OP-1250 fully blocks estrogen-driven proliferation of ER+ breast cancer cells.

OP-1250 is a pure antagonist across the full spectrum of E2 regulated genes.

OP-1250 degrades ERs in multiple cell lines.

OP-1250 shrinks tumors in the HCI-013 PDX model of mutant ERα that models endocrine resistant tumors.

OP-1250 shrinks tumors in multiple xenograft models at 3-10 mg/kg QD.

10 mg/kg OP-1250 achieves high and stable levels in multiple species.

Conclusions:
- OP-1250 is a complete ER-antagonist (CERAN) that blocks AF1 and AF2 of both wild type and mutant ERα.
- OP-1250 is orally bioavailable and achieves high and stable drug levels in multiple species.
- OP-1250 is a POTENT CERAN that shrinks tumors in both wild-type and mutant ESR1 xenograft models.
- OP-1250 is a promising new agent for the treatment of endocrine-resistant breast tumors.

A phase 1 dose escalation and expansion study of OP-1250 alone, and in combination with a PI3K inhibitor, and in combination with a PI3K inhibitor in previously treated patients with ER+ metastatic breast cancer will be initiated in 2020.