US FDA approves Nuvation Bio's taletrectinib for treatment of advanced ROS1-positive non-small cell lung cancer

Nuvation Bio Inc, a global oncology company focused on tackling some of the toughest challenges in cancer treatment, announced that the US Food and Drug Administration (FDA) has approved Ibtrozi (taletrectinib) for the treatment of adult patients with locally advanced or metastatic ROS1-positive (ROS1+) non-small cell lung cancer (NSCLC). Ibtrozi is a highly selective, next-generation oral ROS1 tyrosine kinase inhibitor (TKI) designed to address some of the outstanding challenges of treating ROS1+ NSCLC. It has demonstrated high response rates with durable benefit and intracranial activity and is generally well tolerated, providing a new treatment option for patients with advanced ROS1+ NSCLC.

"The US FDA approval of Ibtrozi marks a major milestone in the evolution of targeted therapy for advanced ROS1-positive NSCLC," said David Hung, founder, president and CEO of Nuvation Bio. "We believe one of the greatest threats to ROS1-positive lung cancer patients is disease progression, especially in the first-line setting. In pivotal trials, Ibtrozi delivered high response rates with sustained durability—truly meaningful benefits for patients. With its clinically proven efficacy and safety profile, we believe Ibtrozi has the potential to become a new standard for what targeted therapies can achieve in this type of lung cancer. With approvals for Ibtrozi now in the US and China, and additional global filings underway, we remain committed to delivering innovative therapies that help patients stay ahead of their disease."

ROS1+ 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 US. The median age at diagnosis for patients with this type of lung cancer is approximately 50 years old, and the disease is more likely to occur in people who have never smoked. Brain metastases are common and a leading cause of disease progression and mortality in this population.

"For people living with advanced ROS1-positive lung cancer, who tend to be diagnosed at a younger age, having another treatment option can make a real difference for them and their loved ones," said Janet Freeman-Daily, co-founder and president of The ROS1ders. "The approval of this new targeted therapy is a meaningful step forward for the advanced ROS1+ lung cancer community and offers hope for patients facing the added challenge of cancer spreading to the brain."

The US FDA approval of Ibtrozi is supported by one of the largest global clinical trial programmes in ROS1+ NSCLC to date, with over 300 patients enrolled in the pivotal TRUST-I and TRUST-II studies.

In TRUST-I, Ibtrozi achieved a confirmed overall response rate (cORR) of 90% in TKI-naïve patients. These findings were reinforced by the TRUST-II results, with a cORR of 85% in TKI-naïve patients. The median duration of response (DOR) was not yet reached for either trial, based

on a cutoff date that is nearly five months later than that of the pooled TRUST-I and TRUST-II analysis published in April in the Journal of Clinical Oncology. For TRUST-I, with a median follow-up for responses of 40 months, the longest DOR was observed at 46.9 months and ongoing. For TRUST-II, with a median follow-up for responses of 19 months, the longest DOR was observed at 30.4 months and ongoing as of October 2024. Given the single-arm nature of the TRUST clinical studies, median progression-free survival (PFS) is not provided in the label.

Across the pivotal studies, consistent results were also observed among patients who were previously treated with a ROS1 TKI (TKI-pretreated). In TRUST-I, treatment with Ibtrozi achieved a cORR of 52% and median DOR of 13.2 months for TKI-pretreated patients, with median follow-up for responses of 33 months. In TRUST-II, treatment with Ibtrozi achieved a cORR of 62%, and as of October 2024 the median DOR was 19.4 months in these patients, with a median follow-up for responses of 19 months.

Brain metastases are among the most common and devastating complications in advanced ROS1+ NSCLC. Ibtrozi was designed to penetrate the central nervous system (CNS) and has demonstrated consistent intracranial responses in patients with measurable brain metastases at baseline. An intracranial response was achieved in 73% of TKI-naive patients (11/15) and 63% of TKI-pretreated patients (15/24).

“Patients living with advanced ROS1+ non-small cell lung cancer and their healthcare providers are in need of new treatment options,” added Nathan Pennell, TRUST study investigator and Professor of Medicine at the Cleveland Clinic. “Ibtrozi’s durability of response and ability to effectively penetrate the brain, coupled with a well-characterized and manageable safety profile, further addresses these critical needs for patients. I believe this now-approved therapy offers providers and patients a promising new option for the treatment of advanced ROS1+ non-small cell lung cancer.” Dr. Pennell is a compensated member of Nuvation Bio’s advisory committee.

Ibtrozi was generally well-tolerated, with most adverse events being low grade, transient and manageable. Patients infrequently (7%) discontinued treatment due to treatment-emergent adverse events (TEAEs). The most common adverse reactions (=20%) included diarrhea (64%), nausea (47%), vomiting (43%), dizziness (22%), rash (22%), constipation (21%), and fatigue (20%). Overall, the majority of CNS events were mild to moderate (~90%) and resolved within days, and dose modifications due to these events were low (~5%). Approximately 90% of reported cases of dizziness were Grade 1 (mild) and transient. Liver enzyme elevations (AST 87%/ALT 85%) and QT prolongation (19%) were manageable with standard monitoring and dose modifications. Ibtrozi is approved as a 600 mg once-daily oral dose, supported by a half-life of approximately 66 hours and broad tissue distribution, including the brain, enabling sustained systemic and CNS exposure.

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