug approval

- On June 11, 2025, the FDA announced the approval of Nuvation Bio's Ibtrozi (taletrectinib), for the **treatment of adult patients with locally advanced or metastatic ROS1-positive non-small cell lung cancer (NSCLC)**.

- ROS1-positive NSCLC is a rare and aggressive form of lung cancer, accounting for approximately 2% of new NSCLC cases, or about 3,000 new diagnoses of advanced disease annually in the U.S.

- Ibtrozi is a central nervous system-active, selective, ROS1 inhibitor.

- The efficacy of Ibtrozi was established in two single-arm, open-label studies (TRUST-I or TRUST-II) in patients with ROS1-positive locally advanced or metastatic NSCLC. The efficacy populations included 157 patients naïve to treatment with a ROS1 tyrosine kinase inhibitor (TKI) and 113 patients who received one prior ROS1 TKI. Patients could be chemotherapy-naïve or have received prior chemotherapy for locally advanced disease. The major efficacy measures were confirmed overall response rate (ORR) and duration of response (DOR).

    - In TKI-naïve patients, the ORR was 90% (95% CI: 83, 95) and 85% (95% CI: 73, 93) in TRUST-I and TRUST-II, respectively. The median DOR was not reached in TRUST-I and was not included in TRUST-II given the shorter duration of follow-up.
    - **In TKI-pretreated patients, the ORR was 52% (95% CI: 39, 64) and 62% (95% CI: 46, 75) in TRUST-I and TRUST-II, respectively**. The median DOR was 13.2 months (95% CI: 7.7, 24.9) in TRUST-I and was not included in TRUST-II given the shorter duration of follow-up.

- Warnings and precautions for Ibtrozi include hepatotoxicity; interstitial lung disease/ pneumonitis; QTc interval prolongation; hyperuricemia; myalgia with creatine phosphokinase elevation; skeletal fractures; and embryo-fetal toxicity.

- The most common adverse reactions (≥ 20%) with Ibtrozi use were diarrhea, nausea, vomiting, dizziness, rash, constipation, and fatigue. The most frequently reported Grade 3 or 4 laboratory abnormalities (≥ 5%) were increased alanine aminotransferase, increased aspartate aminotransferase, decreased neutrophils, and increased creatine phosphokinase.

- The recommended dosage of Ibtrozi is **600 mg orally once daily** on an empty stomach until disease progression or unacceptable toxicity.

    - Patients should be selected for the treatment of locally advanced or metastatic NSCLC based on the presence of ROS1 rearrangement(s) in tumor specimens.
    - An FDA-approved test to detect ROS1 rearrangement(s) for selecting patients for treatment with Ibtrozi is not currently available.

- Nuvation Bio's launch plans for Ibtrozi are pending. Ibtrozi will be available as a 200 mg capsule.