Orphazyme provides regulatory update from FDA on arimoclomol for Niemann-Pick disease type C

June 18, 2021

Orphazyme A/S
Company announcement
No. 16/2021
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Copenhagen – June 18, 2021 – Orphazyme A/S (ORPHA.CO; ORPH), a late-stage biopharmaceutical company pioneering the heat shock protein response for the treatment of rare diseases, today announced it has received a Complete Response Letter (CRL) from the U.S. Food and Drug Administration (FDA) following its review of the new drug application for arimoclomol, a heat shock protein amplifier intended for the treatment of Niemann-Pick disease type C (NPC).

The FDA issued the CRL based on needing additional qualitative and quantitative evidence to further substantiate the validity and interpretation of the 5-domain NPC Clinical Severity Scale (NPCCSS) and, in particular, the swallow domain. Further, the FDA noted in the CRL that additional data are needed to bolster confirmatory evidence beyond the single phase 2/3 clinical trial to support the benefit-risk assessment of the NDA.

A primary endpoint of the phase 2/3 clinical trial was progression in disease severity as measured by the 5-domain NPCCSS. This is a disease-specific measure of disease progression consisting of the five clinically most relevant domains to patients with NPC, caregivers and physicians.

"*We are disheartened by the outcome of the FDA's r eview, given the urgent need for a new therapeutic option for NPC, but we remain committed to working with the regulators, with the goal of delivering arimoclomol to families managing this challenging disease,*" said CEO Christophe Bourdon. He continued: "*We will focus our efforts on pursuing the European regulatory approval, with CHMP opinion expected in Q4 2021 and potential Marketing Authorization in Q1 2022. We are assessing the potential path forward in the U.S. in partnership with the FDA. In the short-term, we will need to reduce our costs substantially and freeze all company efforts not related to clinical and regulatory activities to support approval for NPC*."

Deputy Chairman of the Board of Directors, Bo Jesper Hansen, said: "*As representative for Orphazyme's shareholders and as a shareholder myself , I am extremely disappointed. I strongly believe there is a path forward for Orphazyme based on our pursuit of regulatory approval from the European Medicines Agency and continued dialogue with the FDA. Meeting these milestones in NPC will take great sacrifice from everyone in the organization, while we as a Board assist the management team in protecting as much value as possible*."

Changed outlook for 2021
As stated in Orphazyme's Annual Report 2020, initial outlook for the year was subject to various risks and uncertainties, including but not limited to the timing of regulatory decisions, the success of our commercial efforts and our development activities. The outcome of the FDA decision has significant influence on Orphazyme's outlook for full-year 2021.

Orphazyme now expects operating expenses of DKK 700-720 million (previously DKK 800-850 million) resulting in an expected operating loss of DKK 670-700 million (previously DKK 100-150 million). Cash position at year-end 2021 is expected to be approx. DKK 50 million (previously DKK 350 million).

Orphazyme will provide an update and further information in the coming weeks.

Conference calls and webcasts
Orphazyme will host two conference calls/webcasts on June 18, 2021 at 8.00 AM CET and 2.00 PM CET (8.00 AM EDT) to accommodate European and U.S. time zones. The same information will be provided at both conference calls.

The conference calls can be accessed by dialing:

- United Kingdom, local +44 (0) 8444819752
- Denmark, Copenhagen +45 32720417
- France, Paris +33 (0) 170700781
- Netherlands, Amsterdam +31 (0) 207956614
- Sweden, Stockholm +46 (0) 856618467
- Standard International +44 (0) 2071 928338
- United States, New York +1 6467413167

Event Title: Orphazyme Investor Call

Confirmation code for 8.00 AM CET: 2889481

Confirmation code for 2.00 PM CET (8.00 AM EDT): 9349928

Link for webcast at 8.00 AM CET: *https://edge.media-server.com/mmc/p/q5yie99y*

Link for webcast at 2.00 PM CET (8.00 AM EDT): *https://edge.media-server.com/mmc/p/9k4qohms*

An archive of the teleconferences/webcasts will be made available on Orphazyme's website, www.orphazyme.com, following the call.

For additional information, please contact

Orphazyme A/S

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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 neurovisceral 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 Orphazyme A/S
Orphazyme is a late-stage biopharmaceutical company pioneering the heat shock protein response for the treatment of rare diseases. The company is harnessing amplification of heat shock proteins (or HSPs) in order to develop and commercialize novel therapeutics for diseases caused by protein misfolding, protein aggregation, and lysosomal dysfunction. Arimoclomol, the company's lead candidate, is in clinical development for rare diseases including Niemann-Pick disease type C (NPC) and Gaucher disease. Orphazyme is headquartered in Denmark and has operations in the U.S. and Switzerland. Orphazyme's shares are listed on Nasdaq U.S. (ORPH) and Nasdaq Copenhagen (ORPHA.CO).

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 is in clinical development for NPC and Gaucher Disease. 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.

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 respect of the expected timing of the CHMP opinion and a potential marketing authorization in Europe for arimoclomol for NPC, continuing interactions with the FDA, and the revised financial outlook for full-year 2021, including the anticipated operating expenses, operating loss and cash position. 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.

Attachment

- 16-2021 Orphazyme provides regulatory update from FDA on arimoclomol