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TUPELO TRIAL: A Phase 2, Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial to Evaluate Efficacy, Safety, and Pharmacokinetics of REC4881 in Subjects with Familial Adenomatous Polyposis (FAP) Study Design

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a) **Disclosure of Financial Relationships**: All authors are employees or consultants to Recursion Pharmaceuticals, Inc.

b) **Purpose of the Study:** The TUPELO trial is designed in 2 parts. Part 1 will evaluate the pharmacokinetics (PK) after single and multiple doses of REC-4881 in subjects with Familial Adenomatous Polyposis (FAP) who have previously undergone a colectomy/proctocolectomy.
Part 2 will evaluate the effect of REC-4881, compared to placebo, on rectal/pouch, duodenal, and ampullary adenoma progression in subjects with FAP who have undergone a prior colectomy/proctocolectomy.

c) Methods: This is a multicenter, randomized, double-blind, placebo-controlled two-part basket trial in patients with FAP who have previously undergone a colectomy. There will be approximately 15-25 sites for this trial and approximately 21 participants in Part 1 and 150 participants in Part 2.

d) **Results:** The primary outcome of the TUPELO trial Part 1 include the following: Plasma PK parameters as appropriate, including but not limited to maximum (peak) plasma drug concentration (Cmax), time to reach maximum (peak) plasma concentration following drug administration (Tmax), and area under the plasma concentration-time curve (AUC). The primary outcome of Part 2 is mean change in polyp burden or ampullary lesion size from baseline at 12 months post randomization.

e) Conclusions: TUPELO trial is designed to investigate the efficacy and safety of REC-4881 representing a potential new pharmacologic treatment in patients with FAP who have previously undergone a colectomy/proctocolectomy. Enrollment is ongoing.

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