Nulibry™ (fosdenopterin) – New orphan drug approval

- On February 26, 2021, the FDA announced the approval of BridgeBio Pharma's Nulibry (fosdenopterin), to reduce the risk of mortality in patients with molybdenum cofactor deficiency (MoCD) Type A.

- MoCD Type A is a rare, genetic, metabolic disorder that typically presents in the first few days of life, causing intractable seizures, brain injury and death. Most patients die in early childhood from infections.

    - Before the approval of Nulibry, the only treatment options included supportive care and therapies directed towards the complications arising from the disease.
    - MoCD Type A impacts less than 150 patients globally.

- Patients with MoCD Type A cannot produce a substance known as cyclic pyranopterin monophosphate (cPMP). Nulibry replaces the missing cPMP.

- The efficacy of Nulibry was established on data from three clinical studies (studies 1, 2, and 3) that were compared to data from a natural history study. A total of 13 patients received Nulibry and recombinant *Escherichia coli*-derived cPMP (rcPMP) in the three trials. Efficacy was assessed by comparing overall survival (OS) in pediatric patients treated with Nulibry or rcPMP with an untreated natural history cohort of pediatric patients with genetically confirmed MoCD Type A who were genotype-matched to the treated patients (n = 18).

    - Patients treated with Nulibry or rcPMP had an improvement in OS compared to the untreated, historical control group.

Titration schedule	Nulibry (or rcPMP)	Untreated genotype-matched historical control	Treatment difference (95% CI)
Number of deaths (%)	2 (15%)	12 (67%)	
Kaplan Meier survival probability (95% CI) 1 year 3 years	 92% (57, 99) 84% (49, 96)	 67% (40, 83) 55% (30, 74)	
Mean survival time (95% CI) At 1 year At 3 years	 11 months (9, 13) 32 months (26, 37)	 10 months (8, 12) 24 months (17, 31)	 1 month (-1, 4) 8 months (-1, 16)
Hazard ratio for risk of death (95% CI)	0.18 (0.04, 0.72)		

- A warning and precaution for Nulibry is potential for photosensitivity.

- The most common adverse reactions (> 25%) with Nulibry use were catheter-related complications, pyrexia, viral infection, pneumonia, otitis media, vomiting, cough/sneezing, viral upper respiratory infection, gastroenteritis, bacteremia, and diarrhea.

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- The recommended dosage regimen of Nulibry in patients less than one year of age (by gestational age) is based on actual body weight as shown in the table below. The dose is administered as an intravenous infusion once daily.

Titration schedule	Preterm neonates (gestational age < 37 Weeks)	Term neonates (Gestational age ≥ 37 weeks and above)
Initial dosage	0.4 mg/kg once daily	0.55 mg/kg once daily
Dosage at month 1	0.7 mg/kg once daily	0.75 mg/kg once daily
Dosage at month 3	0.9 mg/kg once daily	0.9 mg/kg once daily

- For patients one year of age or older, the recommended dosage of Nulibry is 0.9 mg/kg (based on actual body weight).

- Nulibry is intended for administration by a healthcare provider. If deemed appropriate by a healthcare provider, Nulibry may be administered at home by the patient's caregiver. If Nulibry can be administered by a caregiver/patient, they should be advised to read the detailed instructions on the preparation, administration, storage, and disposal of Nulibry for caregivers.

- BridgeBio Pharma's launch plans for Nulibry are pending. Nulibry will be available as a 9.5 mg lyophilized powder or cake in a single-dose vial for reconstitution.