# **Supplementary Information**

# Discovery of 7-Hydroxy-6-methoxy-2-methyl-3-(3,4,5-trimethoxybenzoyl)benzo[b]furan (BNC105), a Tubulin Polymerization Inhibitor with Potent Antiproliferative and Tumor Vascular Disrupting Properties.

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Entry	Structure <sup>a</sup>	Inhib. Tubulin polymer-	Inhibition of cancer cell proliferation <sup>c</sup>	Inhib HUVECs <sup>e</sup> IC <sub>50</sub> (nM)
		isation <sup>b</sup>	IC <sub>50</sub> (nM)	
		$IC_{50}(\mu M)$		
1.	OMo	$1.8 \pm 0.2$	<10, 2.9	Activated: 1-10
				Quiescent: 1-10
	Olivie			
	OMe			
	OH			
	OMe			
		15.05	00.110	ND
2.	OMe	$1.5 \pm 0.5$	88 +/- 10	ND
	MeO			
	Mag			
	MeO			
3		15+05	34 +/- 10	ND
5.	OMe MeQ /	1.5 ± 0.5	54 17- 10	
	MeO			
	OMe			
	MeO			

## Table SI-1: Complete listing of novel benzo[b]

Entry	Structure <sup>a</sup>	Inhib. Tubulin polymer- isation <sup>b</sup>	Inhibition of cancer cell proliferation <sup><math>c</math></sup> IC <sub>50</sub> (nM)	Inhib HUVECs <sup>e</sup> IC <sub>50</sub> (nM)
		$IC_{50}$ ( $\mu$ M)		
4.	Meo OMe MeO OH MeO OH MeO OH	$1.3 \pm 0.1$	57, 21	ND
5.	MeO MeO MeO MeO OH	1.5 ± 0.4	1-2	ND
6.	MeO MeO MeO OH OH	<4	3.9, 4.1	Activated: 1-10 Quiescent: 1-10
7.	Meo OMe MeO OMe MeO OMe	1.6 ± 0.2	60, 50	Activated: 10-100 Quiescent: 10-100

Entry	Structure <sup>a</sup>	Inhib. Tubulin polymer- isation <sup><math>b</math></sup> IC <sub>50</sub> ( $\mu$ M)	Inhibition of cancer cell proliferation <sup><math>c</math></sup> IC <sub>50</sub> (nM)	Inhib HUVECs <sup>e</sup> IC <sub>50</sub> (nM)
8.	MeO MeO MeO H		62, 31	Activated: 10-100 Quiescent: 10-100
9.	MeO MeO MeO MeO O MeO O MeO O MeO O MeO O Me	<4	70, 72	Activated: 10-100 Quiescent: 10-100
10.	Meo OMe Meo Me Meo NMe	1.2 ± 0.04	3.9, 4.0	Activated: 1-10 Quiescent: 10-100
11.	MeO MeO MeO MeO MeO NMe	ND	48, 35	Activated: 100-1000 Quiescent: 100-1000

Entry	Structure <sup>a</sup>	Inhib. Tubulin	Inhibition of cancer cell	Inhib HUVECs <sup><math>e</math></sup> IC <sub>50</sub> (nM)
		polymer-	proliferation <sup><math>c</math></sup>	
		$IC_{50} (\mu M)$	IC 50 (IIIVI)	
12.	Meo	$1.3 \pm 0.07$	4, <1	Activated: 0.1-1.0 Quiescent: 0.1-1.0
	MeO NMe			
	ОН			
13.	MeO OMe MeO	ND	4.1, 3.3	ND
	MeO OH			
14.	MeO OMe MeO O	ND	3.0, 3.4	Activated: 1-10 Quiescent: 1-10
	MeO OH			
15.	MeQ OMe MeO O	ND	110, 83	Activated: 100-1000 Quiescent: 100-1000
	MeO NBn			

Entry	Structure <sup>a</sup>	Inhib.	Inhibition of	Inhib HUVECs <sup>e</sup>
		Tubulin	cancer cell	$IC_{50}$ (nM)
		polymer-	proliferation	
		1sation	$IC_{50}$ (nivi)	
16		$\frac{1C_{50} (\mu M)}{ND}$	17.22	Activated: 10, 100
10.		ND	17,22	Activated: 10-100 Ouiescent: 10,100
	MeO			Quiescent. 10-100
	NieO			
	s			
	MeO			
17.	OMe	ND	25, 29	ND
	HO			
	MeO			
	Me			
	N			
	MeO			
	OH			
18.	OMe	ND	3.3; 4.4	Activated: 1-10
				Quiescent: 1-10
	MeO-			
	Me			
	MeO			
	ОН			
10			<u> </u>	
19.	OMe	ND	68; 57	Activated: 10-100
	MeO			Quiescent: 10-100
	MieO 0			
	MeO			
	он /			

Entry	Structure <sup>a</sup>	Inhib. Tubulin polymer-	Inhibition of cancer cell proliferation <sup>c</sup>	Inhib HUVECs <sup>e</sup> IC <sub>50</sub> (nM)
		$IC_{co}(\mathbf{u}\mathbf{M})$	$IC_{50}$ (mvi)	
20.	MeO MeO MeO MeO MeO MeO MeO MeO MeO MeO	ND	21; 14	Activated: 1-10 Quiescent: 10-100
21.	MeO MeO MeO MeO OH	ND	1.6; <1	Activated: 1-10 Quiescent: 1-10
22.	MeO MeO MeO MeO OH	ND	<1; <1	Activated: 0.1-1.0 Quiescent: 0.1-1.0
23.	MeO MeO MeO MeO MeO N MeO N O N O N O N O N O N O N O N O N O N	ND	900; 540	Activated: 100-1000 Quiescent: 100-1000

Entry	Structure <sup>a</sup>	Inhib. Tubulin polymer- isation <sup>b</sup>	Inhibition of cancer cell proliferation <sup><math>c</math></sup> IC <sub>50</sub> (nM)	Inhib HUVECs <sup>e</sup> IC <sub>50</sub> (nM)
24		IC <sub>50</sub> (μM)	29.15	Activated: 10-100
24.	MeO MeO MeO MeO N OEt		27, 15	Quiescent: 10-100
25.	MeO OMe MeO OMe MeO N NH <sub>2</sub> MeO O N O	ND	3.8; 4.0	Activated: 1-10 Quiescent: 1-10
26.	MeO OMe MeO OMe MeO NH	ND	3.6; 4.0	Activated: 1-10 Quiescent: 10-100
27.		ND	540; 600	Activated: 100-1000 Quiescent: 100-1000
28.	MeO MeO MeO MeO NeO NeO NeO NeO NeO NeO NeO NeO NeO N	ND	3.5; 2.4	Activated: 100-1000 Quiescent: 100-1000

Entry	Structure <sup>a</sup>	Inhib. Tubulin	Inhibition of cancer cell	Inhib HUVECs <sup><math>e</math></sup> IC <sub>50</sub> (nM)
		polymer-	proliferation <sup>c</sup>	
		isation <sup>o</sup>	$IC_{50}(nM)$	
29.	MeQ OMe	ND	0.42; 1.7	Activated: 1-10
	Mag			Quiescent: 1-10
	MeO OH			
30.	MeO	$8.7 \pm 0.8$	0.33; 0.75	Activated: 0.1-1.0 Ouiescent: 0.1-1.0
	MeO			
	MeO			
31.	MeO	ND	1.8; 2.3	Activated: 1-10
	MeO			Quiescent: 1-10
	MeO			
32.	OH MeO OMe	ND	1.4: 2.1	Activated: 1-10
			,	Quiescent: 1-10
	MeO			
	MeO´ T OH			
33.	Meo	ND	40; 35	Activated: 10-100 Ouiescent: 10-100
	MeO			Zuroscent. 10 100
	MeO			

Entry	Structure <sup>a</sup>	Inhib. Tubulin polymer- isation <sup><math>b</math></sup> IC <sub>50</sub> ( $\mu$ M)	Inhibition of cancer cell proliferation <sup>c</sup> IC <sub>50</sub> (nM)	Inhib HUVECs <sup>e</sup> IC <sub>50</sub> (nM)
34.		ND	360, 350	Activated: 10-100 Quiescent: 10-100
35.	MeO OMe MeO OMe MeO NMe <sub>2</sub>	ND	300; 310	Activated: 100-1000 Quiescent: 100-1000
36.		ND	0.37; 0.32	Activated: 0.1-1.0 Quiescent: 0.1-1.0
37.		$2.2 \pm 0.4$	0.37; 0.32	Activated: 0.1-1.0 Quiescent: 0.1-1.0
38.		ND	4.5; 5.7	Activated: 10-100 Quiescent: 10-100
39.	MeQ MeQ MeQ N MeQ N MeQ	ND	200, 230	Activated: 100-1000 Quiescent: 100-1000

Entry	Structure <sup>a</sup>	Inhib. Tubulin	Inhibition of cancer cell	Inhib HUVECs <sup><math>e</math></sup> IC <sub>50</sub> (nM)
		polymer- isation <sup>b</sup>	proliferation <sup>c</sup> IC <sub>50</sub> (nM)	
40	OMe	$IC_{50} (\mu M)$	40.35	Activated: 10, 100
40.	MeO MeO	ND	40, 33	Quiescent: 10-100
	MeO			
41.	MeQ MeO MeO	ND	1.5, 0.62	Activated: 0.1-1.0 Quiescent: 0.1-1.0
42.	MeO MeO MeO	ND	6.9, 7.9	Activated: 1-10 Quiescent: 1-10
43.	MeO OMe OH	ND	100-1000 <sup>d</sup>	Activated: 100-1000 Quiescent: 100-1000
	MeO			
44.	Meo OMe O <sub>2</sub> N NO <sub>2</sub> MeO HN NO <sub>2</sub>	ND	>1000 <sup>d</sup>	Activated: 10-100 Quiescent: >1000
	Med			

Entry	Structure <sup>a</sup>	Inhib. Tubulin polymer- isation <sup>b</sup>	Inhibition of cancer cell proliferation <sup><math>c</math></sup>	Inhib HUVECs <sup>e</sup> IC <sub>50</sub> (nM)
		$IC_{50}$ ( $\mu$ M)	1C <sub>50</sub> (IIIVI)	
45.	MeO OMe	ND	1-10 <sup><i>d</i></sup>	Activated: 1-10 Quiescent: 1-10
	MeO MeO N N N N N N N			
	ОН			
46.	MeQ	ND	1-10 <sup><i>a</i></sup>	Activated: 1-10 Quiescent: 1-10
	MeO			
47.	MeO	ND	2.0	Activated: 0.1-1 Quiescent: 1-10
	MeO MeO OH OMe			
48.	MeO /	ND	8.0	Activated: 1-10
	MeO MeO OH			Quiescent: 1-10
49.	MeO <sub>N</sub> / OMe	ND	$1-10^{d}$	Activated: 1-10
	MeO MeO MeO H			Quiescent: 1-10
	NH <sub>2</sub>			

Entry	Structure <sup>a</sup>	Inhib. Tubulin polymer- isation <sup>b</sup>	Inhibition of cancer cell proliferation <sup>c</sup> IC <sub>50</sub> (nM)	Inhib HUVECs <sup>e</sup> IC <sub>50</sub> (nM)
50	OMe	$IC_{50} (\mu M)$	$1-10^d$	Activated: 1-10
	MeO MeO O			Quiescent: 1-10
	MeO OH NH <sub>2</sub>			
51.	Meo	ND	10-100 <sup>d</sup>	Activated: 10-100 Quiescent: 10-100
	MeO			
	MeO OH N-			
52.	MeO OMe MeO	ND	1-10 <sup>d</sup>	Activated: 1-10 Quiescent: 1-10
	MeO OH OH			
53.	MeO	ND	0.1-1 <sup>d</sup>	Activated: 1-10 Quiescent: 1-10
	MeO			
	MeO			
54.	MeO OMe	ND	1-10 <sup>d</sup>	Activated: 1-10
	MeO			
	MeO OH OMe			

Entry	Structure <sup>a</sup>	Inhib. Tubulin polymer- isation <sup>b</sup> $IC_{50}$ ( $\mu$ M)	Inhibition of cancer cell proliferation <sup>c</sup> IC <sub>50</sub> (nM)	Inhib HUVECs <sup>e</sup> IC <sub>50</sub> (nM)
55.	MeO OMe MeO O MeO O MeO O NH <sub>2</sub>	ND	0.1-1 <sup>d</sup>	Activated: 1-10 Quiescent: 1-10
56.	MeO OMe MeO OMe MeO O MeO OH OMe	ND	1-10 <sup>d</sup>	Activated: 1-10 Quiescent: 1-10
57.	MeO MeO MeO OH NH NH	ND	1-10 <sup>d</sup>	Activated: 1-10 Quiescent: 1-10
58.	MeO OMe MeO O MeO O MeO O OH	ND	1-10 <sup>d</sup>	Activated: 1-10 Quiescent: 1-10
59.	MeO OMe MeO O HN MeO O HN MeO O HN MeO O HN	ND	ND	Activated: 1-10 Quiescent: 1-10

Entry	Structure <sup>a</sup>	Inhib.	Inhibition of	Inhib HUVECs <sup>e</sup>
		Tubulin	cancer cell	$IC_{50}(nM)$
		polymer-	proliferation	
		1sation <sup>o</sup>	$IC_{50}$ (nM)	
60	OMe	$IC_{50} (\mu M)$	ND	A stirrete de 100, 1000
60.	MeO	ND	ND	Activated: $100-1000$
	Mag			Quiescent.100-1000
	∫ ∫ ∕_NH			
	MeO			
	ÓН			
61.	MeQ. /	ND	ND	Activated: 100-1000
				Quiescent:10-100
	MeO NH			
	NH <sub>2</sub> .HCl			
	NHO ONH			
	OH			
62.	MeO / OMe	ND	ND	Activated: 1-10
				Quiescent:1-10
	MeO			
	MeOÓÓ			
63	ÓH ``	ND	ND	Activated: 0.1.1.0
05.	MeO	IND.		Oujescent:0.1-1.0
	MeO			<b>C</b>
	OH			
64.	MeO OMe	ND	ND	Activated: 1-10
				Quiescent:1-10
	MeO			
	MeO Ó N-			
	о́н <sup>′</sup>			

Entry	Structure <sup>a</sup>	Inhib. Tubulin polymer- isation <sup>b</sup>	Inhibition of cancer cell proliferation <sup><math>c</math></sup> IC <sub>50</sub> (nM)	Inhib HUVECs <sup>e</sup> IC <sub>50</sub> (nM)
65.	MeO MeO MeO OH N N	ND	ND	Activated: 1-10 Quiescent:1-10
66.	MeO MeO MeO OH N-N N NH2	ND	ND	Activated: 1-10 Quiescent:1-10
67.	MeO MeO MeO OH OH	ND	ND	Activated: 10-100 Quiescent:10-100
68.	MeO MeO MeO OH OH MeO	ND	ND	Activated: 1-10 Quiescent: 1-10

Entry	Structure <sup>a</sup>	Inhib. Tubulin polymer- isation <sup>b</sup>	Inhibition of cancer cell proliferation <sup>c</sup> IC <sub>50</sub> (nM)	Inhib HUVECs <sup>e</sup> IC <sub>50</sub> (nM)
69.	MeO MeO MeO OH	ND	ND	Activated: 10-100 Quiescent: 10-100
70.	HO MeO MeO OH OH O NH O NH O NH <sub>2</sub>	ND	ND	Activated: 1-10 Quiescent: 1-10
71.	HO MeO MeO OH	ND	ND	Activated: 10-100 Quiescent: 100-1000
72.	MeO OMe MeO OMe MeO O MeO Br	ND	500	Tum: 100-1000 Norm: 100-1000
73.	OMe MeO MeO OH	ND	35	Tum: 100-1000 Norm: 100-1000

Entry	Structure <sup>a</sup>	Inhib. Tubulin polymer- isation <sup><math>b</math></sup> IC <sub>50</sub> ( $\mu$ M)	Inhibition of cancer cell proliferation <sup>c</sup> IC <sub>50</sub> (nM)	Inhib HUVECs <sup>e</sup> IC <sub>50</sub> (nM)
74.	F F F MeO OH	ND	800	Tum: >1000 Norm: >1000
75.	MeO OMe MeO OMe MeO O NHMe OH	ND	3.5	Tum: 1-10 Norm: 0.1-1
76.	MeO OMe MeO O MeO O MeO O OH	ND	1.2	Tum: 0.1-1 Norm: 1-10
77.	MeO MeO MeO OH	ND	3.3	Tum: 1-10 Norm: 1-10
78.	MeO MeO MeO MeO NH <sub>2</sub> NH <sub>2</sub> O NH	ND	35	Tum: 1-10 Norm: 10-100

Entry	Structure <sup>a</sup>	Inhib. Tubulin polymer- isation <sup><math>b</math></sup> IC <sub>50</sub> ( $\mu$ M)	Inhibition of cancer cell proliferation <sup>c</sup> IC <sub>50</sub> (nM)	Inhib HUVECs <sup>e</sup> IC <sub>50</sub> (nM)
79.	MeO MeO MeO O MeO O H	3.0	2.4	Tum: 0.1-1 Norm: 10-100
80.	MeO MeO MeO O O O O H	ND	575	Tum: 100-1000 Norm: 100-1000
81.	MeO MeO MeO OH OH	ND	260	Tum: 100-1000 Norm: 100-1000
82.	Meo OMe Meo OMe Meo OMe OMe	1.9±0.4	26±5	Tum: 32 Norm: 44

<sup>a</sup> For synthetic methods and spectral data, see: main text experimental and main text refs 25 and 26.

<sup>*b*</sup> The tubulin concentration was 10  $\mu$ M. Inhibition of extent of assembly, after a 20 min incubation at 30 °C, was the parameter measured: For a description of the method see Verdier-Pinard, P. *et. al. Mol. Pharmacol.* **1998**, *53*, 62-76

<sup>c</sup> Unless otherwise stated the cell line was MCF-7, using the method described in: Verdier-Pinard, P. *et. al. Mol. Pharmacol.* **1998**, *53*, 62-76.

<sup>*d*</sup> The cell line used was MDA-MB-231, see main text experimental for method.

<sup>c</sup> The value is given as a range within which the  $IC_{50}$  value falls, see main text Experimental for method.

#### Synthesis of Compounds:

#### 3-*N*,*N*-Dibenzylamino-4-methoxy-phenylacetylene 17a:

This material was prepared in 4 steps from 2-methoxy-4-iodonitrobenzene:

Step 1, 2-methoxy-4-iodoaniline: A suspension of 2-methoxy-4-iodonitrobenzene (4.00 g, 14.3 mmol) and tin(II) chloride (12.93 g, 57.30 mmol) in 95% ethanol (40 mL) was heated to reflux for 4 h. The solvent was removed under vacuum, and the residue was dissolved in ethyl acetate (100 mL). The organic layer was washed with a 10% sodium bicarbonate solution (100 mL) and brine (100 mL) and dried over MgSO<sub>4</sub>. The solvent was removed under vacuum to afford the title compound as a dark brown oil (2.73 g, 77%) that was used without further purification in the next step. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  6.98 (dd, *J* = 8.78, 2.09 Hz, 1H), 6.97 (d, *J* = 1.81 Hz, 1H), 6.50 (d, *J* = 8.90 Hz, 1H), 3.80 (s, 3H).

Step 2, 2-methoxy-4-iodo-*N*,*N*-dibenzylaniline: To a solution of 2-methoxy-4-iodoaniline (2.73 gm, 11.00 mmol) in dry dimethylformamide (10 mL) under nitrogen was added potassium carbonate (3.35 g, 24.2 mmol), followed by the addition of benzyl bromide (2.9 mL, 24.4 mmol), and the reaction mixture was stirred at 100 °C for 6.5 h (TLC), then cooled to room temperature, diluted with ethyl acetate (80 mL) and washed with 10% aqueous citric acid (3 x 80 mL) and brine (2 x 80 mL). The organic layer was separated and dried over MgSO<sub>4</sub>. The solvent was removed under vacuum to afford a viscous brown oil (4.42 gm, 94%). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.26-7.17 (m, 11H), 7.03 (br s, 1H), 6.60 (d, *J* = 8.50 Hz, 1H), 4.20 (br s, 4H), 3.86 (s, 3H).

Step 3, 3-*N*,*N*-dibenzylamino-4-methoxyphenyl-trimethylsilylacetylene: A solution of 2-methoxy-4-iodo-*N*,*N*-dibenzylaniline (500 mg, 1.16 mmol), Pd(PPh<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub> (25 mg, 0.036 mmol) and triethylamine (320 µL, 2.30 mmol) in dry dichloromethane was deoxygenated by passing nitrogen through the solution for 2 min. To the resulting yellow suspension was added trimethylsilylacetylene (250 µL, 1.77 mmol), followed by the addition of copper (I) iodide (11 mg, 0.058 mmol). The resulting suspension was stirred at room temperature for 1.5 h. The reaction was diluted with dichloromethane (20 mL) and washed with water (20 mL) and brine (20 mL). The organic layer was separated and dried over magnesium sulfate, and the solvent was removed under vacuum to afford the crude product (502 mg) as a brown oil that was used in the next step without further purification. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.25-7.19 (m, 10H), 7.06(dd, *J* = 8.32, 1.94 Hz, 1H), 6.90 (d, *J* = 1.83 Hz, 1H), 6.77 (d, J = 8.35 Hz, 1H), 4.20 (bs, 4H), 3.89 (s, 3H), 0.20 (s, 9H). Step 4, 3-*N*,*N*-dibenzylamino-4-methoxy-phenylacetylene **17a**: To a solution of 3-*N*,*N*-dibenzylamino-4-methoxyphenyl-trimethylsilylacetylene in methanol (5 mL) and tetrahydrofuran (7 mL) was added potassium fluoride (384 mg, 6.6 mmol), and the reaction mixture was stirred at room temperature for 1 h and diluted with ethyl acetate (20 mL). The organic layer was washed with water (2 x 20 mL) and dried over MgSO<sub>4</sub>. The solvent was removed under vacuum to give an orange oil that was purified by column chromatography to give a slightly tan oil (149 mg, 69%) <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.26-7.17(m, 10H), 7.08 (dd, *J* = 8.31, 1.89 Hz, 1H), 6.92 (d, *J* = 1.49 Hz, 1H), 6.79 (d, J = 8.33 Hz, 1H), 4.21 (bs, 4H), 3.90 (s, 3H), 2.98 (s, 1H).



# 5-Ethynyl-1-methyl-1*H*-indole 17b:

A solution of 1-methyl-5-iodoindole (500 mg, 1.95 mmol) in dry 1,4-dioxane (5 mL) was deoxygenated by passing nitrogen through the solution. Trimethylsilylacetylene (323  $\mu$ L, 2.33 mmol), Pd(PPh<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub> (68.3 mg, 0.097 mmol) and copper (I) iodide (11.12 mg, 0.058 mmol) were then added sequentially, and the reaction mixture was stirred for 1 h and filtered through celite. The solvent was removed under reduced pressure and the residue dissolved in tetrahydrofuran (6 mL) and treated with tetrabutylammonium fluoride (2.1 mL, 1 M solution in tetrahydrofuran). The reaction was stirred for 15 min and diluted with ethyl acetate (10 mL). The organic layer was separated, washed with 1 M HCl (aq) (5 mL) and dried over MgSO<sub>4</sub>. The solvent was removed under vacuum, and the crude product was purified by flash chromatography (silica gel, eluent = hexane / diethyl ether 9:1) to afford the title compound as a creamy solid (117 mg, 39%) <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.80 (br s, 1H), 7.34 (dd, *J* = 8.48, 1.43 Hz, 1H), 7.24 (d, *J* = 8.48, 1H), 7.05 (d, *J* = 3.11 Hz, 1H), 6.46 (d, *J* = 3.06 Hz, 1H), 3.77 (s, 3H), 2.99 (s, 3H).

≡ – ∕⊂ NMe \_ N

## 4-Ethynyl-1-methyl-1-H-pyrazole 17f:

When 1-methyl-5-iodoindole was replaced by 1-methyl-4-iodopyrazole in example (**17b**), the identical procedure afforded the title compound as a yellow paste that crystallized on standing (890 mg, 58%). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.57(s, 1H), 7.50 (s, 1H), 3.86 (s, 3H), 2.98 (s, 1H).

### Pharmacokinetic Studies of BNC105 / BNC105P







Figure SI-4: Plasma concentrations of BNC105 following IV administration to male Sprague Dawley rats at nominal dose of 6.0 µmol/kg.

Figure SI-5: Plasma concentrations of BNC105P (closed symbols) and BNC105 (open symbols) following IV administration of BNC105P to male Sprague Dawley rats at a nominal dose of 6.6 µmol/kg.



Table SI-2: Tissue distribution of BNC105 in mice after IV administration of BNC105 and BNC105P. Data represent the dose normalized concentrations of BNC105 at T = 15 min and T = 2 h after IV administration of 6.0 µmol/kg of BNC105 and BNC105P.

Sample	Compound	[BNC105] in tissue (ng/g)					
Time	Doseu	Tumor	Liver	Heart	Spleen	Kidney	Brain
T = 15 min	BNC105	936	794	475	2796	1117	5463
	BNC105P	636	527	725	2854	1121	2695
T = 2 h	BNC105	684	188	406	1310	653	3221
	BNC105P	500	206	358	1276	552	1932