Azafaros Receives FDA Orphan Drug Designation for AZ-3102 in GM2 Gangliosidosis

Leiden, The Netherlands, February 1, 2022 – Azafaros B.V. today announced that the US Food and Drug Administration (FDA) has granted Orphan Drug Designation (ODD) for AZ-3102, a novel oral small molecule, in GM2 gangliosidosis including both Sandhoff and Tay-Sachs diseases. The ODD for GM2 gangliosidosis has been granted based on efficacy demonstrated in a Sandhoff mouse model, including a clear effect on animal survival. These promising preclinical findings support Azafaros' strategy to develop AZ-3102 as a potential disease-modifying treatment for GM1 and GM2 gangliosidoses and other neurogenetic, pediatric, metabolic lysosomal disorders. The company has successfully completed a Phase 1 clinical trial with AZ-3102 in healthy volunteers and will be presenting first-in-human clinical data from the study at the 18th Annual WORLD*Symposium™*, being held from February 7 – 11, 2022, in San Diego, CA.

"This designation from the FDA represents an important milestone in the development of our highly selective, first-in-class dual inhibitor approach with AZ-3102 and provides further validation of our efforts and commitment to provide rare disease patients with new disease-modifying therapeutic options where currently only symptomatic treatments are available," **said Stefano Portolano, Chief Executive Officer of Azafaros**. *"The rapid development of AZ-3102 enabled us to expand its promising preclinical dataset with the first-in-human data that we will present at the WORLDSymposium™ later this month, and we look forward to announcing further updates on our broader clinical program throughout 2022."*

GM2 gangliosidosis, comprising Tay-Sachs, Sandhoff and AB diseases are rare genetic diseases with enzymatic defect causing specific lipids, gangliosides, to accumulate at toxic levels in the brain. As the neurological disease rapidly progresses, subjects living with the disease show a plateau or decline in neurodevelopment, loss of motor skills, difficulties at articulating speech, seizures, and dysphagia leading to aspiration pneumonia, eventually leading to death. The disease prognosis is dismal and it affects mostly infants and young children. AZ-3102 is an orally available azasugar that provides a dual mode-of-action by inhibiting glucosylceramide synthase (GCS) and non-lysosomal glucosylceramidase (GbA2) to reduce harmful lipid accumulation. Azafaros plans to initiate a pivotal Phase 2 study in the second half of 2022.

Orphan Drug Designation by the US FDA provides drug developers with special status and incentives to facilitate the development of therapeutics for rare diseases affecting fewer than 200,000 people in the US. The designation provides seven years of market exclusivity if the drug candidate receives regulatory approval together with exemptions from certain FDA application fees, advice on clinical trial design and tax credits for qualified clinical trial costs.

About AZ-3102

Azafaros' proprietary clinical candidate AZ-3102 is an orally available low-molecular weight azasugar, originally based on discoveries[1] from Leiden University and Amsterdam University Medical Center. It is designed to selectively inhibit two enzymes involved in glycolipid metabolism, called glucosylceramide synthase (GCS) and non-lysosomal neutral glucosylceramidase (GbA2). This dual mode of action aims to reduce toxic glycolipid accumulation. Azafaros completed a first-in-human clinical trial with AZ-3102 in healthy volunteers in 2021 and received Orphan Drug Designation in GM2 Gangliosidosis from the FDA in February 2022.

About Azafaros

Founded in 2018 with a deep understanding of rare genetic disease mechanisms and led by a team of highly experienced industry experts, Azafaros aims to build a pipeline of disease-modifying therapeutics to offer patients and their families new treatment options. The company's lead clinical-staged program is AZ-3102, a highly differentiated, orally available, small molecule with the potential to treat GM1 and GM2 gangliosidosis and other metabolic disorders. By applying its know-how, network, and courage, the Azafaros team challenges traditional development pathways to rapidly bring new drugs to the rare disease patients who need them.

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[1] Ghisadoobe et al., 2014, J Med Chem, doi: 10.1021/jm501181z