Company announcement
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Orphazyme phase 2 study of arimoclomol in Gaucher disease demonstrates marked improvements in key clinical markers

- *Arimoclomol demonstrated a marked and clinically meaningful dose-dependent reduction in liver and spleen size*
- *Primary endpoint demonstrating relative reduction in chitotriosidase levels from baseline was observed, although did not achieve statistical significance*
- *Data supports Orphazyme's intention to proceed with pivotal stage clinical development in Gaucher disease*

Copenhagen, Denmark, June 24, 2020 – Orphazyme A/S (ORPHA.CO), a late-stage biopharmaceutical company pioneering the Heat-Shock Protein response for the treatment of neurodegenerative orphan diseases, today announces topline results from a 6-month phase 2 dose-finding study in Gaucher disease with arimoclomol, an investigational Heat-Shock Protein (HSP) amplifier. The data show a dose-dependent effect of arimoclomol on certain disease-relevant clinical secondary endpoints, such as liver and spleen size. Furthermore, the data demonstrate sustained levels of arimoclomol in the cerebrospinal fluid (CSF), providing further evidence of arimoclomol's ability to cross the blood-brain barrier.

Thomas Blaettler, Chief Medical Officer of Orphazyme, said, "We are very encouraged by the data from this exploratory study which show a clear dose-dependent effect of arimoclomol on liver and spleen size as early as 6 months. Although some aspects of Gaucher disease are well-managed by existing drugs, these therapies do not readily cross the blood-brain barrier, leaving an urgent need for new products that can address the debilitating neurological symptoms of this disease. With its oral administration, ability to cross the blood-brain barrier and the overall body of evidence we have gathered, we are encouraged by the potential for arimoclomol to both address an unmet need in Gaucher disease as well as a range of additional neurodegenerative orphan diseases."

The ORARIGAU-01 trial, a double-blind, randomized, placebo-controlled, phase 2 dose-finding trial in Gaucher disease (GD) type 1 and 3 patients naive to enzyme and/or substrate replacement therapy, was conducted at seven sites in India. A total of 39 patients were randomized 1:1:1:1 to receive placebo or 100mg, 200mg, or 400mg arimoclomol citrate (weight-adjusted) three times per day. The objective of the phase 2 study was to evaluate the response of the three dose levels of arimoclomol on various clinical and disease-specific biomarkers over a 6-month treatment period. Overall, 37 patients were included in the analysis set (2 patients excluded due to negative confirmatory GD genotype), of which 21 were type 1 GD and 16 were type 3 GD patients.

Arimoclomol demonstrated a relative reduction in serum chitotriosidase activity from baseline to 6 months, the primary endpoint, across all dosages compared to placebo ranging from -12% to -29%, although statistical significance was not achieved ($p=0.4$). However, a statistically significant and clinically meaningful dose-dependent reduction in liver size ranging from -15% to -20% relative to placebo was observed (dose trend analysis $p<0.05$). In addition, a clinically meaningful dose-dependent reduction in spleen size ranging from -5 to -21% relative to placebo was observed, although statistical significance was not achieved likely due to small sample size (dose trend analysis $p<0.10$). A post-hoc calculation of the correlation between liver and spleen size was conducted, which supports consistency of effect (correlation coefficient: 0.53). Patients anemic at baseline showed a time-dependent increase in hemoglobin in the highest dose group ($p<0.05$). Consistent with arimoclomol's proposed mechanism of action, we observed a dose-dependent increase in the exploratory biomarker, glycosylsphingosine (lyso-Gb1), possibly indicating release out of the cells of affected organs into the blood.

Arimoclomol was well tolerated with a slightly higher incidence of adverse events (70% placebo; 83% arimoclomol all doses) and serious adverse events compared to placebo (SAEs: none in placebo group; 21% arimoclomol all doses). Three patients died during the trial, one in each arimoclomol group (two were considered non-related to treatment and one death, reported as due to natural causes, was deemed possibly related by the investigator.

Kim Stratton, Chief Executive Officer of Orphazyme, said, "This is the second of our studies to show a positive clinical effect of arimoclomol in lysosomal storage diseases. Together with the phase 2/3 trial results in Niemann-

Pick disease Type C (NPC), these data reinforce the potential of Heat-Shock Protein amplification and give us further confidence in arimoclomol as a potential game-changer for patients with lysosomal storage and neurodegenerative diseases. This further fuels our efforts in diseases with high unmet need such as Gaucher disease, other sphingolipidoses and GCase-deficient Parkinson's disease."

Kim Stratton continued, "There is real momentum here at Orphazyme; we recently initiated a rolling New Drug Application (NDA) submission to the U.S. Food and Drug Administration for arimoclomol in NPC, we plan to submit a Marketing Authorisation Application (MAA) for NPC in Europe in H2 2020 and our pivotal trials in the neurodegenerative diseases, sporadic Inclusion Body Myositis (sIBM) and Amyotrophic Lateral Sclerosis (ALS), are ongoing."

An open-label extension of the phase 2 trial is ongoing across the three weight-adjusted dose levels and Orphazyme will continue to evaluate clinical outcomes, monitor safety, and further explore relevant biomarkers.

Orphazyme plans to proceed with pivotal stage clinical development in Gaucher disease and will discuss these data, along with results from the open-label extension, with Gaucher disease experts and regulators.

Conference call

Orphazyme will be hosting an investor call at which Chief Executive Officer, Kim Stratton, Chief Medical Officer, Thomas Blaettler, and Chief Scientific Officer, Thomas Kirkegaard Jensen, will be presenting the data set for arimoclomol in Gaucher disease. The presentation will be followed by a Q&A session.

The call will be held on **Wednesday, June 24, 2020 at 2.00 PM CET/8.00 AM EDT.**

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Event Title: Orphazyme Investor Call
Confirmation code: **4590874**

The presentation will also be available via webcast: https://edge.media-server.com/mmc/p/r8vk782i

For additional information, please contact

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About Orphazyme A/S
Orphazyme is a biopharmaceutical company pioneering the Heat-Shock Protein response for the treatment of neurodegenerative orphan diseases. The company is focused on developing therapies for diseases caused by protein misfolding, protein aggregation, and lysosomal dysfunction. Arimoclomol, the company's lead candidate, is in clinical development for four orphan diseases: Niemann-Pick disease Type C (NPC), Gaucher Disease, sporadic Inclusion Body Myositis (sIBM), and Amyotrophic Lateral Sclerosis (ALS). The Denmark-based company is listed on Nasdaq Copenhagen (ORPHA.CO). For more information, please visit www.orphazyme.com.

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, crosses the blood-brain barrier, and has now been studied in seven phase 1, four phase 2 and one pivotal phase 2/3 trial. Arimoclomol is in clinical development for NPC, Gaucher Disease, sIBM, and ALS. Arimoclomol has received orphan drug designation (ODD) for NPC, sIBM, and ALS in the US and EU. Arimoclomol has received fast-track designation (FTD) from the U.S. Food and Drug Administration (FDA) for NPC, sIBM and ALS. In addition, arimoclomol has received breakthrough therapy designation (BTD) and rare-pediatric disease designation (RPDD) from the FDA for NPC.

About Gaucher
Gaucher disease is a rare, inherited metabolic disorder causing certain sugar containing fats to abnormally accumulate in the lysosomes of cells, especially within cells of the blood system and nerve cells, thereby affecting organs such as the brain, bone marrow, spleen and liver. The typical systemic symptoms of Gaucher disease, which can appear at any age, include an abnormally enlarged liver and/or spleen and low levels of circulating red blood cells and platelets. These systemic symptoms can be treated by existing enzyme replacement therapy (ERT), and substrate reduction therapy (SRT). The neurological symptoms, although heterogeneous, may include muscle rigidity, loss of movement, seizures, cognitive impairment and vision problems and are unable to be treated by these therapies, given their inability to cross the blood brain barrier (BBB). Gaucher disease is the most common lysosomal storage disorder (LSD) with an estimated incidence of 1:40,000 to 1:60,000, and affecting approximately 15,000 individuals in the United States and Europe combined.

Forward-looking statement

This company announcement may contain certain forward-looking statements. 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, including the clinical development and potential benefits of arimoclomol for Gaucher disease, NPC, sIBM and ALS, 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. 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.