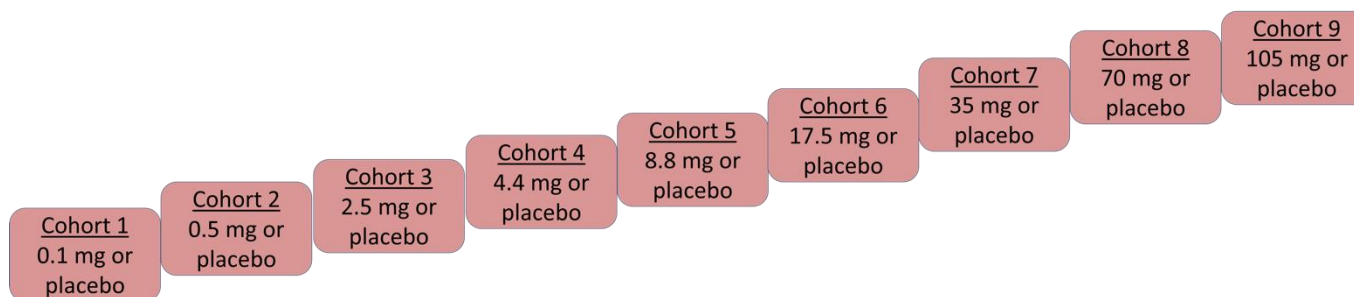


**Figure S1. Overall study design and dose escalation schemes for Parts 1 and 2**

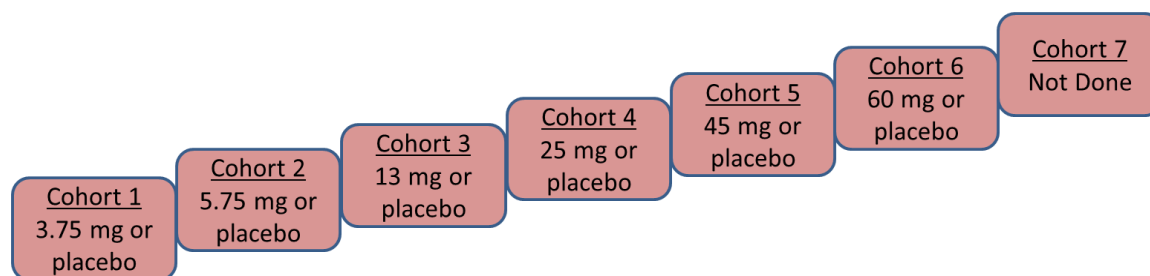
**Single-Rising Dose (SRD)**



Abbreviations: AUC, ; MEE, ; PK, pharmacokinetics.

Maximum 9 cohorts; starting dose 0.1 mg (Cohort 1); Cohorts 2-3: MEE x5-fold; Cohorts 4-9:MEE x2-fold; maximum estimated dose: 122 mg (with unbound AUC 19.8 ng-h/mL). Dosing with TAK-020 progressed to the next cohort after review of the safety, tolerability, and PK data from the previous cohort and the agreement of the principal investigator and the sponsor of the next proposed dose.

**Multiple-Rising Dose (MRD)**



Abbreviation: SRD, single-rising dose.

Maximum 7 cohorts; doses to be determined from SRD; starting dose 3.75 mg (Cohort 1); Cohorts 2 to 7: 2-fold maximum exposure increase per dose increment.