SUPPLEMENTAL DATA

Supplementary Table 1. Antibodies used for immunohistochemistry.

Antibody name	Company and catalog number
anti-NF-κB	CST, 8242S
anti-Nrf2	Abcam, ab137550
anti-8-OHdG	Bioss, bs-1278R
anti-β-tubulin isotype III	Sigma Aldrich, T8578

Supplementary Table 2. Antibodies used for Western blotting.

Antibody name	Company and catalog number
anti-p-AMPK	Cell Signaling Technology (CST), 4185S
anti-AMPK	CST, 2532S
anti-SIRT1	Abcam, ab110304
anti-PGC-1α	Abcam, ab54481
anti-p-ACC	CST, 11818S
anti-COX IV	Proteintech, 11242-1-AP
anti-NDUFS3	Proteintech, 15066-1-AP
anti-TNF-α	CST, 11948S
anti- iNOS	CST, 13120S
anti-ERK	CST, 4695S
anti-β-actin	Abcam, ab8226
anti-p-IκBα	CST, 9246S
anti-IκBα	CST, 4812S
anti-p-Akt	CST, 13038T

anti-AKT	CST, 9272S
anti-p-mTOR	CST, 5536S
anti- mTOR	CST, 2972S
anti-p-NF-κB	CST, 3033S
anti- NF-κB	CST, 8242

Supplementary Table 3. The pharmacokinetic parameters of DW15139 by IV delivery.

IV delivery (10 mg/kg)	Parameter		DW15139	DW14006
Plasma	C_{max}	ng/mL	/	17911.12
	t_{max}	h	/	0.05
	$t_{1/2}$	h	0.36	2.01
	AUC_{0-12h}	h*ng/mL	1269.90	4203.04
DRG	C_{max}	ng/g	831.30	525.38
	t_{max}	h	0.05	0.18
	$t_{1/2}$	h	/	2.74
	AUC_{0-12h}	h*ng/g	295.80	641.06

/ indicates parameter cannot be calculated.

Supplementary Table 4. The pharmacokinetic parameters of DW15139 by PO delivery.

PO delivery (30 mg/kg)	Parameter		DW15139	DW14006
Plasma	AUC_{0-12h}	h*ng/mL	1.63	49.41
DRG	AUC_{0-12h}	h*ng/g	295.80	588.04

/ indicates parameter cannot be calculated. As indicated in **Supplementary Table 3-4**,

after DW15139 (IV or PO) administration, we monitored DW15139 and its hydrolysate

DW14006 in plasma or target tissue (DRG). Plasma and snap-frozen DRG were collected at 8 time points (n = 6/each point, half male and half female C57BL/6 mice) for analysis of DW15139 and DW14006 levels by LC/MS/MS assay. Data are the mean values.

Supplementary Table 5. LD$_{50}$ calculation of DW14006 against C57BL/6 mice (*i.p*)

Groups	Number(n)	Dose(mg/kg)	Log of dose	death rate
1	8	640	2.8062	1
2	8	512	2.7093	1
3	8	409.60	2.6124	1
4	8	327.68	2.5154	1
5	8	262.14	2.4185	0.5
6	8	209.72	2.3216	0

LD$_{50}$=lg^{-1}{Xm-i($\sum$p-0.5)} (Xm: the highest dose converted to logarithm; i: Difference of dose logarithm between adjacent groups; $\sum$p: sum of death rate)

LD$_{50}$= lg^{-1}{2.8062-0.0969(4.5-0.5)} = 262.1682 mg/kg.