NPC Community Notification

18 June, 2021

Orphazyme is deeply disappointed to share with the global NPC community that we have 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 for the treatment of NPC. By issuing a CRL, the FDA is indicating that Orphazyme's application for arimoclomol has not been approved in its current form. We will continue to work with the FDA to understand its feedback and evaluate whether there is a path forward in the U.S.

The FDA issued the CRL based on needing additional evidence to substantiate the validity and interpretation of the 5-domain NPC Clinical Severity Scale (NPCCSS) and, in particular, the swallow domain. The 5-domain NPCCSS is a disease-specific measure of disease progression consisting of the five clinically most relevant domains to patients with NPC, caregivers and physicians.

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.

We recognize this is disheartening news for the community and share in your frustration, knowing there is an urgent need for a new therapeutic option for people living with NPC.

While we review the FDA's letter and determine next steps, we want to share a few points with the community:

- At this time, we intend to maintain our existing expanded access program (EAP) and ongoing clinical trials in NPC. Our aim is to avoid a disruption in access for individuals who are currently receiving arimoclomol for NPC.

- We are evaluating all potential pathways in partnership with the FDA to advance our NPC clinical development program in the U.S. and will keep the community apprised of next steps.

- We also remain focused on supporting our pending application with the European Medicines Agency (EMA) for arimoclomol approval in NPC. We expect an opinion from the Committee for Medicinal Products for Human Use (CHMP) in Q4 2021, with the potential for Marketing Authorization in Europe in Q1 2022.

We are grateful to everyone who has joined us on the journey so far, including our esteemed investigators, clinician partners, advocacy community and the families and individuals who participated in our clinical trials. Your collective support, guidance, and trust has and continues to be instrumental to addressing the significant unmet need for

NPC patients. We value our relationship with you and will continue to provide updates on our path forward. Orphazyme's mission since our inception has been to pioneer new treatments for patients and families in urgent need and we remain committed to this work.

Learn more at www.orphazyme.com or contact@orphazyme.com.