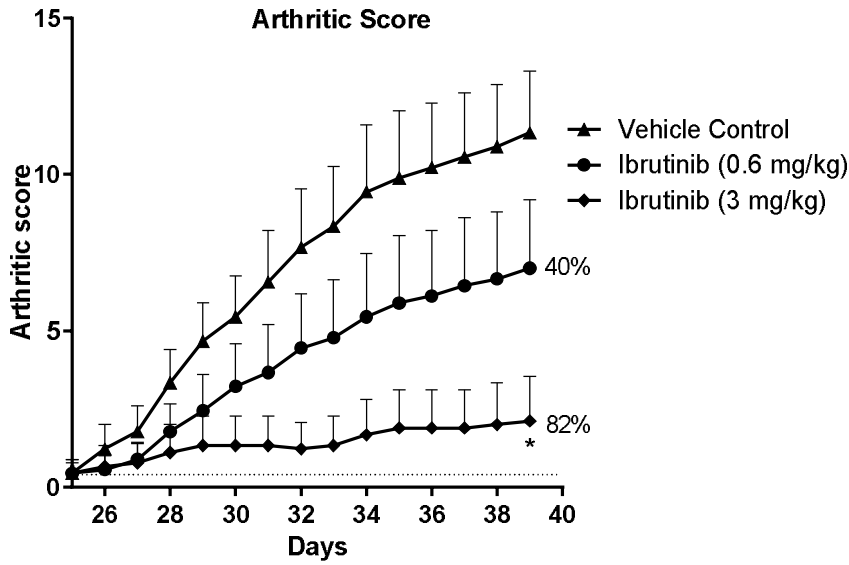
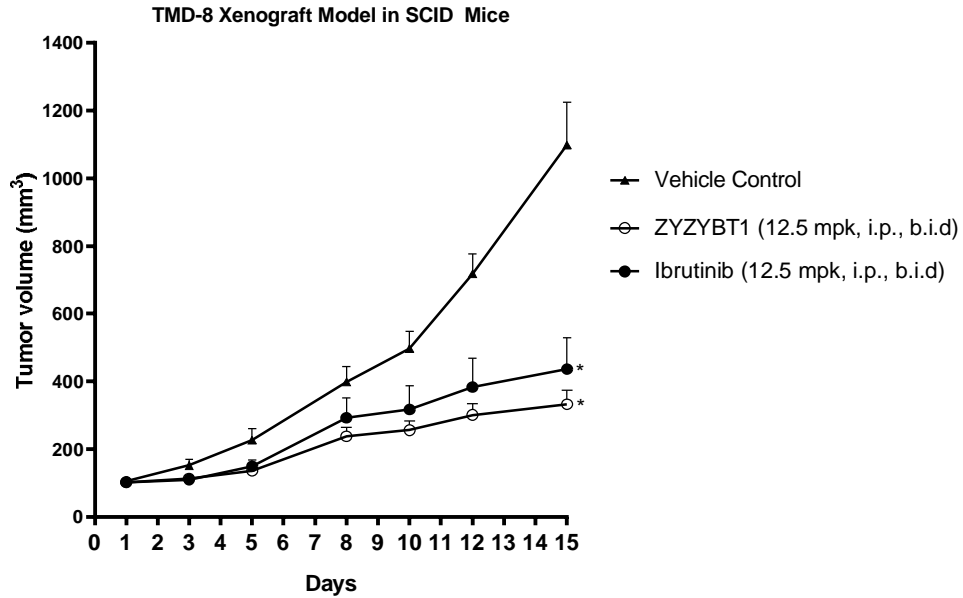


**Supplementary Table 1: Pharmacokinetic data for ZYBT1 in Wistar rats and mice**

<b>Species</b>	<b>Route/Dose</b>	<b>T<sub>max</sub> (h)</b>	<b>C<sub>max</sub> (ng/mL)</b>	<b>AUC<sub>last</sub> (ng.h/mL)</b>
Wistar rat	PO; 3 mg/kg	0.25	649	908
	PO; 10 mg/kg	2.00	820	2730
	PO; 30 mg/kg	2.00	1264	4716
	PO; 100 mg/kg	4.00	2877	13185
	PO; 300 mg/kg	4.00	6141	80662
SCID mice	PO; 0.2 mg/kg	0.25	10.48	8.63
	PO; 1 mg/kg	0.25	61.8	174.80
	PO; 3 mg/kg	0.25	703.04	588.03
	PO; 5 mg/kg	1	429.03	1124.68
	PO; 15 mg/kg, BID	8.50	6272.60	13476.17

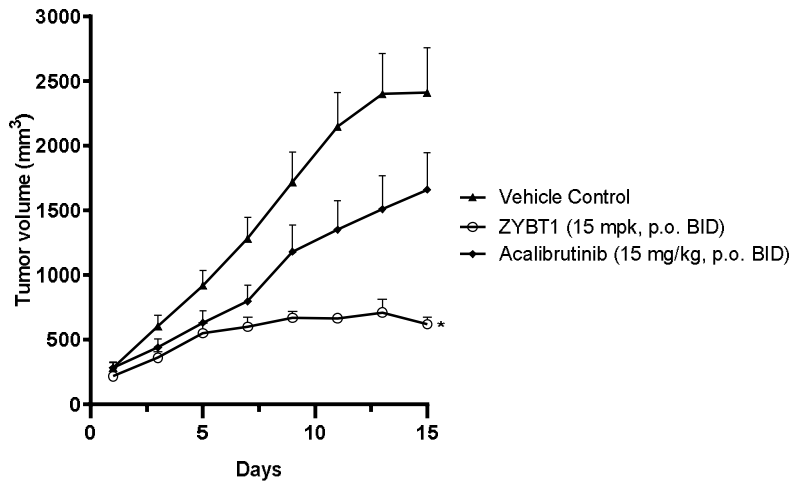


**Supplemental Figure S1. Effect of ibrutinib on clinical score in collagen-induced arthritis (CIA) model.** Mice with established CIA were divided into separate groups consisting of 10 mice each. Groups were treated vehicle or ibrutinib (0.6 & 3mg/kg, QD) for 14 consecutive days. The data represent the mean arthritic scores. Error bars represent SEM. \*, P < 0.05 when compared with vehicle control

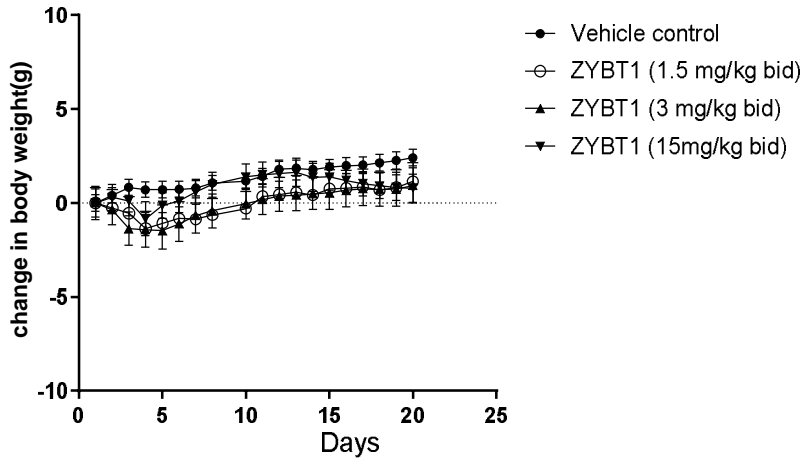


**Supplemental Figure S2. Suppression of tumor volume in TMD8 DLBCL xenograft model by ZYBT1 and ibrutinib.** Mice with established tumor reaching around 100 mm<sup>3</sup> were divided into different groups of 10 mice each. Groups were untreated vehicle or treated with ZYBT1 or ibrutinib (12.5 mg/kg, BID, intra peritoneal) for 14 consecutive days. The data represents the mean tumor volume. Error bars represent SEM. \*, P < 0.05 when compared with vehicle control.

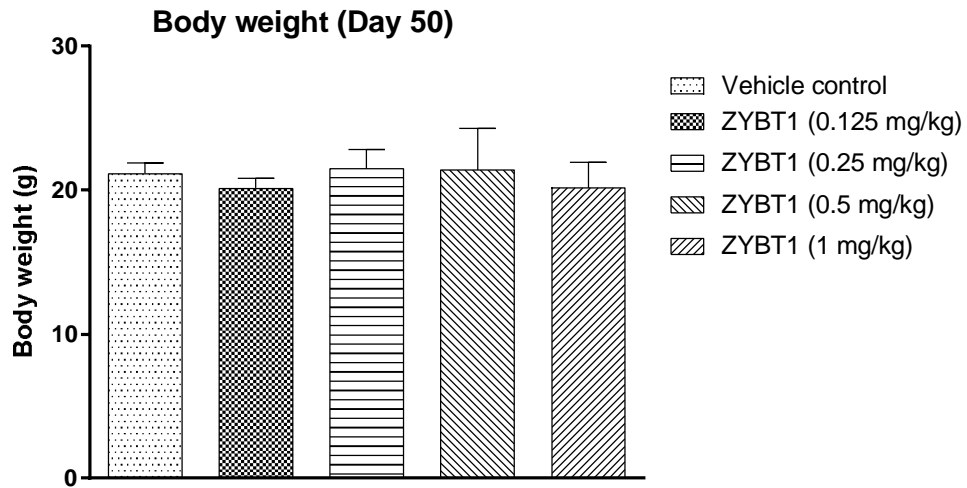
TMD-8 Xenograft Model in SCID Mice



**Supplemental Figure S3. Suppression of tumor volume in TMD8 DLBCL xenograft model by ZYBT1 and acalibrutinib.** Mice with established tumor reaching around 250 mm<sup>3</sup> were divided into different groups of 10 mice each. Groups were untreated vehicle or treated with ZYBT1 or acalibrutinib (15 mg/kg, BID, p.o.) for 14 consecutive days. The data represents the mean tumor volume. Error bars represent SEM. \*, P < 0.05 when compared with vehicle control



**Supplemental Figure S4: Effect of ZYBT1 on change in body weight in TMD8 DLBCL xenograft model by ZYBT1.** Mice with established tumor reaching around 100 mm<sup>3</sup> were divided into different groups of 10 mice each. Groups were untreated vehicle or treated with ZYBT1 (1.5, 3 & 15 mg/kg, p.o, BID) for 20 consecutive days. The data represents the mean body weight. Error bars represent SEM. \*, P < 0.05 when compared with vehicle control



**Supplemental Figure S5: Effect of ZYBT1 on body weight after three weeks of treatment in collagen-induced arthritic mice model.** Mice with established CIA were divided into separate groups consisting of 10 mice each. Groups were treated vehicle or ZYBT1 (0.125, 0.25, 0.5 & 1 mg/kg, OD) for three weeks. The data represent the mean body weight. Error bars represent SEM. \*,  $P < 0.05$  when compared with vehicle control