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VIA Electronic Delivery

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RE: Lack of Transparency and Patient Inclusion Throughout NASH Regulatory Process

Dear Dr. Enzmann and Dr. Toerner:

Over the past several decades, liver diseases have relentlessly risen to become one of the leading causes of death and illness worldwide. Research also shows that despite impacting up to 6% of adults globally, one serious chronic liver disease, Nonalcoholic Steatohepatitis (NASH) is currently underdiagnosed, underreported, and undertreated. NASH is all set to be the biggest draw in hepatology resources for some time to come if it continues untreated: time, knowledge and expertise, resources and donated livers needed for transplantation.

Whilst it is true that there is no “silver bullet” response for a disease as widespread, complex, and multi staged as NASH, there is absolutely an unmet need in terms of clinical intervention for this life-or-death condition. The NASH patient community is not under the illusion that any one therapy will resolve the full spectrum of NASH issues yet, without some sort of medical solution, many of these patients remain on a very dangerous path that leads to more serious liver disease and death.

As patients, for many of whom addressing this disease is literally a life-and- death issue, we were extremely disappointed by the Food and Drug Administration’s (FDA) decision to cancel the Advisory Committee for the first pharmacological treatment for NASH, obeticholic acid (OCA). This was an unexpected U-turn from FDA, which has worked hard in recent years to form, and uphold, meaningful partnerships with patient communities.

Advisory Committees act as a vital tool for key stakeholders like patients to provide independent advice that will contribute to the quality of the agency's regulatory decision-making and lend credibility to the product review process. By choosing to not hold an Advisory Committee, the FDA in turn chose to deny patients their first opportunity to speak: to provide their perspectives on the balance between treatment risks and

benefits, and discuss the urgency and need for therapies that stop liver fibrosis progression.

FDA followed this disappointing decision by choosing to send out a Complete Response Letter (CRL) indicating the benefits of OCA did not outweigh its risks. Yet, it is mystifying to imagine how the risk/reward relationship was assessed without properly hearing from patients affected by NASH first. An act such as this, performed in a non-transparent way, not only puts current patients at risk, but also endangers further research into complex conditions such as NASH.

The goals of both the European Medicines Agency (EMA), and the FDA to foster scientific excellence and protect the public health by assuring the safety, efficacy and security of medical therapies are ones that we share. We understand that both the FDA and the EMA hope to establish shared expectations, trust, and reliability between themselves and the patient community. This is why it is critical for all regulatory agencies to acknowledge the patient voice, maintain transparency in their decisions, and appreciate the real world urgency and benefit of a therapy to an impacted patient population.

We also understand that the current COVID-19 pandemic is putting unprecedented pressure on the world's health care systems. However, there is no pause button for any patient's condition. As important public health strategies and resources are applied globally to mitigate further spread of COVID-19, liver disease progression among affected individuals continues.

It is vital for the FDA to clarify their understanding of acceptable risk-benefit trade-offs from the patient perspective, and why they chose to make their decision on the first treatment for NASH behind closed doors. We also hope that as the EMA advances in their process, they look to actively expand their efforts to include the patient perspective consistently.

Overall, NASH drugs are a need, not a want. We respectfully ask for the FDA to please inform the NASH community of their position on these critical issues, and for both EMA and FDA to consider the patient voice throughout their regulatory process. It is vital for all regulatory agencies to be transparent in their decisions, and ensure that all individuals and families impacted by NASH receive the attention they deserve.

Thank you for your consideration.

Regards,

European Liver Patients Association
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