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## Product Data Sheet

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Product Name: Inolitazone

Cat. No.: GC13204

### Chemical Properties

Cas. No. 223132-37-4

Chemical Name 5-(4-((6-(4-amino-3,5-dimethylphenoxy)-1-methyl-1H-benzo[d]imidazol-2-yl)methoxy)benzyl)thiazolidine-2,4-dione

SMILES CC1=CC(OC2=CC3=C(N=C(COC4=CC=C(CC5C(NC(S5)=O)=O)C=C4)N3C)C=C2)=CC(C)=C1N

Formula  $C_{27}H_{26}N_4O_4S$  M.Wt 502.58

Solubility Soluble in DMSO Storage Store at -20°C

General For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.

Structure

### Protocol

#### Cell experiment:

DRO90-1 (DRO) and ARO81 (ARO) cells are plated in 12-well culture plates in triplicate for each condition at an initial concentration of  $2 \times 10^4$  cells/well. After overnight incubation, cells are treated with either Inolitazone, Rosiglitazone, Troglitazone, GW9662, or Paclitaxel diluted in DMSO at concentrations indicated in figure legends. All cells receive identical volumes of DMSO and are exposed to each drug for 6 days with medium and drug changed every 48 h. After 6 days, cells are washed with PBS, trypsinized and counted by Beckman Coulter Counter[1].

**Caution: Product has not been fully validated for medical applications. For research use only.**

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### Animal experiment:

Mice[1] Suspensions of  $1 \times 10^6$ /0.1 mL DRO or ARO cells in RPMI medium are injected subcutaneously in one flank of 3-4 week athymic female nude mice. Mice are changed to specialized diets either 1 week prior or 1 week after tumor implantation and randomly assigned to experimental or control groups with 10 mice per group. Diets consisted either placebo, 0.00025%, 0.0025%, or 0.025% Inolitazone formulated into the diet. Mice weighed between 20-25 g and consume on average 4 g of food per day. For combinatorial studies either placebo, 10 mg/kg or 15 mg/kg paclitaxel is injected i.p. twice weekly. Tumors are measured every 3-4 days for 35 days with calipers and tumor volumes are calculated by the formula:  $0.5236(a \times b \times c)$ , where a is the shortest diameter, b is the diameter perpendicular to a and c is the diameter height.

### References:

[1]. Copland JA, et al.  
Novel high-affinity  
PPARgamma agonist  
alone and in  
combination with  
paclitaxel inhibits  
human anaplastic  
thyroid carcinoma  
tumor growth via  
p21WAF1/CIP1.

Oncogene. 2006 Apr  
13;25(16):2304-17.

[2]. Marlow LA, et al.  
Reactivation of  
suppressed RhoB is a  
critical step for the  
inhibition of  
anaplastic thyroid  
cancer growth.

Cancer Res. 2009 Feb  
15;69(4):1536-44.

### Background

Description: IC50 Value: 0.8 nM [1] Inolitazone(RS5444) is a novel high-affinity PPARgamma agonist,

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which activates PPARgamma with an EC50 about 1/50th that of rosiglitazone and has no effect on RIE cells that do not express PPARgamma. *in vitro*: In vitro, the IC50 for growth inhibition is approximately 0.8 nM while anaplastic thyroid carcinoma (ATC) tumor growth was inhibited three- to fourfold in nude mice. siRNA against PPARgamma and a pharmacological antagonist demonstrated that functional PPARgamma was required for growth inhibitory activity of RS5444. RS5444 upregulated the cell cycle kinase inhibitor, p21WAF1/CIP1 [1]. RS5444 inhibited culture growth and caused irreversible G1 arrest, but did not induce apoptosis. In addition, RS5444 caused dramatic changes in cellular morphology which were associated with increased motility and diminished cellular adherence, but no increase in the ability of such cells to digest and invade Matrigel [2]. Treatment with RS5444 leads to the up-regulation of RhoB and subsequent activation of p21, and that silencing of RhoB by RNAi blocks the ability of RS5444 to induce p21 and to inhibit ATC cells proliferation [3]. *in vivo*: The median peak efatutazone blood level was 8.6 ng/mL for 0.15-mg dosing vs 22.0 ng/mL for 0.3-mg twice daily dosing [4]. Although efatutazone treatment did not reduce percentage of mice developing invasive cancer, it significantly reduced prevalence of noninvasive cancer and total number of cancers per mouse and increased prevalence of well-differentiated cancer subtypes not usually seen in this mouse model [5]. Clinical trial: CS-7017 in Combination with Carboplatin/Paclitaxel in Subjects with Stage IIIb/IV Non-small Cell Lung Cancer (NSCLC). Phase 1b

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