Azafaros Announces Enrollment of First Patient in Phase 2 RAINBOW Study Evaluating AZ-3102 in GM2 and NP-C Patients

- **RAINBOW study design enables rapid advancement into the company's planned Phase 3 efficacy trial**

Leiden, The Netherlands, June 8th 2023 – Azafaros B.V. today announced that the first patient has been enrolled into its Phase 2 RAINBOW study (NCT05758922). The clinical trial is being conducted in Brazil and the US and will evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics across two doses of its lead asset, AZ-3102, in patients with GM2 gangliosidosis and Niemann-Pick disease type C (NP-C).

AZ-3102 is a novel, orally available, brain-penetrant azasugar, engineered to have a unique, dual mode of action by inhibiting two key enzymes involved in the metabolism of glycosphingolipids. Azafaros is developing the compound as a potentially disease-modifying treatment in severe metabolic disorders including GM1 and GM2 gangliosidoses and NP-C. Enrollment of the first patient in the study is an important milestone for Azafaros in its mission to bring new treatment options to these patients and their families.

The Phase 2 RAINBOW study is a **ra**ndomized, double-bl**in**d, place**bo**-controlled, multicenter, 12-**w**eek trial assessing the safety, tolerability, pharmacokinetics, and pharmacodynamics of AZ-3102 in patients with GM2 gangliosidosis and NP-C. The study will enroll 12 patients in total (6 with GM2 and 6 with NP-C), aged 12 to 20 years, each of whom will receive either the low dose, high dose, or a placebo. Patients who complete the 12-week study period will be offered a double-blind extension if approved by the country's health authorities. The aim of the short study is to determine the clearance of AZ-3102 from the body and the effect of two different doses in patients to identify the target dose for Azafaros' planned Phase 3 pivotal study.

Dr. Daniel Almeida do Valle, a Paediatric neurologist at the Hospital Infantil Pequeno Príncipe in Curitiba, Brazil, where the first patient has been enrolled, said: *"A childhood diagnosis of GM2 of NP-C is devastating for patients and their families. There is a great need to provide more treatment options to improve the lives of these patients. The safety and tolerability of AZ-3102 has already been seen in healthy volunteers and I am excited to be working with Azafaros to take AZ-3102 further with the Phase 2 RAINBOW trial. This will help us to further our clinical development of AZ-3102, which has great potential to become a treatment option for patients*."

Prof. Dr. Roberto Giugliani, Chief of the Medical Genetics Clinical Research Group at the Hospital de Clinicas de Porto Alegre and Lead Principal Investigator for the study, said: *"Children who suffer from GM2 and NP-C are currently dependent on limited and, in some cases, mostly supportive treatment options. AZ-3102 has the potential to truly impact the course of these devastating disorders. Based on the favorable safety and tolerability profile that Azafaros demonstrated in its Phase 1 healthy volunteer study, the Phase 2 RAINBOW trial will now examine these parameters in patients to identify the optimal dose for further clinical development."*

Stefano Portolano, Chief Executive Officer of Azafaros, said: *"Today's announcement demonstrates our commitment to address the significant unmet medical needs of GM2 and NP-C patients. The design of the RAINBOW study allows us to move quickly and advance AZ-3102 as a potentially transformative treatment for these patients by defining the optimal dose for a pediatric population in a Phase 3 efficacy study, which we plan to initiate in 2024."*

About AZ-3102

AZ-3102 is an orally available azasugar with a unique dual mode of action, developed as a potential treatment for rare lysosomal storage disorders with neurological involvement, including GM1 and GM2 gangliosidoses and Niemann-Pick disease type C (NP-C).

At the start of 2023, AZ-3102 received three Rare Pediatric Disease Designations (RPDD) from the United States Food and Drug Administration (FDA) for the treatment of GM1 and GM2 gangliosidoses, and NP-C. The asset also received Orphan Medicinal Product Designation (OMPD) from the European Medicines Agency (EMA) for the treatment of GM2 gangliosidosis, as well as an Innovation Passport from the UK Medicines and Healthcare Products Regulatory Agency (MHRA) for the treatment of GM1 and GM2 gangliosidoses.

In 2022, the compound received Fast Track Designation for GM1 and GM2 gangliosidoses as well as NP-C and Orphan Drug Designations (ODD) for GM2 gangliosidosis (Sandhoff and Tay-Sachs Diseases) and NP-C from the FDA.

About GM1 and GM2 Gangliosidoses

GM1 gangliosidosis and GM2 gangliosidosis (Tay-Sachs and Sandhoff diseases) are lysosomal storage disorders caused by the accumulation of GM1 or GM2 gangliosides, respectively, in the central nervous system (CNS), resulting in progressive and severe neurological impairment and early death. These diseases mostly affect infants and children, and no disease-modifying treatments are currently available.

About Niemann-Pick Disease Type C (NP-C)

Niemann-Pick disease type C (NP-C) is a progressive, life-limiting neurological lysosomal storage disorder caused by mutations in the NPC1 or NPC2 gene and aberrant endosomal-lysosomal trafficking, leading to the accumulation of various lipids, including gangliosides in the CNS. The onset of disease happens throughout the lifespan of an affected individual, from prenatal life through adulthood. The mainstay of therapy is symptom management.

About Azafaros

Azafaros is a clinical-stage company founded in 2018 with a deep understanding of rare genetic disease mechanisms, a compound library from Leiden University, 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-stage program is AZ-3102, a small molecule azasugar, orally available and brain penetrant, with the potential to treat GM1 gangliosidosis and GM2 gangliosidosis (Tay-Sachs and Sandhoff diseases) and Niemann Pick disease type C (NP-C). 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. Azafaros is supported by a syndicate of leading Dutch and Swiss investors including Forbion, BioGeneration Ventures, BioMedPartners, and Schroders Capital.

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