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Orphazyme announces publication of results from its Phase 2/3 trial of arimoclomol in Niemann-Pick disease type C in the Journal of Inherited Metabolic Disease

- *Arimoclomol was well-tolerated with a statistically significant and clinically meaningful effect on disease progression*

Copenhagen –August 23, 2021 – Orphazyme A/S (ORPHA.CO; ORPH), a late-stage biopharmaceutical company, today announced that results from a Phase 2/3 trial of arimoclomol, an investigational heat-shock protein amplifier, in Niemann-Pick disease type C (NPC) have been published in the peer-reviewed *Journal of Inherited Metabolic Disease (JIMD)*. The online publication is available here.

"*We are pleased to share the data from our Phase 2/3 trial in JIMD. NPC is a rare, inherited progressive neurodegenerative disorder with a high unmet medical need for disease-modifying treatment options. This trial demonstrated a statistically significant and clinically meaningful treatment effect of arimoclomol in NPC supported by significant and consistent effects across several disease- and pharmacodynamic biomarkers. We believe these data establish the potential of arimoclomol as an efficacious and well-tolerated disease-modifying treatment for NPC*" said Thomas Blaettler, Chief Medical Officer at Orphazyme.

The Phase 2/3 trial (NPC-002; ClinicalTrials.gov identifier: NCT02612129), was a prospective, randomized, double-blind, placebo-controlled study. Fifty patients aged 2–18 years were randomized 2:1 to arimoclomol:placebo, stratified by miglustat use. Routine clinical care was maintained. Arimoclomol was administered orally three times daily. The primary endpoint was change in 5-domain NPC Clinical Severity Scale (NPCCSS) score from baseline to 12 months, as described by Mengel et al.[1] and Patterson et al.[2]. The 5-domain NPCCSS comprises the domains determined to be most clinically relevant to patients, caregivers, and clinicians: ambulation, cognition, fine motor skills, speech, and swallowing (Cortina-Borja et al.[3]). A recent validation of the 5-domain NPCCSS shows that a change of 1 point or greater on the total score constitutes a clinically meaningful change for caregivers/patients and physicians (Patterson et al[2]).

At 12-months, a significant treatment effect in favor of arimoclomol of −1.40 points (95% CI: −2.76, −0.03; p = 0.046) was observed, corresponding to a 65% relative reduction in annual disease progression. In the prespecified subgroup of patients receiving miglustat as routine care, arimoclomol resulted in stabilization of disease severity with a treatment difference of −2.06 in favor of arimoclomol (p = 0.006). In the pre-specified subgroup of patients ≥4 years of age the mean treatment difference was −1.80 in favor of arimoclomol (p=0.016), corresponding to 82% relative reduction in annual disease progression.

Arimoclomol was well-tolerated, with adverse events occurring in 88.2% of patients receiving arimoclomol and 75.0% of patients receiving placebo. Fewer patients had serious adverse events with arimoclomol (14.7%) versus placebo (31.3%).

Christophe Bourdon, Chief Executive Officer at Orphazyme added, "*We are committed to serving the NPC community and are working expeditiously to deliver this potential new medicine to patients. Arimoclomol is under regulatory review in Europe, with an anticipated CHMP opinion in Q4 2021, and we continue to evaluate the path forward in the U.S. following the recent FDA response.*"

References:

1. Mengel E, Bembi B, Del Toro M, et al (2020) Clinical disease progression and biomarkers in Niemann–Pick disease type C: a prospective cohort study. Orphanet J Rare Dis 15: 328.
2. Patterson MC, Lloyd-Price L, Guldberg C, et al (2021) Validation of the 5-domain Niemann-Pick type C Clinical Severity Scale. Orphanet J Rare Dis 16: 79.
3. Cortina-Borja M, Vruchte D, Mengel E, et al (2018) Annual severity increment score as a tool for stratifying patients with Niemann-Pick disease type C and for recruitment to clinical trials. Orphanet J Rare Dis 13: 143. doi:110.1186/s13023-13018-10880-13029.

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About Niemann-Pick disease type C
Niemann-Pick disease type C (NPC) is a rare, genetic, progressively debilitating, and often fatal neurodegenerative disease. It belongs to a family known as lysosomal storage diseases and is caused by mutations leading to defective NPC protein. As a consequence, lipids that are normally cleared by the lysosome accumulate in tissues and organs, including the brain, and drive the disease pathology. We estimate the incidence of NPC to be one in 100,000 live births and the number of NPC patients in the United States and in Europe to be approximately 1,800 individuals. There are no approved treatments for NPC in the U.S.

About arimoclomol
Arimoclomol is an investigational drug candidate that amplifies the production of heat shock proteins (HSPs). HSPs can rescue defective misfolded proteins, clear protein aggregates, and improve the function of lysosomes. Arimoclomol is administered orally, and has now been studied in 10 Phase 1, four Phase 2, and three pivotal Phase 2/3 trials. Arimoclomol has received Orphan Drug Designation (ODD) for NPC in the US and EU. Arimoclomol has received Fast-Track Designation (FTD), Breakthrough Therapy Designation (BTD), and Rare Pediatric Disease Designation (RPDD) from the U.S. Food and Drug Administration (FDA) for NPC. On June 17, 2021, Orphazyme received a Complete Response Letter from the FDA regarding its New Drug Application for arimoclomol for the treatment of NPC. A marketing authorization application (MAA) for arimoclomol in NPC has been filed with the European Medicines Agency and is under review.

About Orphazyme A/S
Orphazyme is a late-stage biopharmaceutical company developing arimoclomol for Niemann-Pick disease type C (NPC). Orphazyme is headquartered in Denmark and has operations in the U.S. and Switzerland. ADSs representing Orphazyme's shares are listed on Nasdaq U.S. (ORPH) and its shares are listed on Nasdaq Copenhagen (ORPHA).

Forward-looking statement
This company announcement may contain certain forward-looking statements under the U.S. Private Securities Litigation Reform Act of 1995 and otherwise, including in its intention to pursue regulatory approval for arimoclomol in the United States and Europe and the timing of clinical data. Although the Company believes its expectations are based on reasonable assumptions, all statements other than statements of historical fact included in this company announcement about future events are subject to (i) change without notice and (ii) factors beyond the Company's control. These statements may include, without limitation, any statements preceded by, followed by, or including words such as "target," "believe," "expect," "aim," "intend," "may," "anticipate," "estimate," "plan," "project," "will," "can have," "likely," "should," "would," "could", and other words and terms of similar meaning or the negative thereof. Forward-looking statements are subject to inherent risks and uncertainties beyond the Company's control that could cause the Company's actual results, performance, or achievements to be materially different from the expected results, performance, or achievements expressed or implied by such forward-looking statements, including the risks and uncertainties that are described in the Risk Factors section of the Company's Annual Report on Form 20-F for the year ended December 31, 2020 filed with the U.S. Securities and Exchange Commission (SEC) on March 2, 2021, the Company's Report on Form 6-K filed with the SEC on June 11, 2021, and other filings Orphazyme makes with the SEC from time to time. These documents are available on the "Investors & Media" section of Orphazyme's website at www.orphazyme.com. Except as required by law, the Company assumes no obligation to update these forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in the forward-looking statements, even if new information becomes available in the future.