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895 RAT CARCINOGENICITY STUDY WITH GW501516, A PPAR DELTA AGONIST.

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GW501516, a non-genotoxic PPARδ agonist, was assessed for carcinogenic potential by daily administration (oral gavage) to Han Wistar rats for a period of 104 weeks. Males were given 0, 5, 15 or 30 mg/kg/day for the first 6 weeks of the study. For the remainder of the study males were given 0, 5, 20 or 40 mg/kg/day. Females were given 0, 3, 10 or 20 mg/kg/day for the entire study. GW501516 produced test article-related neoplastic findings in multiple tissues at all doses. Increased mortality was seen with females given GW501516 at all doses and uterine endometrial adenocarcinoma contributed to death in a high proportion of these animals. Neoplasms considered test-article related occurred in the liver (hepatocellular adenoma at ≥ 10 mg/kg/day), urinary bladder (transitional cell carcinoma in males given 20 and 40 mg/kg/day), thyroid (follicular cell adenoma at ≥ 3 mg/kg/day and carcinoma in males at ≥ 20 mg/kg/day), tongue (squamous cell papilloma in males at 5 mg/kg/day and 40 mg/kg/day), stomach (squamous cell papilloma in males at ≥ 5 mg/kg/day and a female at 20 mg/kg/day, and carcinoma in a male at 40 mg/kg/day and a female at 3 mg/kg/day), skin (inverted squamous cell papilloma in males at ≥ 5 mg/kg/day and females at 3 or 20 mg/kg/day), Harderian glands (adenoma in males at ≥ 5 mg/kg/day and adenocarcinoma in a male at 40 mg/kg/day), testes (interstitial cell adenoma at 40 mg/kg/day), ovary (Sertoli cell adenoma at ≥ 10 mg/kg/day) and uterus (polyp and endometrial adenocarcinoma at ≥ 3 mg/kg/day). Some of the tumor types observed in this study have not been reported with either PPARα or PPARγ agonists and may reflect tumor promotion mediated through PPARδ agonism.