Six Issues to Consider for Rare Disease Pre-IND Meetings

PREMIER PERSPECTIVES

Careful planning is important for all early drug development programs, but it is particularly critical in rare diseases where study populations are limited and precedents for drug development are lacking. Pre-IND meetings with the FDA give sponsors the opportunity to discuss their unique development challenges and determine where regulatory flexibility can be justified.

While the topics explored during pre-IND meetings may vary depending on the drug, development stage, and target indication, here are six issues rare disease sponsors should consider prior to engaging with the FDA:

1. Chemistry, Manufacturing, and Controls (CMC). CMC submissions to the IND are required to support each phase of drug development. Sponsors should be prepared to clearly summarize the type and amount of CMC information to be submitted in the IND and justify the appropriateness of this information in supporting their proposed clinical trials.

2. Nonclinical Studies. Where the proposed clinical indications are for the treatment of rare disease, the FDA can exercise flexibility in nonclinical programs and, in some cases, may allow abbreviated or deferred nonclinical studies. Sponsors should be prepared to discuss whether the completed nonclinical studies and the proposed nonclinical study plan are sufficient to support proof of concept and inform the safety of the investigative drug.

3. Clinical Pharmacology. Given that clinical trial precedents which inform dosing and usage in rare disease populations may be limited, sponsors should carefully plan the clinical pharmacology aspects of their drug development plans. Information from these studies and analyses can inform study design and provide supportive evidence of efficacy. As with nonclinical studies, the FDA can exercise flexibility in determining which clinical pharmacology studies are required, and when these studies need to be conducted.

4. Clinical Considerations. The FDA has no specified minimum number of patients needed to establish drug safety and efficacy. Although the approval standard is the same for drugs that treat rare diseases as those that treat non-rare diseases, the FDA has the flexibility to exercise the broadest possible scientific judgment in applying that standard in the rare disease setting. Sponsors should be prepared to discuss the benefits and risks of the drug, the seriousness of the disease, and the level of unmet medical need.

5. Expedited Programs. A pre-IND meeting is also an opportunity for sponsors to consult with the FDA on how to use the expedited programs available for development and regulatory review. These expedited programs include fast track designation, breakthrough therapy designation, priority review designation, accelerated approval, and regenerative medicine advanced therapy (RMAT) designation. Of note, fast track designation is unique in that it can be requested with the IND if there is sufficient nonclinical evidence.

6. Companion Diagnostics. Investigative drugs that are intended for use in a biomarker-defined subtype of patients may require a companion diagnostic. If a companion diagnostic is needed, sponsors should be prepared to discuss drug-diagnostic co-development early in the drug development program.

The pre-IND meeting is often the first regulatory communication with the FDA regarding a development program. By proactively preparing for this meeting, sponsors can set themselves up for productive discussions which may help in identifying areas of regulatory flexibility.

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