Clinical Trial Review Board Meeting
Agenda Item Meeting Minutes

Date: 19 February 2004

Agenda Item: Double-blind, placebo-controlled, dose determination, efficacy, safety, and tolerability study of BG00012 in patients with relapsing remitting MS

Support: * **Support with Minor Revisions:** *

Not Support: * **Rework Required:** X

Attendees: The following people were present during the discussion of the above-referenced agenda item.

TITLE	NAME or NAME OF DESIGNEE	PRESENT
Clinical Project Manager	Rebecca Conaghan	Yes
CTRB Chairperson	Carmen Bozic	Yes
Medical Director	Gilmore O'Neill	Yes
Medical Writer	Ed Berkhoff/Anne Read	Yes
Vice President, Drug Safety and Medical Information	John Ferguson	Yes
Senior Vice President, Medical Research	Whaijen Soo	Yes
Senior Vice President, Regulatory Affairs	Nadine Cohen	No
Vice President, Biometrics and Data Management	Laura Meyerson	No
Vice President, Preclinical and Clinical Development Sciences	Jim Green	No
Other(s)	Hans Peter Hasler, Bill Sibold, Bob Hamm, John Oram, Carey Smith, Dale Spriggs, Ying Zhu, Boyd Hanson, Minhua Yang, Sven Lee, Deborah Kinch, Susan Horne, Mary Spellman, Chris Tenhoor, Sharon MacBain, Paul Flyer, Al Sandrock, James Stella, Susan Goelz, Cara Lansden, Theresa Pondrebrac, Barry Ticho	

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Summarized Discussion

- Gilmore O'Neill presented the concept to the CTRB. Four options were included in the presentation as shown in the table below:

Option	Dosing Regimes					
#1		240 mg/day 2 div dose	360 mg/day 3 div dose	480 mg/day 2 div dose	720 mg/day 3 div dose	
#2	120 mg/day Single dose		360 mg/day 3 div dose	480 mg/day 2 div dose	720 mg/day 3 div dose	
#3	120 mg/day Single dose		360 mg/day 3 div dose		720 mg/day 3 div dose	
#4					720 mg/day 3 div dose	1080 mg/day 3 div dose

The discussion focused on Options 1, 2, and 3. Option 4 was discarded.

- Dosing emerged as the most critical issue. Option 2 appeared confusing to some CTRB members. Commercial representatives were not in favor of a 240 mg dose because this dose might affect the marketing strategy of the 720 mg dose under development for psoriasis. Regulatory representatives were concerned that bypassing a 240 mg dose might raise questions with regulatory agency reviewers. Research representatives felt that a true dose ranging study was only reflected in Option 3, or possibly adding a 120 mg arm to Option 1.
- Reformulation of study drug was discussed (i.e., developing a 60 mg capsule in addition to the 120 mg capsule now available). However, this was thought to be not possible due to time constraints.
- BID dosing was discussed and it was thought that this dosing regimen was beneficial on many different levels.

Summarized Action Plan

- The concept was not approved. The team was instructed to seek alignment amongst the different interests (i.e., research and commercial) and reconvene an ad hoc CTRB a soon as possible, preferably the week of February 23rd, with an updated and agreed upon study design.