

# Technology Licensing Opportunity

Non-Confidential Summary



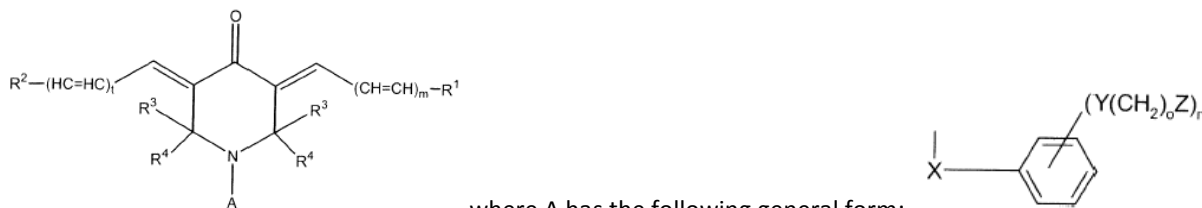
## NOVEL CYTOTOXIC COMPOUNDS WITH ANTICANCER POTENTIAL ROI# 12-015

### **Opportunity:**

Commercial rights to a broad range of structurally related compounds with cytotoxic effects are available. These compounds are potentially more efficacious and safer alternatives or adjuncts to existing anticancer drugs.

### **Background:**

Anticancer drugs are generally highly toxic and many interact with nucleic acids, which can cause carcinogenesis and mutagenesis. Researchers at the University of Saskatchewan have prepared novel clusters of alkylating agents which were designed to interact with thiol groups while avoiding reactions with the amino and hydroxy moieties of nucleic acids. These findings led to an evaluation of the hypothesis that thiol-alkylators, such as the 4-piperidones shown below, could be cytotoxic and yet be well tolerated in mammals.



where A has the following general form:

### **Invention:**

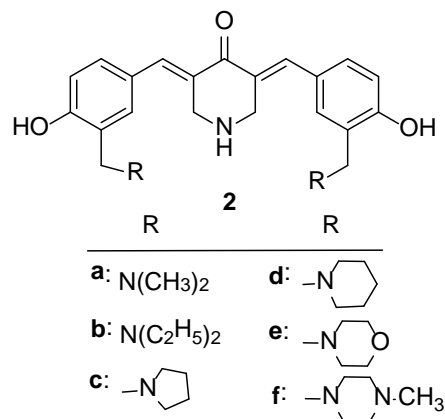
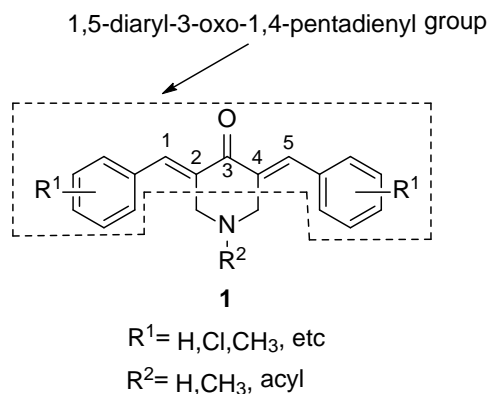
Current research deals with the mounting of the 1,5-diaryl-3-oxo-1,4-pentadienyl pharmacophore on different molecular scaffolds including a piperidine ring **1**. This structural arrangement permits successive alkylations of cellular thiols which has been shown to cause greater toxicity to tumours than normal cells on occasions. Many of these compounds have multidrug resistance (MDR)-revertant properties and are well tolerated in mice.

A representative compound (2a, below) was found to be very effective on seven human colon cancer cell lines screened by the National Cancer Institute, USA ( $IC_{50}$  values in  $\mu M$  are in parentheses) namely HCT116 (1.20), HCT15 (2.29), HT29 (0.89), HCC2998 (1.70), KM12 (1.00), COLO 205 (1.05) and SW-620 (1.26). In addition, the compounds in series **2** below display significant potencies towards human Molt4/C8, CEM, HL-60, HSC-2, HSC-3, and HSC-4 neoplasms and are significantly less toxic to human HGF, HPC and HPLF nonmalignant cells.

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### **Perceived Advantages:**

1. The structures are novel and therefore neoplasms, and especially drug-resistant ones, should be sensitive to these compounds. Excellent candidates for use in antibody - drug conjugate therapeutics.
2. Various related analogues in series **1** have the following properties displaying (i) greater toxicity towards tumours than normal cells (ii) excellent tolerance by mice and (iii) MDR-revertant characteristics. Hopefully the compounds in series **2** will follow suit. These properties are in contrast to currently available medication where toxicity and inactivity to MDR- tumours is often observed.
3. If one or more of the compounds in series **2** are active in vivo, then the coadministration of an established drug used in treating CRC such as 5-fluorouracil (5FU) with a compound in series **2** should be undertaken. The aim of this exercise is to reduce the dose of 5FU and hence ameliorate the toxicity of this drug.

### **Researchers:**



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### **Patent Status:**

US Patent Application No. 62/170227

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