INDICATION and IMPORTANT SAFETY INFORMATION

INDICATION

JIDEYTRO™ (zidesamtinib) is indicated for the treatment of adult patients with locally advanced or metastatic *ROS1*-positive non-small cell lung cancer (NSCLC) who received a prior ROS1 kinase inhibitor.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS:

Warnings and Precautions reflect the pooled safety population (N=446) who received JIDEYTRO at a dose of 100 mg orally once daily until disease progression or unacceptable toxicity in ARROS-1.

Central Nervous System (CNS) Adverse Reactions (AR):

- Dizziness, ataxia, cognitive and psychiatric disorders occurred in 25% of patients; of these, 2.5% were Grade 3 or 4. One patient (0.2%) with brain metastases experienced a Grade 3 seizure.
- Dizziness, including vertigo, presyncope, and positional dizziness, occurred in 12% of patients; of these, 0.2% were Grade 3. Dosage interruption for dizziness was required in 0.4% and dose reduction in 0.7% of patients.
- Ataxia, including gait disturbance and balance disorder, occurred in 2% of patients; all were Grade 1 or 2.
- Cognitive impairment occurred in 9% of patients; of these, 1.6% were Grade 3 or 4. Cognitive impairment included memory impairment (3.1%), cognitive disorder (1.6%), hallucination (1.1%), delirium (1.1%), aphasia (0.9%), amnesia (0.7%), confusional state (0.7%), anterograde amnesia (0.2%), disturbance in attention (0.4%), and slow speech (0.2%). Dose interruption for cognitive impairment was required in 1.3% of patients.
- Psychiatric disorders occurred in 6% of patients; of these, 0.7% were Grade 3 or 4. Psychiatric disorders included anxiety (3.1%), depression (1.3%), agitation (0.7%), affect lability (0.4%), irritability (0.4%), abnormal behavior (0.2%), depressed mood (0.2%), personality change (0.2%), psychotic disorder (0.2%), and suicidal ideation (0.2%). Dosage interruption for psychiatric disorders was required in 0.9% of patients.
- Advise patients to avoid engaging in hazardous tasks requiring mental alertness and motor coordination, such as operating machinery or driving a motor vehicle if they are experiencing CNS reactions.
- Monitor patients for CNS adverse reactions and suicidal thoughts and behaviors during treatment with JIDEYTRO. Withhold and then resume at the same or reduced dose upon improvement or permanently discontinue JIDEYTRO based on severity.

QTc Interval Prolongation:

- JIDEYTRO can cause QTc interval prolongation, which can increase the risk for ventricular tachyarrhythmias (e.g., torsades de pointes) or sudden death. JIDEYTRO has not been studied in patients with a history of QTcF >450 msec on more than one assessment prior to initiation.
- Of the 435 patients who underwent at least one post-baseline electrocardiogram (ECG) assessment, 2% experienced an increase in QTcF of >60 msec compared to baseline after receiving JIDEYTRO and 0.2% increase in QTcF to >500 msec. QTc prolongation led to dose interruption in 0.4% of patients.

- Evaluate ECGs and electrolytes prior to administration of JIDEYTRO and monitor periodically during treatment. Adjust the frequency of monitoring based on risk factors such as known long QT syndromes, clinically significant bradyarrhythmias, severe or uncontrolled heart failure, and concomitant medications associated with QTc interval prolongation.
- Withhold, then resume at the same or reduced dose, or permanently discontinue JIDEYTRO based on severity.

Interstitial Lung Disease (ILD)/Pneumonitis:

- JIDEYTRO can cause severe or life-threatening ILD or pneumonitis.
- ILD/pneumonitis occurred in 1.8% of patients, including Grade 3 or 4 in 0.4%.
- ILD/pneumonitis led to dose interruption in 0.7%, dose reduction in 0.2%, and permanent discontinuation in 0.4% of patients.
- Monitor patients for new or worsening pulmonary symptoms indicative of ILD/pneumonitis. Immediately withhold JIDEYTRO in patients with suspected ILD/pneumonitis, then upon recovery resume at the same or reduced dose or permanently discontinue based on severity.

Skeletal Fractures:

- JIDEYTRO can increase the risk of skeletal fractures.
- Five patients (1.1%) experienced skeletal fractures. Grade 3 ankle fractures occurred in two patients (0.4%). Dose interruptions for fractures occurred in 0.4% of patients.
- Promptly evaluate patients with signs or symptoms of fractures.

Myalgia with Creatine Phosphokinase (CPK) Elevation:

- JIDEYTRO can cause myalgia with creatine phosphokinase (CPK) elevation.
- Myalgia occurred in 13% of patients. Based on laboratory values, concurrent myalgia with increased CPK occurred in 2.1% of patients.
- Advise patients to report unexplained muscle pain or tenderness. Monitor serum CPK levels prior to administration of JIDEYTRO and every 2 weeks during the first month of treatment and then every 1 to 2 months and as clinically indicated in patients reporting unexplained muscle pain or tenderness. Withhold, then resume JIDEYTRO at the same or reduced dose, or permanently discontinue JIDEYTRO based on severity.

Pancreatic Toxicity:

- JIDEYTRO can cause pancreatic toxicity. In the pooled safety population, among the subgroup of patients who underwent pancreatic lab testing, increased amylase and lipase levels occurred in 22% and 25%, respectively, with Grade 3 increased lipase in 8% of patients. Grade 3 lipase elevation resulted in JIDEYTRO dose reduction in one patient. In the pooled safety population, Grade 3 pancreatitis occurred in one patient (0.2%).
- Evaluate amylase and lipase prior to administration of JIDEYTRO and monitor periodically during treatment. Based on the severity of the adverse reaction, temporarily withhold, reduce the dose, or permanently discontinue JIDEYTRO.

Embryo-Fetal Toxicity:

- Based on literature reports in humans with congenital mutations leading to changes in tropomyosin receptor kinase (TRK) signaling, findings from animal studies and its mechanism of action, JIDEYTRO can cause fetal harm when administered to a pregnant woman.
- Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with JIDEYTRO and for 6 months after the last dose.
- Advise male patients with female partners of reproductive potential to use effective contraception during treatment with JIDEYTRO and for 3 months after the last dose.

ADVERSE REACTIONS:

- The most common adverse reactions (≥15%) were edema, peripheral neuropathy, constipation, fatigue, and dyspnea.
- The most common Grade 3 or 4 laboratory abnormalities (≥2%) were increased lipase, increased CPK, increased triglycerides, decreased lymphocytes, and decreased hemoglobin.
- Clinically relevant adverse reactions in <10% of patients receiving JIDEYTRO were cognitive disorders, psychiatric disorders, stomatitis, ataxia, ILD/pneumonitis, QTc prolongation, pancreatitis, and ankle fracture.

DRUG INTERACTIONS:

Strong and Moderate CYP3A Inhibitors:

- Avoid concomitant use of JIDEYTRO with a strong or moderate CYP3A inhibitor as this could increase JIDEYTRO exposure, which may increase the risk of JIDEYTRO adverse reactions.

Strong and Moderate CYP3A Inducers:

- Avoid concomitant use of JIDEYTRO with strong or moderate CYP3A inducers as this could decrease JIDEYTRO exposure, which may decrease the effectiveness of JIDEYTRO.

Please see Full Prescribing Information.