Type B Meeting Minutes

Sponsor: [Redacted Biopharma Inc.]
Product: [Investigational Oncology Agent XYZ-101]
IND Number: [######]
Date of Meeting: June 12, 2025
Meeting Type: Type B (Pre-IND)
Meeting Format: Teleconference
FDA Division: Division of Oncology 1 (DO1), Office of Oncologic Diseases, CDER

Subject: Use of i3+3 Design for Phase 1 Dose-Escalation Study

Discussion Point #3:
Sponsor proposal to use the i3+3 design with equivalence interval [0.25, 0.35] for determining dose escalation and de-escalation decisions in the proposed Phase 1 first-in-human trial.

FDA Feedback:
The FDA appreciates the sponsor's effort to adopt a model-assisted design with a structured decision framework, such as the i3+3 design. However, the Agency does not agree with the proposed equivalence interval of [0.25, 0.35], as it raises concerns regarding alignment with acceptable safety standards for first-in-human oncology trials.

Specifically, FDA considers an upper boundary of 0.35 for the equivalence interval to be too permissive, especially when the target toxicity rate is 0.30. Such an interval would tolerate escalation or dose retention decisions at estimated DLT rates up to 35%, which exceeds conventional Phase 1 tolerability expectations.

The Agency recommends that the upper bound of the equivalence interval should be set below 0.33, consistent with the maximum acceptable DLT probability in most early-phase oncology settings. For example, the FDA would not object to an interval such as [0.25, 0.30] or [0.25, 0.32], which provides a more conservative framework to safeguard patient safety while still permitting escalation when appropriate.

The sponsor is encouraged to revise the equivalence interval accordingly and resubmit the updated Statistical Analysis Plan (SAP) for further review. The FDA also reminds the sponsor that equivalence intervals should reflect clinical judgment and consensus on tolerability, not merely statistical convenience.

Action Items:
- Sponsor to revise i3+3 design to reflect a more appropriate equivalence interval (e.g., [0.25, 0.30])
- Sponsor to provide revised SAP and decision algorithm logic table in the IND submission
- FDA to review updated submission upon receipt

These minutes reflect FDA's understanding of the meeting discussions and do not constitute final regulatory approval.