Jazz Pharmaceuticals Showcases New Clinical and Translational Data for Modeyso™ (dordaviprone) in H3 K27M-mutant Diffuse Midline Glioma at SNO 2025

November 11, 2025

Data highlight continued progress in Jazz's brain tumor research and demonstrate the company's commitment to advancing treatment options for patients with rare and aggressive brain tumors

For U.S. media and investors only

DUBLIN, Nov. 11, 2025 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced that the company will present five abstracts at the 2025 Society for Neuro-Oncology (SNO) Annual Meeting taking place November 19-23 in Honolulu, Hawaii. The presentations will feature both clinical and preclinical research evaluating Modeyso™ (dordaviprone), as well as new preclinical data featuring JZP3507 (formerly ONC206) in central nervous system (CNS) tumors, reflecting Jazz's growing impact and innovation in neuro-oncology.

Key presentations include:

- New translational research characterizing potential molecular pathways associated with sensitivity to dordaviprone and exploring how targeted combination strategies may help to enhance response.
- Preclinical data evaluating how dordaviprone may influence the tumor immune environment to inform future research on rational immunotherapy combinations.

"These presentations at SNO represent the collective progress of our dedicated research team within Jazz and our academic collaborators who share a relentless commitment to improving outcomes for patients living with devasting brain tumors," said Joshua E. Allen, Ph.D., chief scientific officer, oncology, Jazz Pharmaceuticals. "The SNO presentations provide new insights into how treatment might be further optimized in the future for patients with brain cancer. The continued advancement of *Modeyso* and our ongoing research across many areas, including the JZP3507 (ONC206) program, reflect our belief that through scientific innovation and persistence, we will continue to bring new hope to patients and families who urgently need better options."

The full SNO abstracts are available here. The full list of Jazz presentations at SNO 2025 are:

Topic	Author	Presentation Details
EGFR metabolically suppresses differentiation in H3 K27M-mutant diffuse midline glioma	Sunjong Ji, Robert Doherty, Mateus Mota, Siva Kumar Natarajan, Daniel de la Nava, Peter Sajjakulnukit, Erik R. Peterson, Tiffany Adam, Michael Niculcea, Katie Vo, Kelsey Wink, Subramaniam Bavani, Yadavilli Sridevi, Javad Nazarian, Joanna J. Phillips, Sabine Mueller, Mariella Filbin, David A. Solomon, Daniel R. Wahl, Costas Lyssiotis, Tingting Qin, Alexander Beck, Pavithra Viswanath, Nicholas Nuechterlein, Sebastian M. Waszak, Sriram Venneti, Carl Koschmann	**Type:** Oral Abstract **Session:** Pediatric Abstracts – Session I **Date:** Friday, November 21, 10:49-10:54 a.m. HST **Number:** TMET-51
Dordaviprone (ONC201) in a pediatric patient with recurrent H3 K27M-mutant diffuse glioma and leptomeningeal disease	Gabriel Batistella, Felipe D'Almeida Costa, Tomás Freddi, Nicholas Wojtynek, David Korones	**Type:** Poster **Session:** Poster and Networking Session **Date:** Friday, November 21, 11:30 a.m.-12:45 p.m. HST **Number:** CTP-15
Allosteric ClpP agonist ONC206 alters mitochondrial metabolism and stress response to elicit apoptosis in meningioma	Andrew K. Lee, Cristina Maranto, Scott Foster, Varun V. Prabhu, Joshua E. Allen	**Type:** Poster **Session:** Poster and Networking Session **Date:** Saturday, November 22, 11:45 a.m.-1:05 p.m. HST **Number:** TMET-26
ONC206 inhibits tumor growth and is a potential novel therapeutic strategy for	Theophilos Tzaridis, Jingbo Liu, Joshua E. Allen, Varun V. Prabhu, Robert J. Wechsler-Reya, Tobey MacDonald	**Type:** Poster **Session:** Poster and

refractory medulloblastoma		Networking Session **Date:** Saturday, November 22, 11:45 a.m.-1:05 p.m. HST **Number:** EXTH-70
Leveraging the immunomodulatory effects of dordaviprone (ONC201) to induce long-term survival response in diffuse midline glioma patients and models	Clara Savary, Mika L. Persson, Evangeline R. Jackson, Ryan J. Duchatel, Tuan Vo, Izac J. Findlay, Alicia M. Douglas, Liesl Bramberger, Daniel de la Nava, Bryce C. Thomas, Holly P. McEwen, Tyrone S. Beitaki, Laura Rodriguez de la Fuente, Yolanda Colino-Sanguino, Fatima Valdes Mora, Martin R. Larsen, Pouya Faridi, Jeff Holst, Jemma Mayall, Cassie N. Kline, Andrea T. Franson, Sriram Venneti, Hubert Hondermarck, Jay Horvat, Brett Nixon, Rodrigo Cartaxo, Javad Nazarian, Esther Hulleman, Sabine Mueller, Nicholas A. Vitanza, Carl Koschmann, Marta M. Alonso, Tiago Ferreira Carvalheiro, Jasper van der Lugt, Matthew D. Dun	**Type:** Oral Abstract **Session:** CNS Rare Tumor Abstracts – Session II **Date:** Sunday, November 23, 11:34-11:39 a.m. HST **Number:** DDDR-38

About H3 K27M-Mutant Diffuse Midline Glioma
H3 K27M-mutant diffuse midline glioma is a rare and highly aggressive brain tumor that primarily affects the midline structures of the brain and spinal cord.[1,2] It is characterized by a specific genetic mutation (H3 K27M) that disrupts epigenetic regulation and drives tumor growth.[4] Most commonly diagnosed in children and young adults, patients with this type of glioma often face an extremely poor prognosis, with limited therapeutic options and very low survival rates following recurrence.[3] Median survival is approximately one year from diagnosis and 5.1 months after progressing following frontline therapy.[7]

About Modeyso ™ (dordaviprone)
Modeyso (dordaviprone) (formerly known as ONC201) is approved by the U.S. Food and Drug Administration (FDA) for the treatment of H3 K27M-mutant diffuse midline glioma in adult and pediatric patients one year of age and older with progressive disease following prior therapy.[4] *Modeyso* is an oral small molecule administered once weekly. *Modeyso* is a mitochondrial caseinolytic protease P (ClpP) agonist and also inhibits the dopamine-2 (D2) receptor. In vitro, dordaviprone activated the integrated stress response, induced apoptosis, and altered mitochondrial metabolism, leading to restored histone H3 K27 trimethylation in H3 K27M-mutant diffuse glioma.[4]

Modeyso received accelerated approval in August 2025 based on a pre-specified integrated efficacy analysis of 50 adult and pediatric patients with recurrent H3 K27M-mutant diffuse midline glioma enrolled across five open-label clinical studies (ONC006, ONC013, ONC014, ONC016, and ONC018). Continued approval may be contingent upon verification and description of clinical benefit, including in the ongoing Phase 3 ACTION trial (NCT05580562), which is evaluating the safety and clinical benefit of dordaviprone [5] in newly diagnosed patients with H3 K27M-mutant diffuse glioma following radiotherapy. *Modeyso* was developed by Chimerix prior to its acquisition by Jazz Pharmaceuticals in April 2025.

Modeyso (dordaviprone) is only approved in the United States.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS
Hypersensitivity
MODEYSO can cause severe hypersensitivity reactions.

In the pooled safety population, Grade 3 hypersensitivity reactions occurred in 0.3% of patients receiving MODEYSO. Signs and symptoms of hypersensitivity may include rash, hives, fever, low blood pressure, wheezing, or swelling of the face or throat.

Inform patients about the signs and symptoms of hypersensitivity reactions and instruct them to seek immediate medical attention if symptoms occur.

If clinically significant hypersensitivity or anaphylaxis occur, immediately interrupt MODEYSO and initiate appropriate medical treatment and supportive care. Based on the severity of the adverse reaction, temporarily interrupt or permanently discontinue MODEYSO.

QTc Interval Prolongation
MODEYSO causes concentration-dependent QTc interval prolongation, which can increase the risk for ventricular tachyarrhythmias (e.g. torsades de pointes) or sudden death.

In patients who received MODEYSO and underwent at least one post baseline ECG, QTcF increase of >60 msec compared to baseline and QTcF >500 msec occurred in 6% and 1.2% of patients, respectively.

Monitor ECGs and electrolytes prior to initiation and periodically during treatment, as clinically indicated. Increase the frequency of monitoring in patients with congenital long QT syndrome, existing QTc prolongation, a history of ventricular arrhythmias, electrolyte abnormalities, heart failure, or who are taking strong or moderate CYP3A4 inhibitors.

Avoid concomitant use with other agents known to prolong the QT interval. If concomitant use cannot be avoided, increase the frequency of monitoring and separate administration of MODEYSO and QT-prolonging product.

Interrupt or reduce the dose of MODEYSO in patients who develop QT prolongation; permanently discontinue in patients with signs of life-threatening arrhythmias.

Embryo-Fetal Toxicity
MODEYSO 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 MODEYSO and for 1 month after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with MODEYSO and for 1 month after the last dose.

ADVERSE REACTIONS

Serious adverse reactions occurred in 33% of the 376 patients who received MODEYSO. Serious adverse reactions in >2% of patients included hydrocephalus (5%), vomiting (4.3%), headache (3.2%), seizure (2.4%), and muscular weakness (2.1%). Fatal adverse reactions occurred in 1% of patients who received MODEYSO, including cardiac arrest (0.5%), intracranial hemorrhage (0.3%), and encephalopathy (0.3%).

The most common adverse reactions (≥20%) reported in clinical trials with MODEYSO were fatigue (34%), headache (32%), vomiting (24%), nausea (24%), and musculoskeletal pain (20%). The most common (≥2%) Grade 3 or 4 laboratory abnormalities were decreased lymphocytes (7%), decreased calcium (2.7%), and increased alanine aminotransferase (2.4%).

DRUG INTERACTIONS

Strong and Moderate CYP3A4 Inhibitors

Avoid concomitant use of MODEYSO with strong and moderate CYP3A4 inhibitors. If concomitant use cannot be avoided, reduce the MODEYSO dose as recommended and monitor for toxicity.

Strong and Moderate CYP3A4 Inducers

Avoid concomitant use of strong and moderate CYP3A4 inducers with MODEYSO.

USE IN SPECIFIC POPULATIONS

Lactation

There are no data on the presence of MODEYSO in human milk because of the potential for serious adverse reactions from MODEYSO in breastfed children, advise women not to breastfeed during treatment with MODEYSO and for 1 week after the last dose.

Pediatric Use

The safety and effectiveness of MODEYSO have not been established in patients less than 1 year of age. Dosing has not been established for patients weighing less than 22 pounds (10 kg).

Please refer to the full Prescribing Information, available here, including both Patient Information and Instructions for Use, for complete safety and administration information.

About Jazz Pharmaceuticals

Jazz Pharmaceuticals plc (Nasdaq: JAZZ) is a global biopharma company whose purpose is to innovate to transform the lives of patients and their families. We are dedicated to developing potentially life-changing medicines for people with serious diseases – often with limited or no therapeutic options. We have a diverse portfolio of marketed medicines, including leading therapies for sleep disorders and epilepsy, and a growing portfolio of cancer treatments. Our patient-focused and science-driven approach powers pioneering research and development advancements across our robust pipeline of innovative therapeutics in oncology and neuroscience. Jazz is headquartered in Dublin, Ireland with research and development laboratories, manufacturing facilities and employees in multiple countries committed to serving patients worldwide. Please visit www.jazzpharmaceuticals.com for more information.

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[1] Yang, Z., Sun, L., Chen, et al. New progress in the treatment of diffuse midline glioma with H3K27M alteration. *Heliyon*. 2024;*10*(2).

[2] National Cancer Institute. Diffuse Midline Glioma: Diagnosis and Treatment. Updated August 20, 2024. Accessed June 20, 2025. https://www.cancer.gov/rare-brain-spine-tumor/tumors/diffuse-midline-gliomas

[3] Bagley, S. J., Umemura, et al. Prognostic Features of Recurrent Midline and H3 K27M-Mutant Glioma. *Cancers*. 2025; 17(13):2107. https://doi.org/10.3390/cancers17132107

[4] MODEYSO (dordaviprone) Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc.

[5] ClinicalTrials.gov. ONC201 in H3 K27M-mutant Diffuse Glioma Following Radiotherapy (the ACTION Study) (ACTION). Updated June 6, 2025. Accessed June 20, 2025. Study Details | ONC201 in H3 K27M-mutant Diffuse Glioma Following Radiotherapy (the ACTION Study) | ClinicalTrials.gov

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