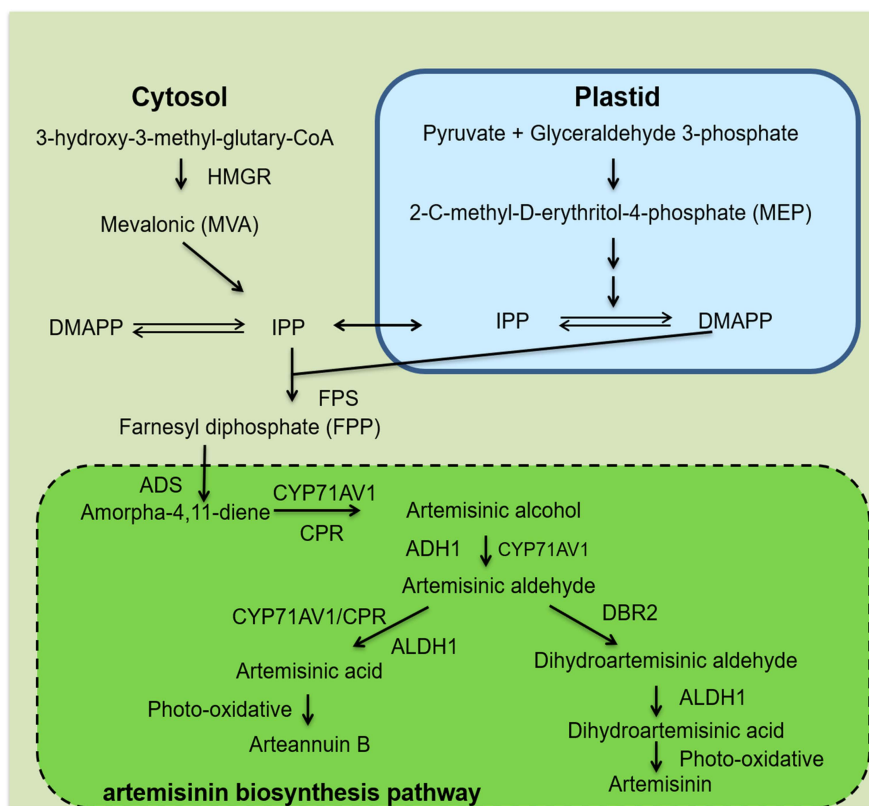
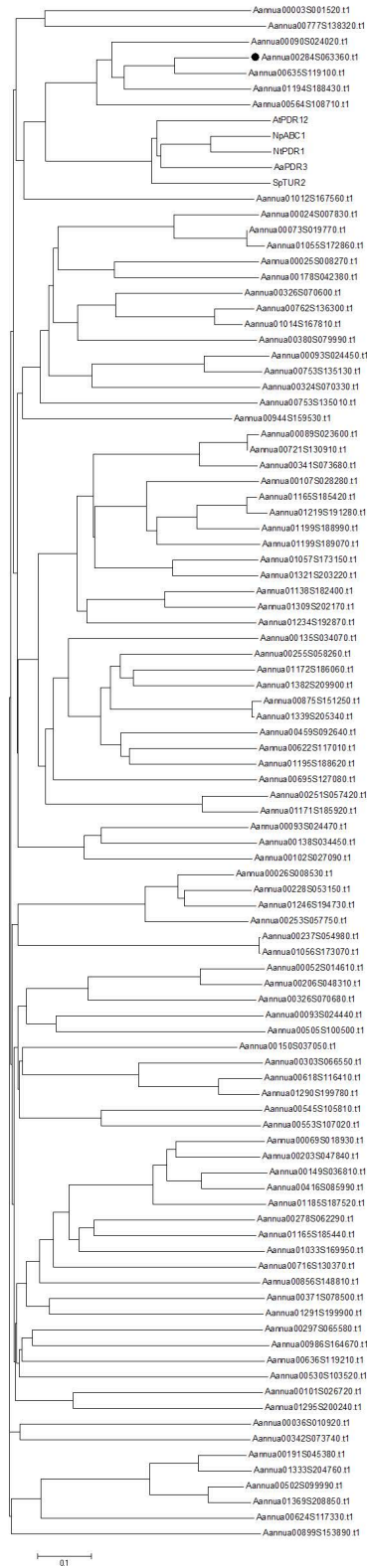


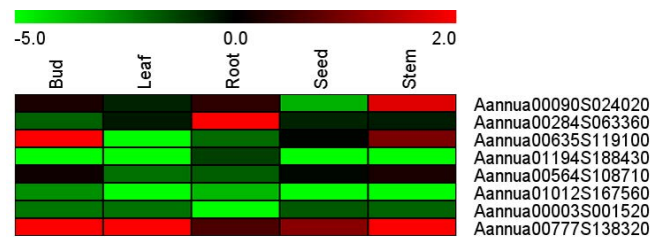
## Supplementary Information



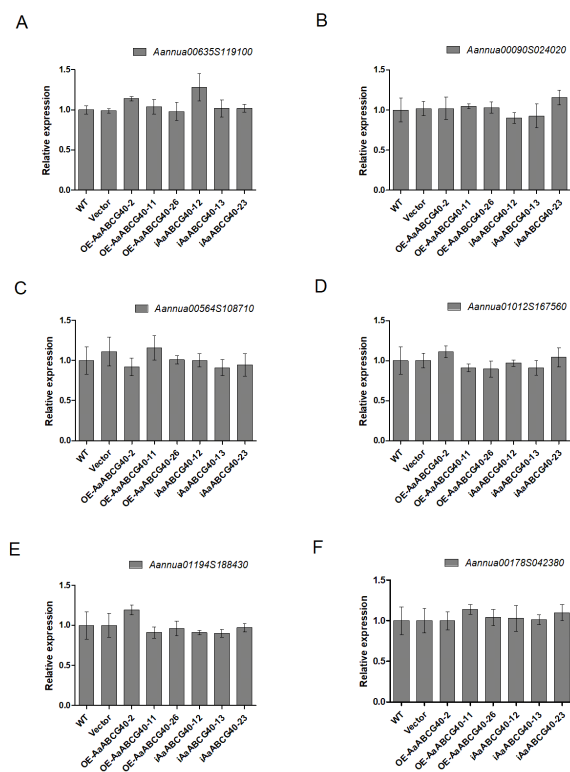
**Figure S1. The artemisinin biosynthetic pathway.** HMGR, 3-hydroxy-3-methylglutaryl-CoA reductase; DXS, 1-deoxyxylulose 5-phosphate synthase; DXR, 1-deoxyxylulose 5-phosphate reductoisomerase; DMAPP, dimethylallyl diphosphate; IPP, isopentenyl diphosphate; FPS, farnesyl diphosphate synthase; ADS, amorpha-4,11-diene synthase; CYP, cytochrome P450; CYP71AV1, cytochrome P450-dependent hydroxylase; CPR, cytochrome P450 oxidoreductase; DBR2, double bond reductase 2; ALDH1, aldehyde dehydrogenase 1; ADH1, alcohol dehydrogenase; CYB5, cytochrome b5 monooxygenase.



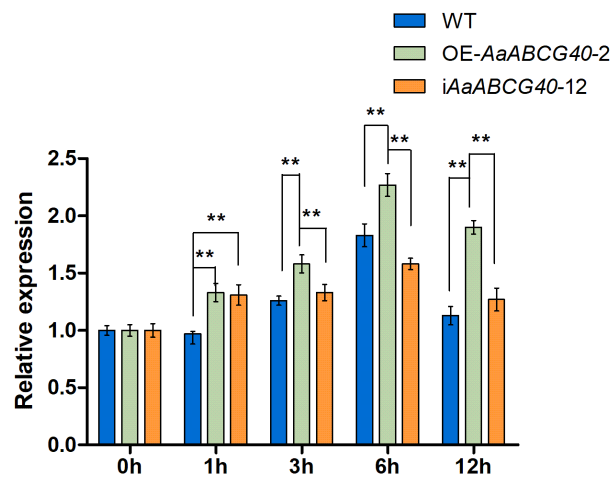
**Figure S2. Phylogenetic tree showing the relationship ABC transporters in *A. annua* compared with AtPDR12 from *Arabidopsis*.** The tree presented here is a neighbor-joining tree based on amino acid sequence alignment. The candidate gene *AaABCG40* is marked by the black circle.



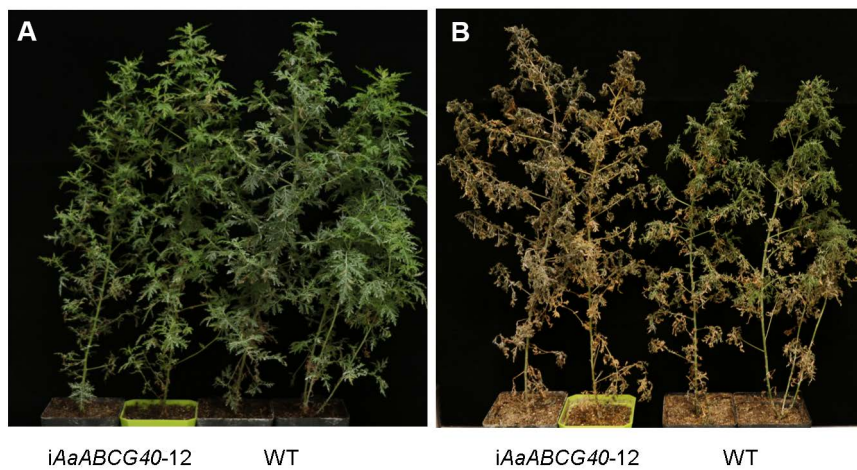
**Figure S3. Hierarchical cluster analysis of 8 PDR transporter genes in *A. annua*.** The color scale at the top represents the value of log-transformed reads per kilobase per million of mapped reads.



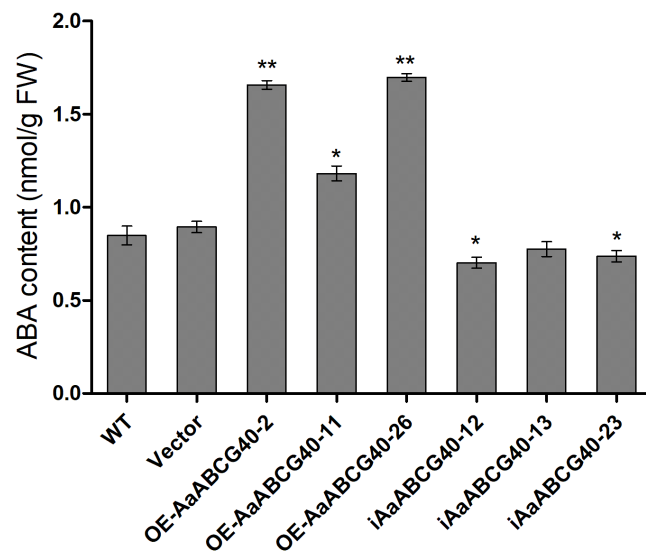
**Figure S4. Comparative analyses of *AaABCG* gene expression in wild type (WT), plants transformed with the empty vector (EV), *AaABCG40*-overexpression and *AaABCG40*-RNAi plants. (A) Relative expression of Aannua00635S119100 in WT, EV and *AaABCG40* transgenic *A. annua* lines. (B) Relative expression of Aannua00090S024020 in WT, EV and *AaABCG40* transgenic *A. annua* lines. (C) Relative expression of Aannua00564S108710 in WT, EV and *AaABCG40* transgenic *A. annua* lines. (D) Relative expression of Aannua01012S167560 in WT, EV and *AaABCG40* transgenic *A. annua* lines. (E) Relative expression of Aannua01194S188430 in WT, EV and *AaABCG40* transgenic *A. annua* lines. (F) Relative expression of Aannua00178S042380 in WT, EV and *AaABCG40* transgenic *A. annua* lines. The error bars represent the means  $\pm$  SD from three biological replicates.**



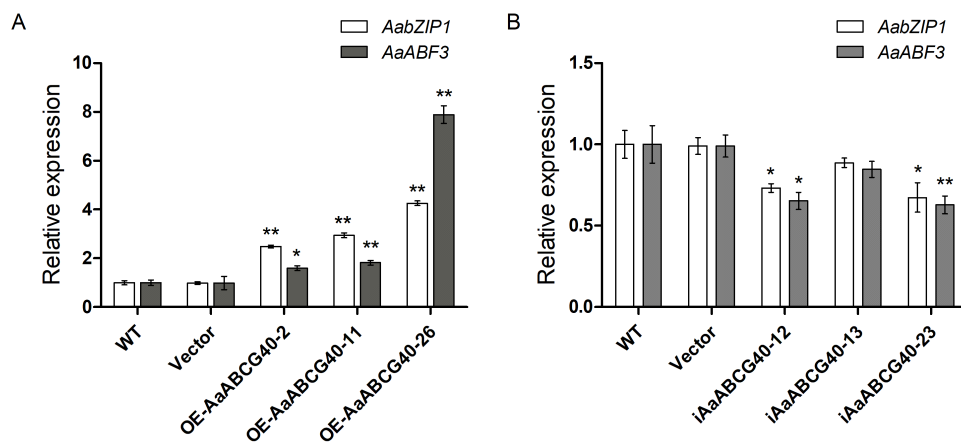
**Figure S5. Relative expression of *AaCYP71AV1* in wild type (WT), OE-*AaABCG40-2* and *AaABCG40*-RNAi-12 plants with the ABA treatment. *ACT1N* was used as internal control. The error bars represent the means  $\pm$  SD from three replicates.  $P < 0.05$ ,  $P < 0.01$ , student's *t*-test.**



**Figure S6. *AaABCG40*-RNAi transgenic *A. annua* showed worse tolerance under drought stress. (A)** Two-month-old cutting seedlings of *AaABCG40*-RNAi transgenic plants and wild-type *A. annua* plants were cultivated in pots and watered well in the growth chamber under a 16-h light/8-h dark cycle at 25°C for a week. **(B)** Water was withheld for 14 days.

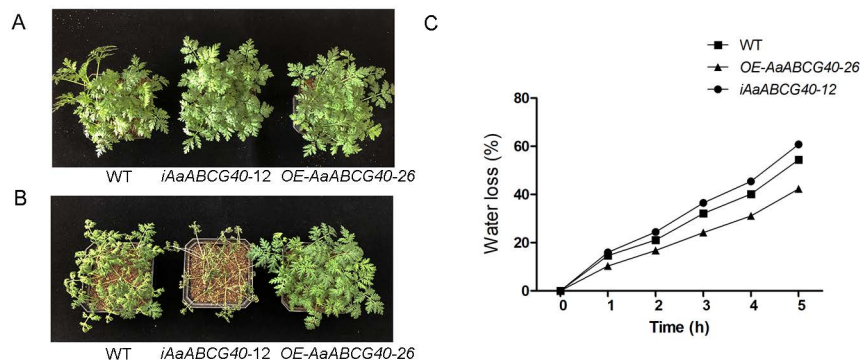


**Figure S7. ABA levels measured in the leaves of wild type (WT), OE-AaABCG40-2 and AaABCG40-RNAi-12 plants.** The error bars represent the means  $\pm$  SD from three replicates.  $P < 0.05$ ,  $P < 0.01$ , student's *t*-test.



**Figure S8. Relative expression of *AaZIP1* and *AaABF3* in wild type (WT), plants transformed with the empty vector (EV), *AaABCG40*-overexpression and *AaABCG40*-RNAi plants. (A) Relative expression of *AaZIP1* and *AaABF3* in WT, EV and *AaABCG40*-overexpression transgenic *A. annua* lines. (B) Relative expression of *AaZIP1* and *AaABF3* in WT, EV and *AaABCG40*-RNAi transgenic *A. annua* lines. *ACTIN* was used as internal control. The error bars represent the means  $\pm$  SD from three technical replicates.  $P < 0.05$ ,  $P < 0.01$ , student's *t*-test.**





**Figure S9. The next generation of *AaABCG40*-overexpression transgenic *A. annua* showed better tolerance under drought stress.** (A) The seeds of OE-AaABCG40-26 transgenic plant and wild-type *A. annua* plants were cultivated in pots and watered well in the growth chamber under a 16-h light/8-h dark cycle at 25°C for one month. (B) Water was withheld for 20 days. (C) Time course of water loss from the leaves of 4-week-old wild-type and OE-AaABCG40-26 *A. annua* plants. Three independent experiments were performed, and three independent plants were used to calculate. The error bars represent the means  $\pm$  SD from three technical replicates.

**Table S1.** Primers used in this study.

No.	Primer name	Use	Primer sequence 5'-3'	Restriction enzyme
1	AaABCG40-FP1	cloning	TGTAACAATGGATGGAAGTACTGGAAT	-
2	AaABCG40-RP1	cloning	CGACTGCAATCCAATACCAGTAAGC	
3	AaABCG40-FP	qPCR	GGGAAACAAACGATTTTATCCAGAGC	
4	AaABCG40-RP	qPCR	CCAAGGAAAGTAAGAGCCACAGCATA	
5	$\beta$ -actin-FP	qPCR	CCAGGCTGTTTCTGCTCTGTAT	
6	$\beta$ -actin-RP	qPCR	CGCTCGGTAAGGATCTTCATCA	
7	BamHI-AaABCG40-FP	cloning	CTCTCTCTCCAACCTGGATCCATGGAAGTACTGGAATA	<i>BamHI</i>
8	AaABCG40-Spel-RP	cloning	CCCTTGCTCACCATACTAGTTCTTCTGGAAATTAAGGAT	<i>SpeI</i>
9	AaABCG40-RNAi-FP	cloning	CACCGGTGAACGAGTTCCTTGCC	
10	AaABCG40-RNAi-RP	cloning	CATCGAAGGTAATTGAATGTGGTTC	
11	Pro- AaABCG40-FP	cloning	TTGGTGTGTTTGTTCCTATTTATG	
12	Pro- AaABCG40-RP	cloning	CTTTATCCAGTCAGTTCATCCATTG	
13	PstI-ProAaABCG40 -FP	cloning	TGCACTGCAGTTGGTGTGTTTGTTCCTAT	<i>PstI</i>
14	ProAaABCG40-BamHI-RP	cloning	CGGGATCCTGTTACAAAAGATCAATTGATC	<i>BamHI</i>
15	AaADS-F	qPCR	GGACTAGTTCAGGCTATG	
16	AaADS-R	qPCR	AAGCATGTAATTGACCACC	
17	AaCYP71AV1-F	qPCR	TCATTTTCTGCTGCTT	
18	AaCYP71AV1-R	qPCR	CCAGTTTGCCTCAGTA	
19	AaDBR2-F	qPCR	ACTGCTGGTGGCTTTCTTA	
20	AaDBR2-R	qPCR	ACCCTCGACTTGTTCCTTA	
21	AaALDH1-F	qPCR	CAGTTTCTGACCCAAATCCAGTTGA	
22	AaALDH1-R	qPCR	TCGGAGTAGTTGGTCACAT	
23	PDR196-AaABCG40-FP	cloning	AGTGGATCCCCGGGCTGCAGATGGATGGAAGTACTGGAATA	
24	PDR196-AaABCG40-RP	cloning	CTTGATATCGAATTCCTGCAGTTATCTTCTGGAAATTAAG	
25	PDR196-AtPDR12-FP	cloning	AGTGGATCCCCGGGCTGCAGATGGAGGGAAGTACTGTTTACC	
26	PDR196-AtPDR12-RP	cloning	GTACCGGGCCCCCTCGAGCTATCGTTTTTGGAAATTGA	
27	Aannua00178S042380-RT-FP	qPCR	CTCAACTCCGTGGTCCAACCTCT	
28	Aannua00178S042380-RT-RP	qPCR	TATTGAACCAGAAAATGGACGGCT	
29	Aannua00635S119100-RT-FP	qPCR	TCCCGTGAAGAAAATGACGAAGA	

30	Aannua00635S119100-RT-RP	qPCR	ATCTTCATCAGCGGCATTCACAA	
31	Aannua01194S188430-RT-FP	qPCR	AGGAGCACGAAGCAGAAGCCAAA	
32	Aannua01194S188430-RT-RP	qPCR	TGTAAAGACGCCAGTTTCAATGC	
33	Aannua00090S024020-RT-FP	qPCR	AGGACACAAGATAACGACGAGGA	
34	Aannua00090S024020-RT-RP	qPCR	CAACAAGCGTAAACTCGCCTCCAG	
35	Aannua00564S108710-RT-FP	qPCR	GCTTGGGCACAATGGGTGGGTAT	
36	Aannua00564S108710-RT-RP	qPCR	AATAGCCTTGTCTAATGGAGGGAGT	
37	Aannua00178S042380-RT-FP	qPCR	TACTGAATGGGGTAACAGGGAAG	
38	Aannua00178S042380-RT-RP	qPCR	ATTGAACCAGAAAATGGACGGCT	
39	AabZIP1-RT-FP	qPCR	CGATGTTTCCGAAGCCGTAT	
40	AabZIP1-RT-RP	qPCR	TGCTAACCCGTCCGATGA	
41	AaABF3-RT-FP	qPCR	GCTGCTTTCAACTTCAACACTTC	
42	AaABF3-RT-RP	qPCR	ATAAATCACGTTGAGCCATGCT	