Orphazyme reports positive arimoclomol data from open-label phase 2/3 extension in Niemann-Pick disease Type C

- *12-month data from open-label extension trial show sustained effect in reducing disease progression over two years*
- *New genetic sub-group analysis recommended by US Food and Drug Administration supports robustness of results*
- *Filling of New Drug Application in US on track for H1 2020, with expected approval in H1 2021*

Copenhagen, Denmark, January 3, 2020 – Orphazyme A/S (ORPHA.CO), a biopharmaceutical company pioneering Heat-Shock Protein response for the treatment of neurodegenerative orphan diseases, today announces 12-month interim data from an open-label extension of a phase 2/3 study of arimoclomol, an investigational product candidate in development for Niemann-Pick disease Type C (NPC).

The long-term data demonstrate a continued positive impact on disease progression over two years. Furthermore, separate data from a post-hoc genetic sub-group analysis of patients provides more evidence of the efficacy of arimoclomol.

Collectively, these new data strengthen the regulatory marketing applications for arimoclomol in the US and Europe. Orphazyme plans to submit a New Drug Application (NDA) for arimoclomol in NPC to the US Food and Drug Administration (FDA) in H1 2020 and a Marketing Authorization Application (MAA) in Europe in H2 2020.

Thomas Blaettler, Chief Medical Officer, commented, "*We are highly encouraged by the 12-month results from our open-label extension study. Arimoclomol had a sustained effect on disease progression over two years. Furthermore, patients initially randomized to placebo in the placebo-controlled trial experienced a 90% reduction in disease progression when switched to arimoclomol treatment".*

Kim Stratton, Chief Executive Officer, said: "These new data confirm our commercial preparations for the launch of arimoclomol in the US as well as in other key markets. We look forward to seeking approval and bringing this innovative treatment to the market to address the significant unmet need in this devastating disease. Arimoclomol is a very promising compound which has the potential to change lives for the better, and we are continuing its development in three other indications: Amyotrophic Lateral Sclerosis (ALS), sporadic Inclusion Body Myositis (sIBM), and Gaucher disease".

Arimoclomol phase 2/3 trial results in NPC confirmed

In 2019, the UK Medicines and Healthcare products Regulatory Agency (MHRA) performed a routine inspection of the clinical research organization that conducted the trial on behalf of Orphazyme. Following a process agreed upon with the MHRA, data from the trial were re-analyzed and overall efficacy and safety previously reported was confirmed. Treatment with arimoclomol adjunct to routine clinical care resulted in a treatment difference of -1.34 (same as previously reported) and a p-value = 0.0537 as measured by the primary endpoint, 5-domain NPC Clinical Severity Scale (5-domain NPCCSS).

New genetic sub-group analysis further supports robustness of phase 2/3 trial results

In NPC, Homozygous functional null mutations are predictive of early onset and rapid progressive disease course. FDA recommended to analyze the influence of the homozygous mutations on the study results. In the placebo-controlled phase of the trial, all patients homozygous for functional null mutations (n=3) were under 4 years and randomized to the arimoclomol treatment group (accounting for 3 of 4 arimoclomol patients in this subpopulation). When this imbalance of treatment allocation is taken into account, arimoclomol has a statistically significant effect on disease progression compared to placebo (p-value 0.024).

Sustained effect with continued reduction in disease progression

Results from the 12-month open-label extension of the phase 2/3 randomized placebo-controlled trial (CT-ORZY-NPC-002) demonstrate sustained benefit of arimoclomol over a two-year period and further evidence of its efficacy and safety profile. Forty-one patients completed the 12-month double-blinded part of the CT-ORZY-NPC-

002 trial and continued into the open-label extension, where all patients received arimoclomol treatment. Patients who switched from placebo to arimoclomol treatment experienced similar reduction of disease progression as observed earlier in those patients randomized to arimoclomol treatment in the placebo-controlled trial as measured by the 5-domain NPCCSS (0.23 progression in the open-label extension vs 2.0 progression in the placebo-controlled trial).

Patients who received arimoclomol for a total of two years showed greater progression in the open-label extension compared to the placebo-controlled part. This was mainly due to patients under 4 years with continued aggressive disease course. In the pre-defined subgroups of patients 4 years and older and patients receiving miglustat as part of their routine clinical care, early treatment initiation with arimoclomol resulted in greater benefit than delayed start of treatment, indicating that the disease course was modified by the treatment.

Arimoclomol was safe and well-tolerated over 24 months.