Supplementary Data

Supplementary Table 1. Definitions of Terms

Active controls: As opposed to placebo controls, active controls are subjects who receive standard of care treatment rather than the investigational treatment.

Allocation \ randomization: With randomization, participants are assigned to intervention groups by chance. In non-randomized studies, participants are expressly assigned to intervention groups through a method such as physician choice.

Blinding \ masking: In open-label studies, no masking is used, so subjects and investigators both know the identity of the intervention assignment (e.g., drug or placebo). In single-blind studies, one party (either the investigator or participant) is unaware of the intervention assignment. In double-blind studies, two or more parties are unaware of the intervention assignment.

Device: Defined by the FDA at: http://www.fda.gov/medicaldevices/deviceregulationandguidance/overview/classifyyourdevice/ucm051512.htm. The definition of a device is broad and serves primarily to distinguish devices from other regulated products such as drugs, which function based on chemical action. A device can be "an instrument, apparatus, implement, machine, contrivance, implant, *in vitro* reagent, or other similar or related article, including a component part, or accessory which is intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease."

Interventional study: Individuals are assigned based on a protocol to receive specific interventions. Subjects may receive diagnostic, therapeutic, or other types of interventions. The assignment of the intervention may or may not be random. The individuals are then followed and outcomes are assessed.

Observational study: Outcomes are assessed in pre-defined groups of individuals. Subjects in the study may receive diagnostic, therapeutic, or other interventions, but the investigator does not assign specific interventions to the subjects of the study.

Parallel assignment: Participants are assigned to one of two or more groups in parallel for the duration of the study.

Phase 0 study: Exploratory trials, involving very limited human exposure, with no therapeutic or diagnostic intent (e.g., screening studies or microdose studies).

Phase 1 study: Initial studies to determine the metabolism and pharmacologic actions of drugs, to identify side effects associated with increasing doses, and to gain early evidence of effectiveness; often includes healthy participants.

Phase 2 study: Conducted to evaluate the effectiveness of interventions for particular indications in patients with the disease or condition under study, and to determine the common short-term side effects and risks.

Phase 3 study: Expanded trials, after preliminary evidence suggesting effectiveness of the drug has been obtained, intended to gather additional information to evaluate or confirm the overall benefit-risk relationship of the drug, and provide an adequate basis for regulatory approval and labeling.

Phase 4 study: Studies of marketed, FDA-approved drugs to delineate additional information including the drug's risks, benefits, and optimal use, often in larger populations.