To assess the toxicokinetics (TK) of CBX129801 in Cynomolgus monkeys following a single weekly subcutaneous injection for 28 doses.

Methods
Four groups received subcutaneous injections of CBX129801 at 0.4, 1.33, 3.31 and 4.0 mg/kg/week for 28 doses. Blood samples were collected 0, 12, 24 and 48 hours after each dose during the 7-week recovery period at predetermined time. Additional samples were collected during the recovery period on Days 196, 210, 226 (6-month recovery) and 287, 301 and 315 (9-month recovery). The plasma was assayed for CBX129801 by a validated LC-MS assay.

Results
Following the first subcutaneous injection of CBX129801 at 0.4, 1.33 and 4.0 mg/kg mean C\text{max} values were 81.3, 222 and 274 nM and at 0.4, 1.33 and 4.0 mg/kg in females, respectively. C\text{max} mean values in males were substantially lower than in females. C\text{max} mean values in females were 917, 175 and 356 nM at 0.4, 1.33 and 4.0 mg/kg, respectively. Corresponding mean AUC\text{0-24} values were 215, 1060 and 3410 nM∙day in males and 469, 1670 and 3410 nM∙day in females. AUC\text{0-24} values in females were similar between gender and dose groups and ranged from 2.9 to 3.31 day ∙ nM in males and 3.31 to 4.0 mg/kg in females. CBX129801 exposure increased as a function of dose in a dose-proportional manner and was similar between genders. CBX129801 appeared to undergo a steady state within 18-days and maintained high concentrations throughout the entire dosing period. Plasma concentrations of CBX129801 mortality decreased over time and were substantially low by the end of the recovery period. As a result of the lowered exposure, the drug was not detected in excreta.

Conclusion
Upon subcutaneous administration in monkeys, CBX129801 exposure showed high inter-individual variability, similar between genders and dose groups. CBX129801 mean C\text{max} values were similar between gender and dose groups and ranged from 2.9 to 3.31 day ∙ nM in males and 3.31 to 4.0 mg/kg in females. Day 1 apparent T\text{1/2} values were similar between gender and dose groups and ranged from 2.9 to 3.31 day. Apparent T\text{1/2} in females were 2.29 to 3.31 day and 2.29 to 3.31 day in males. Corresponding mean AUC\text{0-24} values were 215, 1060 and 3410 nM∙day in males and 469, 1670 and 3410 nM∙day in females. Corresponding mean AUC\text{0-24} values were similar between gender and dose groups and ranged from 2.9 to 3.31 day ∙ nM in males and 3.31 to 4.0 mg/kg in females. CBX129801 exposure increased as a function of dose in a dose-proportional manner and was similar between genders. CBX129801 mortality decreased over time and were substantially low by the end of the recovery period. As a result of the lowered exposure, the drug was not detected in excreta.

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