

## Supplementary information Fig. S8 VPA and EPZ6438 promote the regenerative response in ENR-organoids

- a, Representative images of ENR-organoids with and without VPA/EPZ6438.
- **b**, Quantification of total/Lgr5-GFP-expressing organoid number at different passages (n = 4 wells).
- c, qPCR analyses of Clu and regenerative genes expression in organoids cultured under the indicated conditions (n = 2 wells). P values were determined by two-sided unpaired t-test.
- **d**, Heatmap displaying the expression of an injury-induced regenerative signature in different organoids (n = 3 mice).
- e, f, Representative images (e) and quantification of organoid number (f) cultured under

the indicated conditions with or without 6 Gy  $\gamma$ -irradiation. Scale bars, 100  $\mu$ m. (n = 4 wells).

\*\*\*P < 0.001; \*\*P < 0.01; All experiments were independently replicated at least three times with similar results.