Rowbotham et al.: Efficacy and safety of the α4β2 neuronal nicotinic receptor agonist ABT-894 in patients with diabetic peripheral neuropathic pain

Supplementary Text. Description of adaptive dropping-arm design employed in Study 1

Methods:

An adaptive dropping-arm design was employed for Study 1. An interim efficacy evaluation was implemented as planned for Study 1, which took place when 125 subjects (approximately 25 per arm) completed the Week 6 visit (including those who discontinued prior to the Week 6 visit). At the interim evaluation, the posterior probabilities **P** (D_i **>** δ **| Data**) were calculated, where D_i was the difference between the ABT-894 dose group *i,* (*i* = 1 mg, 2 mg, or 4 mg BID ABT-894) and the placebo group in terms of the change from baseline to the last non-missing observations at or prior to Week 6 visit on the 24-hour average pain, and δ = 0.5. A non-informative prior was used. If the observed dose response curve was monotonically increasing across ABT-894 doses, and the lowest dose (1 mg) satisfied **P (**D_i **>** δ **| Data) < 0.20**, then the enrollment to this dose group would be discontinued while the subjects who had already enrolled into this dose group would continue to finish the scheduled visits.

Results:

At the interim efficacy evaluation conducted for Study 1, the posterior probabilities were 0.48, 0.13 and 0.16 for 1 mg, 2 mg, and 4 mg BID ABT-894 dose groups, respectively. The pre-specified algorithm of dropping a study arm was not met and the study continued to completion without any design modification.