Supporting Information

The discovery of a novel inhibitor of apoptotic protease activating factor-1 (Apaf-1) for ischemic heart: synthesis, activity and target identification

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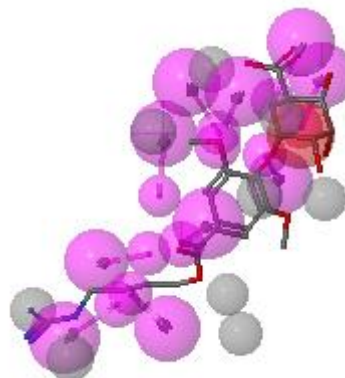
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Table S1. The predicted target candidates for kinases of compound ZYZ-488 using PharmMapper server[1]

Note that in silico targets screening was performed within an in-house pharmacophore databae, named PharmTarget DB, which contains more than 7000 receptor-based pharmacophore models, and only those kinases at the top 300 (about 9%) in the ranked list were extracted and summarized.

Rank[a]	PDB	Target	Fit	Normalized	Molecular and pharmacophore

ID	Name	Score	Fit Score	Aligned Model[b]
			Compound ZYZ-488	
22	1Z6T APAF-1	4.476	0.4069	

[a] The ranked list of hit target pharmacophore models, which are sorted by fit score in descending order;

[b] The molecule and pharmacophore were aligned by PharmMapper, and the molecule-pharmacophore alignment poses were displayed via a modified version of Jmol applet. The pharmacophore features are schemed by color: Hydrophobic, cyan; Positive, blue; Negative, red; Donor, green, Acceptor, magenta; Aromatic, yellow;

[c] The result for compound 2 can be freely accessed and downloaded from the PharmMapper server via

http://59.78.96.61/pharmmapper/result.php?job_id=14099133002

1.   Liu, X., et al., *PharmMapper server: a web server for potential drug target identification using pharmacophore mapping approach.* Nucleic acids research, 2010. **38**(suppl 2): p. W609-W614.

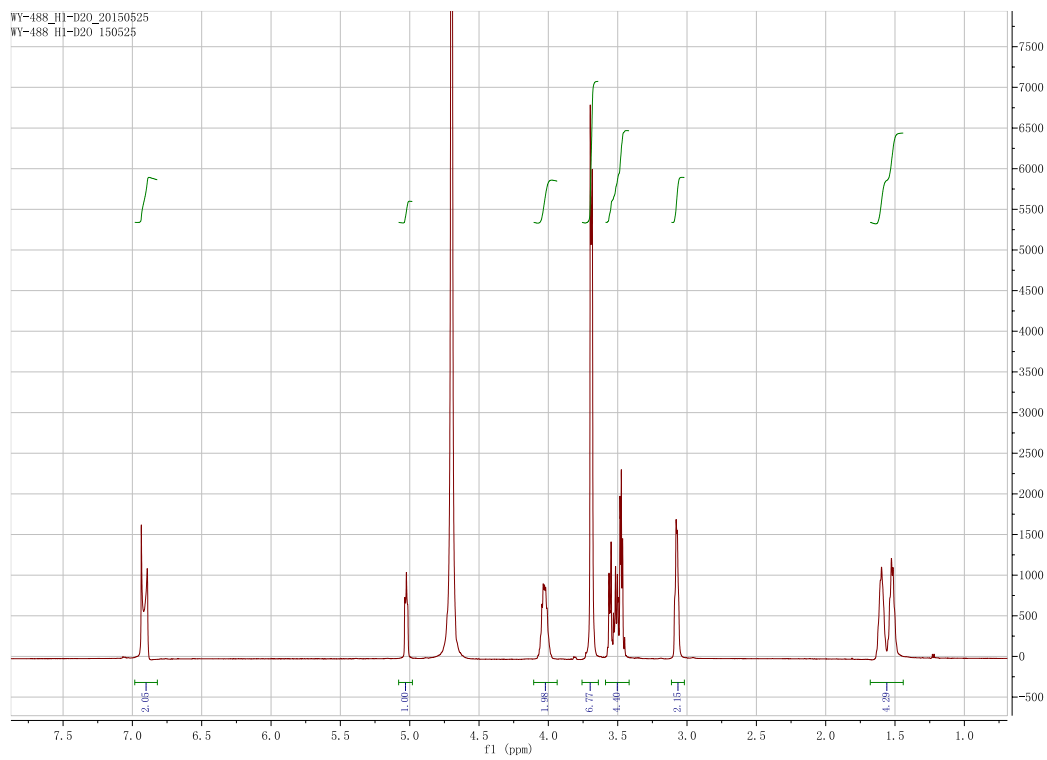**Figure S1. ^{1}H NMR(600MHz,D$_2$O) for compound ZYZ-488**

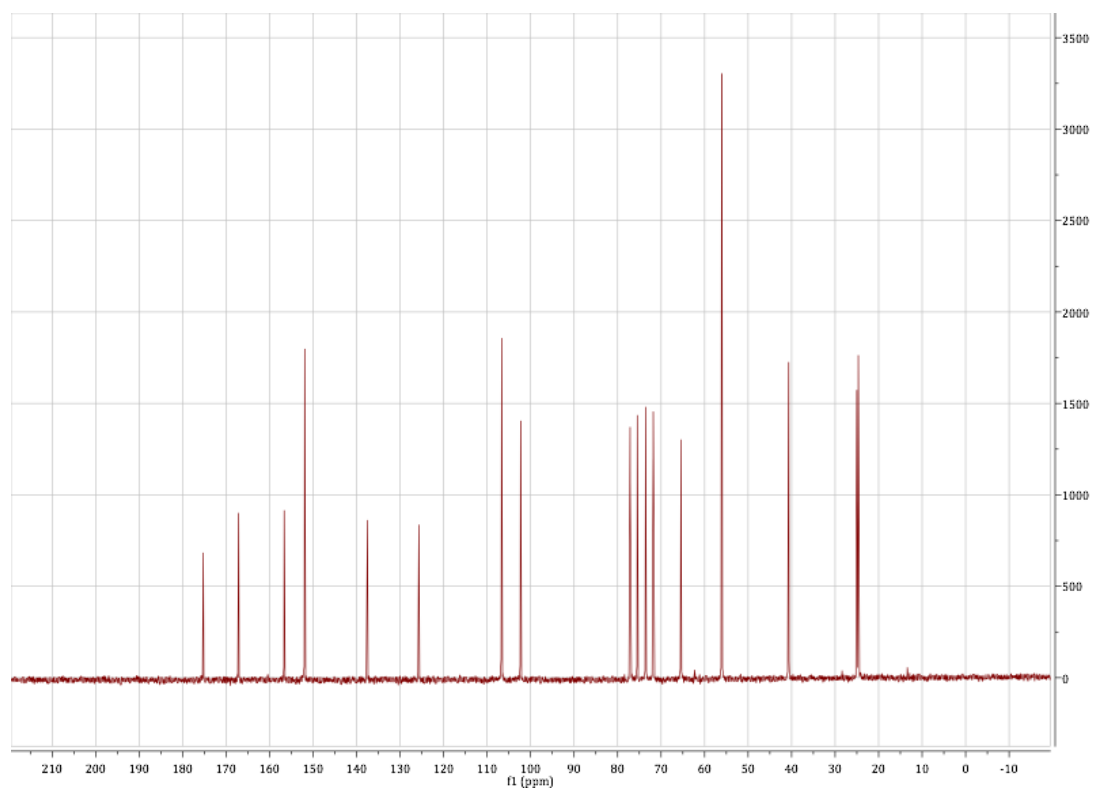**Figure S2. ^{13}C NMR(150MHz,D$_2$O) for compound ZYZ-488**
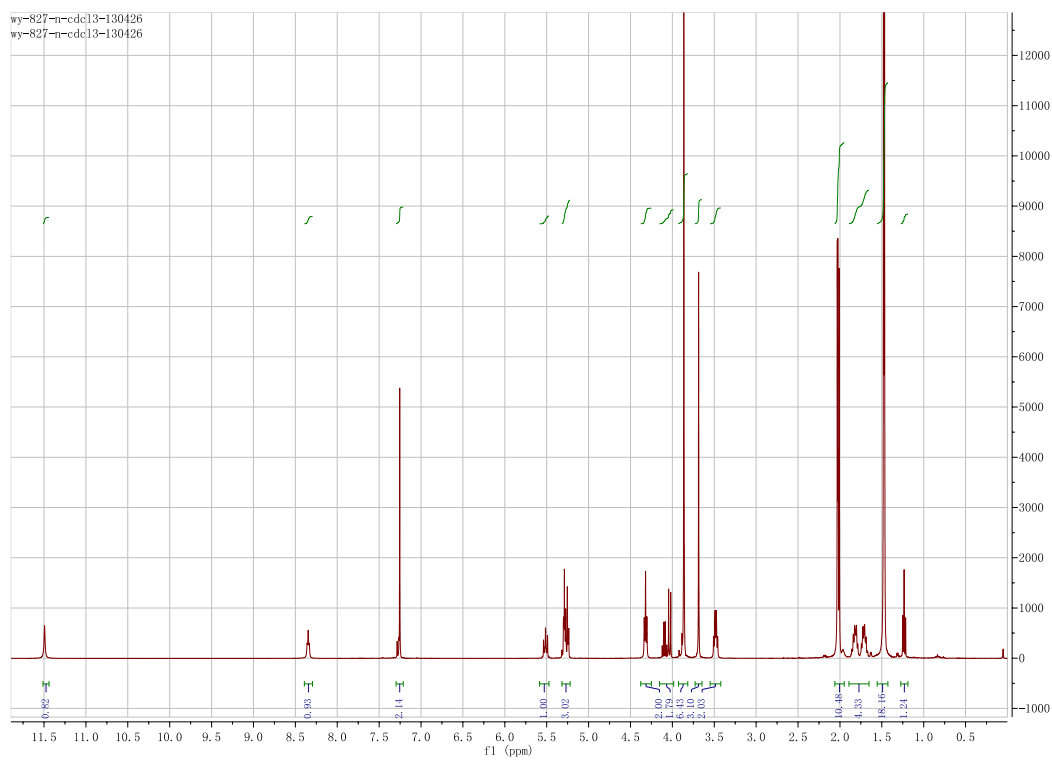
Figure S3. ^{1}H NMR(400MHz, CDCl$_3$) for compound 7

Figure S4. ^{13}C NMR(100MHz, CDCl$_3$) for compound 7
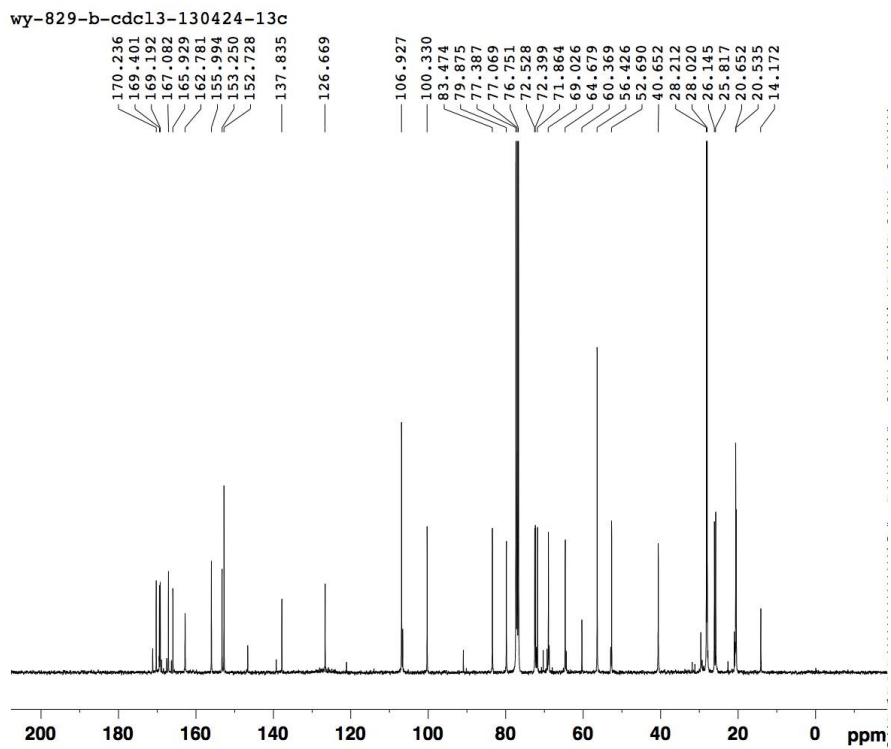
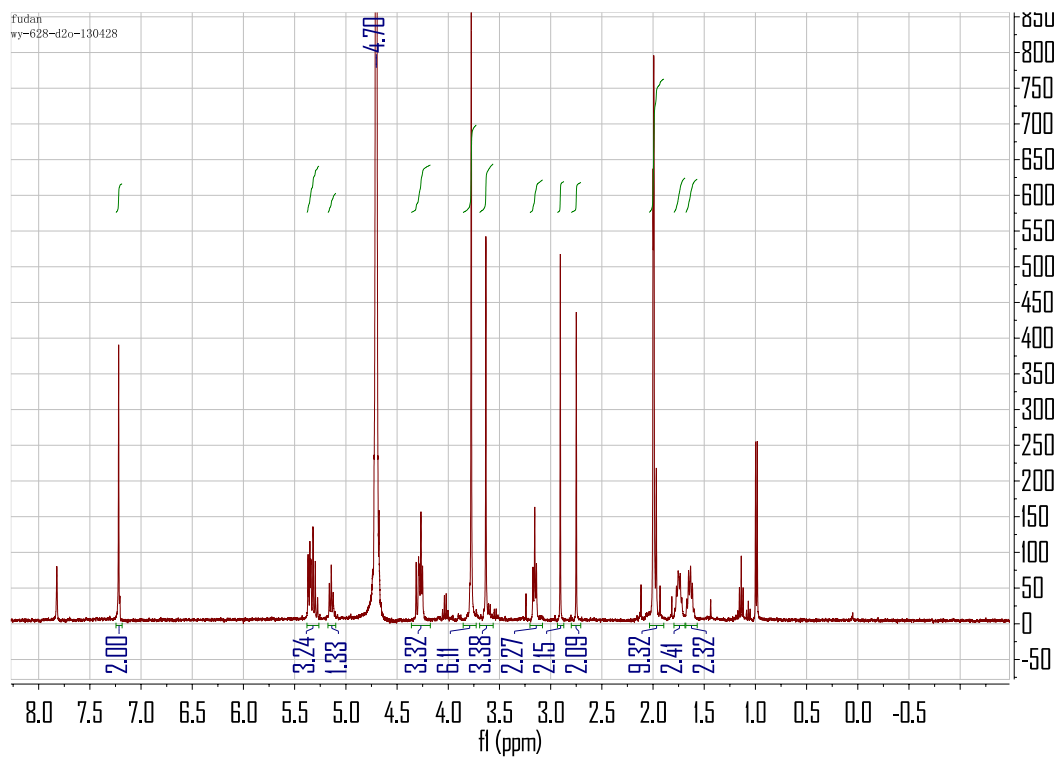**Figure S5. ^{1}H NMR (400MHz, D$_2$O) for compound 8**

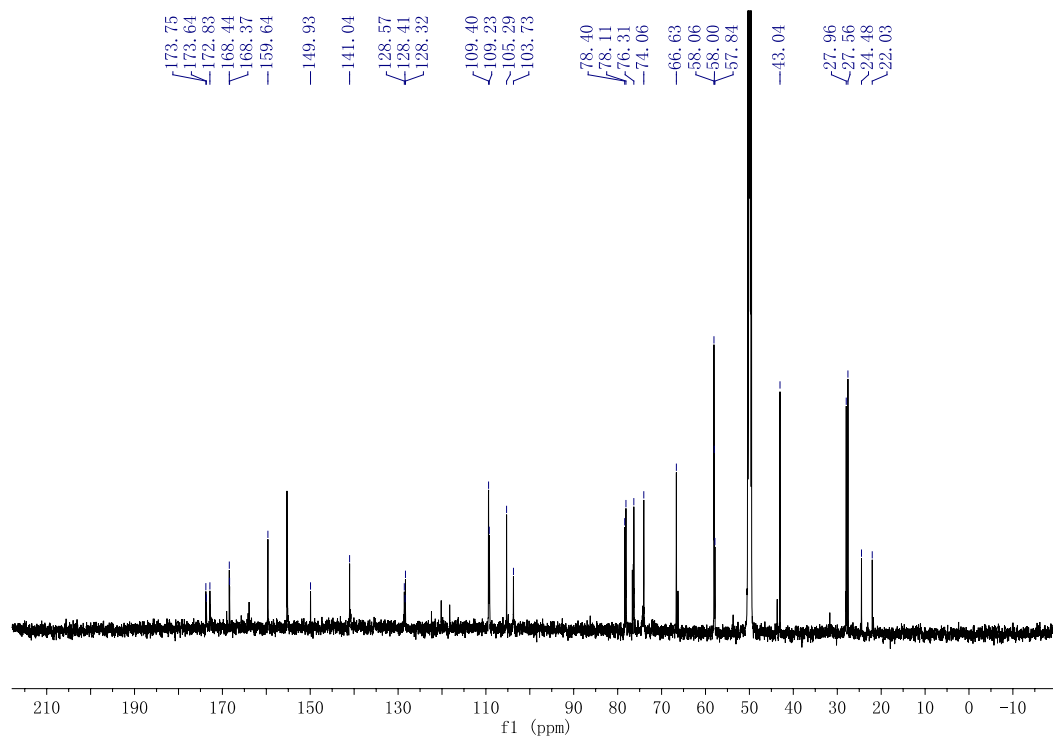**Figure S6.** ^{13}C NMR (150MHz, CDOD$_3$) for compound 8

Figure S7. The effect of ZYZ-488 on expression of Apaf-1 under normoxic or hypoxic condition.
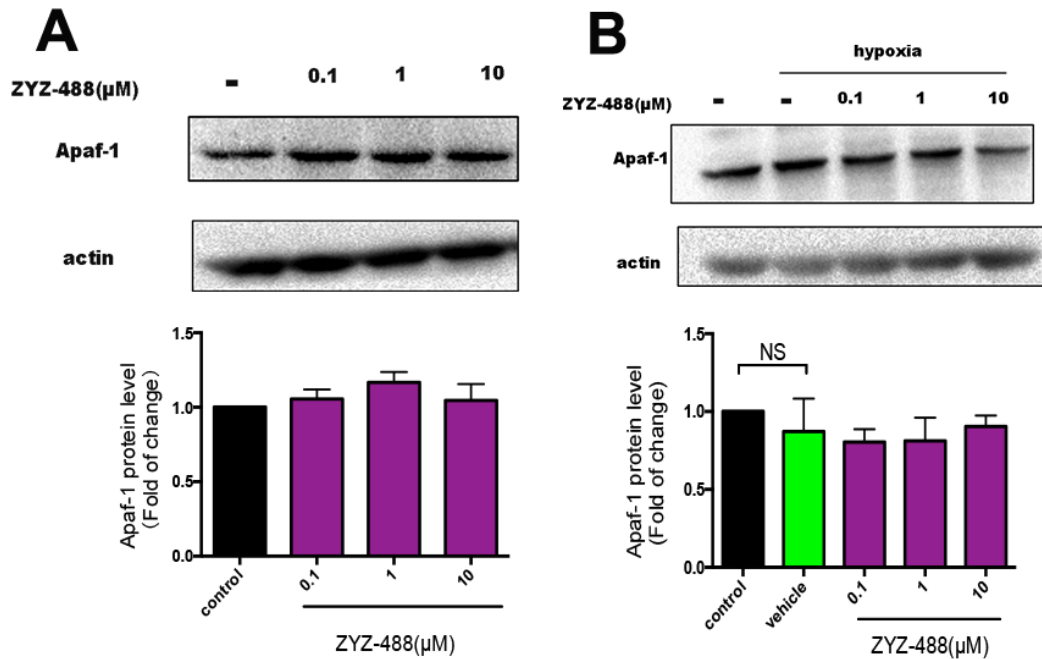

Figure S7. The effect of **ZYZ-488** on expression of Apaf-1 under normoxic or hypoxic condition. H9c2 cells were incubated with indicated concentrations of **ZYZ-488** for 12 h. Then Apaf-1 protein level under normoxic condition was analyzed by Western blot (A). H9c2 cells were culture under hypoxic condition for another 12h to analyze the Apaf-1 protein level under hypoxic condition. Data are the mean ±S.E.M of results from at least three independent experiments.

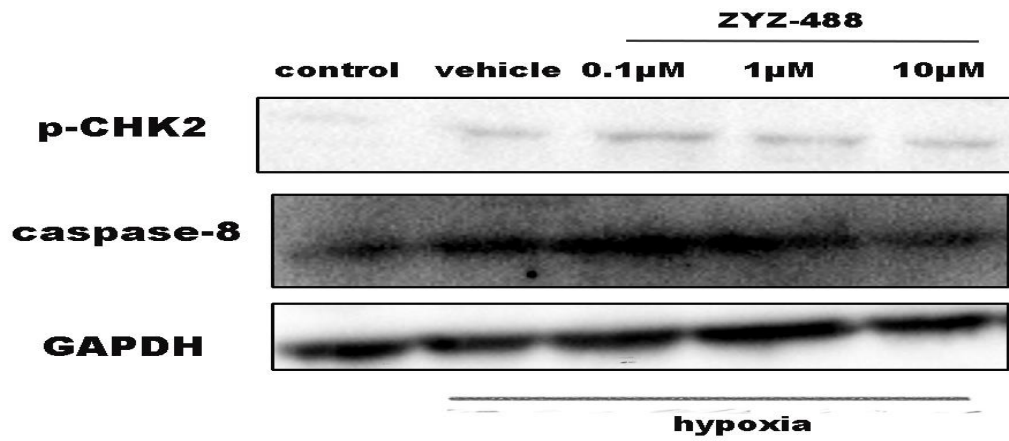**Figure S8. Effect of ZYZ-488 on CHK-2 phosphorylation and activation of caspase-8.**

Figure S9. Silencing effect of siApaf-1

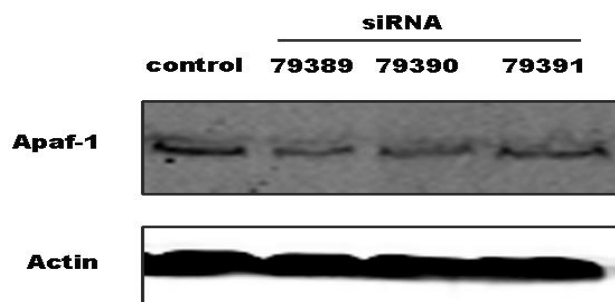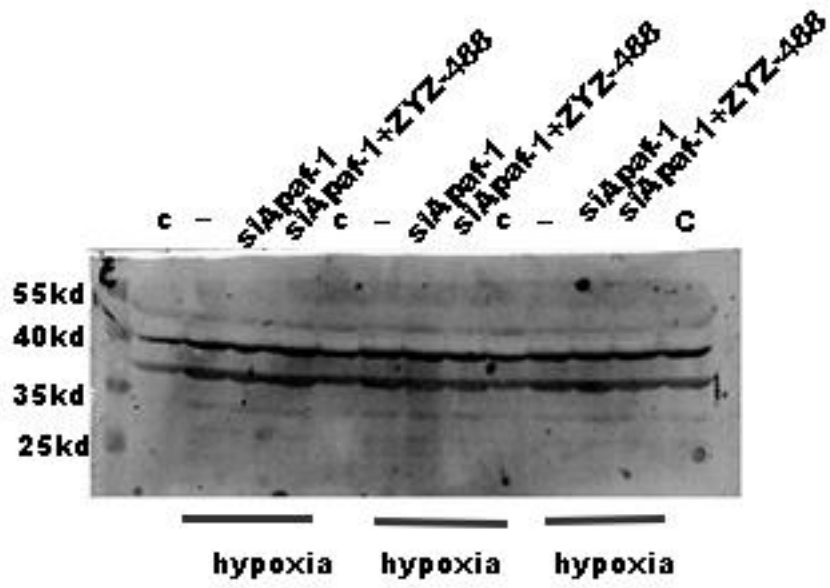**Figure S10. The full-length blots of figure 8.**

Figure S11. The full-length blots of figure 9.

Figure S12. The full-length blots of figure S7 and S8.