BG00012 SMT Meeting
06 July 2006

Attendees: [redacted]
C. Lansden (CL), R. Lingamanemi (RL), [redacted]
[redacted] G. O'Neill (GON), [redacted]
[redacted] M. Yang (MY)

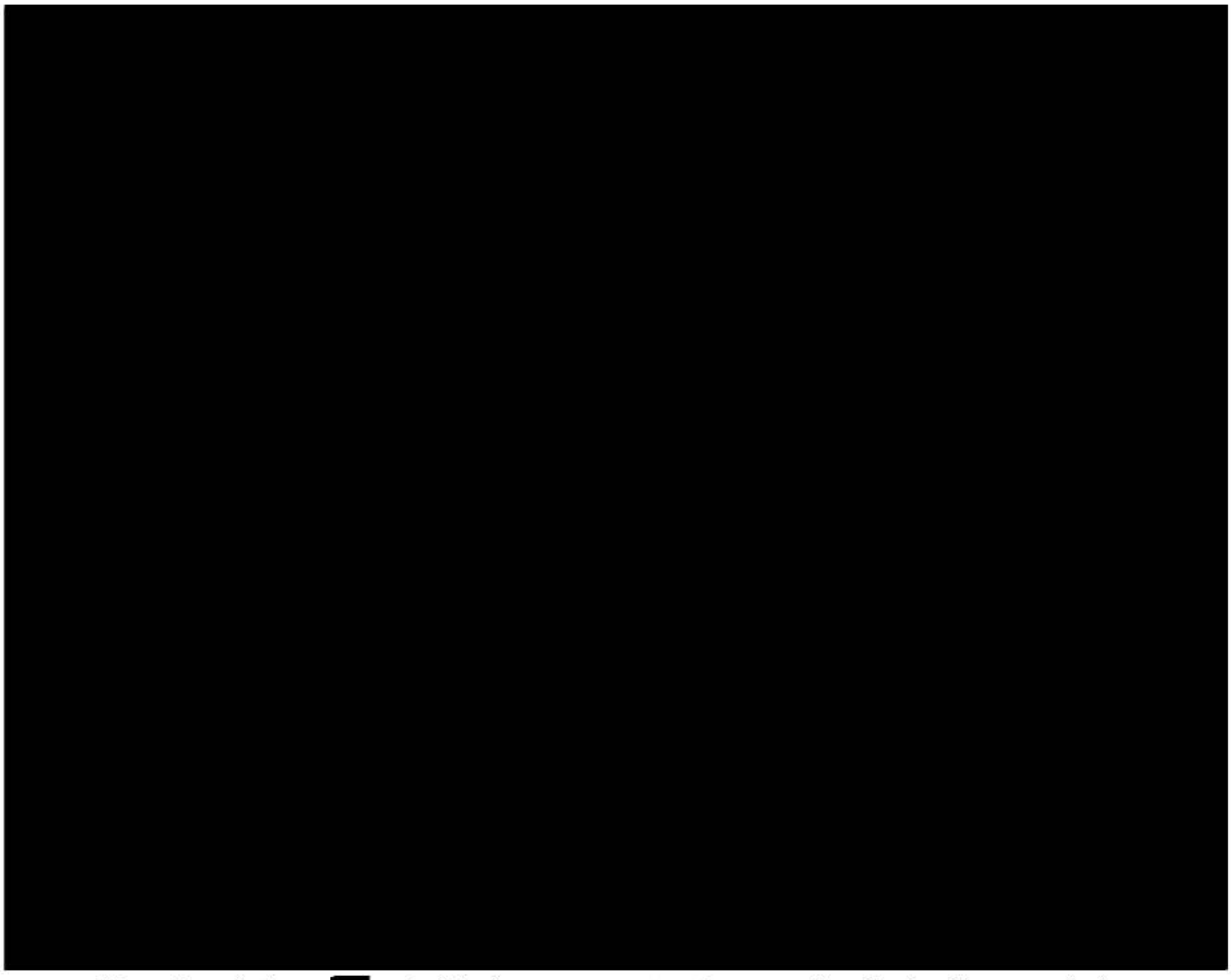
AGENDA ITEMS

I. Discussion of Comments to the Protocol Drafts:
- **109MS301 – Double-blind, monotherapy**
- **109MS302 – 3-Arm reference comparator**

I. Discussion of Comments to Protocol Drafts

- The team agreed to discuss comments to the 109MS301 (301) Study as any changes to this protocol will most likely need to be carried over to the 109MS302 (302) Study as well.

[redacted]



- Dose Escalation: [redacted] asked in her comments why no rationale for dose escalation was provided? No clinical data – only observations – exist to support dose escalation helps the patients to tolerate higher doses of BG12, no rationale will be provided.
- Dose Reduction: The team discussed the question of allowing subjects to dose reduce vs. discontinuing the study due to tolerability issues. Study C-1900 allowed subjects to reduce to 120mg TID for 1 month if they could not tolerate their assigned dose level of BG12. After 1 month the subject would re-challenge at the higher dose level, if unable to tolerate the higher dose level following re-challenge, subjects would be allowed to continue the study at the reduced dose of 120 mg TID.
    - GON and MY are in favor of allowing the same dose reduction process in 301 and 302 and allow subjects to stay in the study at a reduced dose (120 mg TID) if unable to tolerate the 240 TID level. MY stated she would prefer to have data on subjects taking some level/amount of BG12 vs. data on subjects who are not on any treatment or have subjects discontinue the study.
    - CL questioned what impact would allowing a lower (120 mg TID) dose level have on the dose rationale for 240 mg TID?

- [redacted] questioned if there would be a risk to the label with allowing decreased dose?
- Safety [redacted] noted that tolerability issues would need to be reported as AEs as they were in C-1900 in order to document reason for reduced dosing.
- Although, not all concerns with dose reduction were resolved, it was agreed a section regarding dose reduction will be included in the protocol. Language to be taken from C-1900.

Due to time constraints the team was not able to discuss issues specific to the 109MS302 protocol.

[redacted]