Figure 1


Figure 2

A Parental and secondary mutant in vitro coculture


Figure 3


Figure 4
A capan-1

CAPAN-1.B2.S*
ddPCR to assess
CAPAN-1/CAPAN-1.B2.S* ratio
Day 0


B


Animal

D


Figure 5

B



D
Starting ratio of secondary mutant:parental
Starting ratio of secondary mutant:parental



F

H


> - Vehicde
> - Olapanb ( $50 \mathrm{mg} / \mathrm{kg}$ daily; p.o.) $(n=6)$
> - AZD-1775 $(30 \mathrm{mg} / \mathrm{kg}$ : Wice daľy; p.o. $(n=6)$
I


- Olaparib ( $50 \mathrm{mg} / \mathrm{kg}$; daily; p.o.) $(n=6)$
- AZD-1775 (30 mg/kg: wico daly; p.o) $(n=6)$

G



## Table 1

| $\begin{aligned} & \text { Cell } \\ & \text { line } \end{aligned}$ | Reference sequence for BRCA2 CAGCAAGTGGAAAATCTGTCCAGGTATCAGATGCT | CRISPR- <br> Induced <br> mutation | Subcloned <br> colonies <br> sequenced <br> (\#) | Estimated <br> allele <br> frequency |
| :---: | :---: | :---: | :---: | :---: |
| CAPAN-1 | CAGCAAG-GGAAAATCTGTCCAGGTATCAGATGC | N/A | 20 | 1.00 |
| $\begin{aligned} & \text { CAPAN- } \\ & 1 . \mathrm{B}^{2} .3^{*} \end{aligned}$ | CAGCAAG-GGAAAATCTGTCCAGGTATCAGATGC | $\begin{aligned} & \text { CAPAN- } \\ & 1 \text { ( } 6174 \mathrm{del} \text { ) } \end{aligned}$ | 20 | 0.59 |
|  | CAGCAAG-GGAAAAT CAGGTATCAGATGC | 5-bp Deletion |  | 0.41 |

Sequencing of BRCA2 in CAPAN1.B2.S*

Table 2

| Cell line | Reference sequence for BRCA1 <br> CAATCCTAGCCTTCCAAGAGAAGAAAAAGAAGAGAAACTAGAAACAGTTAAAGTGTCTAATAATGCTGAAGACCCCAAAGATCTCATGTTAAG | CRISPR- <br> Induced mutation | Subcloned colonies sequenced <br> (产) | Estimated <br> allele <br> frequency |
| :---: | :---: | :---: | :---: | :---: |
| StM149 | CAA-CCTAGCCTTCCAAGAGAAGAAAAMGAAGAGAAACTAGAAACAGTTAAAGTGTCTAATAATGCTGAAGACCCCAAAGATCTCATGITAAG | 1/4 | 20 | 1.00 |
| stm149.B1.s* | CAA-cctag - Tang | $\begin{aligned} & 80-b_{p} \\ & \text { Deletion } \end{aligned}$ | 20 | 0.66 |
|  | CAA-CCTAGCCTTCCAAGAGAAGAAAAAGAAGAGAAACTAGAAACAGTTAAAGTGTCTAATAATGCTGAAGACCCCAAAGATCTCATGTTAAG | STM149 (2289delT) |  | 0.33 |

Sequencing of BRCA1 in SUM149.B1.S*

