BG00012 MS Clinical Development Team

Team Minutes

To: **Program/Clinical Development Team**

From: Cara Lansden

Date: 07 September 2005

Re: CDT Meeting Discussion Minutes – 07 September 2005

[redacted]

Pre-IND Meeting Outcome

Delays to the timeline:

- The Pre-IND meeting was held on Thursday, 01 Sep. The FDA did not agree to the pre-clinical bridging argument and require another non-rodent study prior to beginning Phase 3, and for various reasons, it was suggested that the study should be done in primates. This could result in a delay of about 12-18 months to the Phase 3 program. The impact on timelines will be discussed in more detail at the Program Team level when [redacted] is present.
- The main clinical issues for the IND filing raised by FDA were the [redacted]
    - For the IND, FDA wants us to [redacted] in Phase 3.
- With the delay to the start of Phase 3 due to the additional pre-clinical study, should we push out the IND filing for MS, the QTc study or Food Effect study? It was agreed that it was preferable to file the IND and continue planning for the QTc interval study in Q1 06, and have everything ready for an EOP2 meeting. Based on the Pre-IND meeting, if we have a good pre-clinical plan in the IND, it will be accepted by FDA. FDA also said that our data supports the QTc Interval study.

DECISION: CDT will still file the IND in October

- Also, we could begin Phase 3 studies in the EU, since those Regulatory agencies (with the exception of Denmark and France) are currently satisfied with the data package. The downside is that we would not have FDA feedback on one of our pivotal clinical studies being run in EU.

- FDA said they would accept outside US studies as long as they were done ethically – we can get more feedback at EOP2.

Clinical Development Plan:

- The option with 2 placebo-controlled monotherapy studies with combination safety was acceptable by the FDA. G. O'Neill clarified that FDA said they expected long phase 3 studies of UP TO 2 years duration.
- However, FDA gave strong warning that although they believe placebo-controlled studies are acceptable, the MS Societies have claimed they were unethical and FDA may not accept placebo-controlled studies in future.
- FDA would accept an all-comers design and an Active Comparator designed for superiority in lieu of a placebo-controlled study. A dose-response study with the lowest dose being as efficacious as placebo would be the least acceptable.
- FDA suggested that BIIB should be canvassing MS practitioners about whether they considered placebo-controlled studies ethical.