Understanding the **Complete Response Letter** that Ultragenyx Received from the FDA

On July 11th, Ultragenyx announced that it received a complete response letter (CRL) from the U.S. FDA for UX111, an investigational gene therapy for patients with Sanfilippo syndrome Type A (MPS IIIA). We understand that any delay in making this potential treatment available to families who are waiting is devastating.

We also recognize that this news may be confusing, especially since CRLs are a technical part of the regulatory review process, and this is the first time the Sanfilippo community has encountered one. **Unfortunately, there is now a delay in when the FDA will make a decision on UX111.**

Complete Response Letter (CRL):

The FDA's way of saying **"revise and resubmit"** – aspects of the application need to be updated before FDA can complete its review and make a decision.

The details of a CRL vary across drug applications.

Before any medicine is approved to reach patients in the U.S., a company must provide the FDA with a package of all their research results, safety testing, and manufacturing details.

For gene therapies like UX111, this package is called a Biologics License Application (BLA).

When the FDA reviews a BLA, they want to make sure the product is high-quality, safe for patients, effective at treating the disease, and manufactured consistently.

One of the responses the FDA can provide when reviewing the BLA is a CRL. Receiving a CRL means that the review of the BLA has stopped and the FDA review will only continue when changes have been made and resubmitted. Once a BLA is resubmitted, a new review cycle starts.

Key Facts About the UX111 CRL

While the FDA has not yet fully reviewed or made any determinations regarding the clinical trial data, the FDA did not raise concerns about the quality of product manufactured to date, safety, or effectiveness of the gene therapy.

The CRL **focuses on FDA's observations** about the facilities and processes used in manufacturing UX111.

Ultragenyx believes all of the FDA's observations are readily addressable and **our priority is to resolve them** so that we can resubmit the BLA as soon as possible for review.

What happens next? What's the timeline?

We understand that time matters for children with Sanfilippo syndrome Type A. **We are moving with urgency and doing everything we can to resolve the FDA's observations to ensure FDA has the information it has requested in order to begin reviewing the BLA.** We cannot provide specific timelines right now, but we want to explain next steps involved in the process as we move forward.

Prior to receiving the CRL, Ultragenyx was already in the process of responding to FDA's observations. We are continuing to address the observations.

Our Steps Forward

Ultragenyx prepares for a meeting with the FDA by developing a briefing document and agenda, and then submits a request for a meeting.

The FDA schedules the meeting.

The meeting with FDA takes place with the goal to agree on the planned resolution of the observations.

Once we have alignment with the FDA on what will be included in the application, Ultragenyx plans to resubmit the BLA.

The FDA will re-review the BLA. This step typically takes the FDA up to 6 months to review and make a decision.

What about access or regulatory decisions outside the U.S.?

Our immediate focus is on resolving the observations in the CRL and working to resubmit the BLA so that FDA review of UX111 can continue.

Our desire is for patients and families around the world to have access to a safe and effective treatment option, and at this time, we believe the fastest path to achieve that goal starts with FDA approval in the U.S. We will share details about our international plans as information becomes available.

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Like you, it is our goal to bring this potential treatment to children with Sanfilippo syndrome Type A as soon as possible. Our team is committed to ensuring the availability of UX111, while respecting the FDA's review process.

Together, we remain committed to this shared goal.

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