

# **Discovery and clinical introduction of first-in-class imipridone ONC201**

## **Supplementary Material**

### **Supplementary Table 1. Summary of ONC201 *in vivo* anti-cancer efficacy studies.**

Note: s.c.: subcutaneous, IP: intraperitoneal, PO: oral, IV: intravenous, NA: not applicable, CSC: cancer stem cell

Tumor type	Mouse model	Dose, Route	Frequency	ONC201	Efficacy	Comparison	Combination	CSC-efficacy	Reference
Lymphoma	Eμ-myc transgenic	25 mg/kg, PO	1x/week		Prolonged survival	NA	NA	NA	1
Acute Myeloid Leukemia	Patient-derived cells serially passaged in NSG mice (i.v.)	5 μM, <i>in vitro</i>	48hrs in vitro		Prolonged survival	NA	NA	Yes	7
Glioblastoma	T98G s.c.	30 mg/kg, PO	single dose		Partial regression	slightly better than bevacizumab	NA	NA	1
	SF767 intracranial	25 mg/kg, PO	single dose		Prolonged survival	survival better than bevacizumab	bevacizumab+ONC201 further improved survival	NA	1
	MGPP-3 s.c.	25 mg/kg, IP	3x/week		Partial regression followed by progression	ABT263 response similar to ONC201	ABT263+ONC201 tumor regression better than single agent	Yes	30
Colorectal	SW480/RKO/HCT116 p53 null s.c.	30/50/100 mg/kg, IP and PO	single dose		Stasis	NA	NA	NA	1
	HCT116 wt/p53 null and DL-D-1 s.c.	12.5/25/50/80/100 mg/kg	single dose, 1-2 doses/week		Partial regression	similar or slightly better than rTRAIL	NA	NA	1, 2
	HCT116 p53 null, intracanal	IP/IVPO	1x/2-3weeks					NA	1
	HCT116 p53 null, intracanal	25 mg/kg, PO	1x/week		slightly reduced primary tumor and decreased metastasis	better than bevacizumab	bevacizumab+ONC201 improved primary tumor reduction and decreased lung metastasis	NA	1
	DL1, Ad5fluor+ CSCs s.c., passage, limiting dilution	50 mg/kg IP	1x/week		Partial regression, reduction of passage decreased tumor initiation and CSC markers	superior to 5-Fluorouracil	NA	Yes	26
Head and Neck	Fadu squamous cell, s.c.	50 mg/kg, PO	2x/week		Partial regression followed by progression	radiation resistant	ONC201+radiation slightly better than single agent	NA	
Breast	MDA-MB-231 (triple-negative)	50/100 mg/kg IP	single dose		Partial regression	superior to rTRAIL	NA	NA	1
Lung	H460 (non-small cell)	30 mg/kg, IP	single dose		Partial regression	superior to docetaxel	complete regressions in combination with paclitaxel/docetaxel	NA	1
Hepatocellular	HepG2	25 mg/kg, PO	1x/week		Partial regression	superior to Sorafenib	complete regressions with ONC201+sorafenib	NA	35
Pancreatic	Panc-1 s.c.	30 mg/kg, PO	daily		Partial regression and prolonged survival	superior tumor regression compared to gemcitabine	ONC201+gemcitabine improved tumor regression and survival	NA	41

Supplemental Figure 1. Pharmacokinetics of single dose ONC201 in (A) Sprague Dawley rats and (B) beagle dogs.

