Supplementary material: Pharmacogenetic analyses of imputed non-genotyped markers in genomic regions identified in the genome-wide analyses

To explore the extent of the associated genomic regions, all HapMap phase II SNPs within 100kb upstream and downstream of markers identified at genome-wide or suggestive significance levels of significance were imputed and tested for association using Markov Chains algorithm (with 50 iterations) implemented in the MACH software (1,2). A broader region (200kb each side) was imputed for the Chromosome 1 associated locus, as a 100kb window was not sufficient to capture the full extent of the associated region.

Figure S3: Chromosome 1 associated region and response to antidepressants in the whole sample. Negative decadic logarithm of the uncorrected probability of false positive (p values) is plotted against chromosomal location of genotyped (full circles) and imputed (empty circles) SNP markers. P-values smaller than 5x10-6 (suggestive significant) are in blue. The graph covers 100kbp upstream and downstream from the strongest associated genotyped marker (rs2136093).

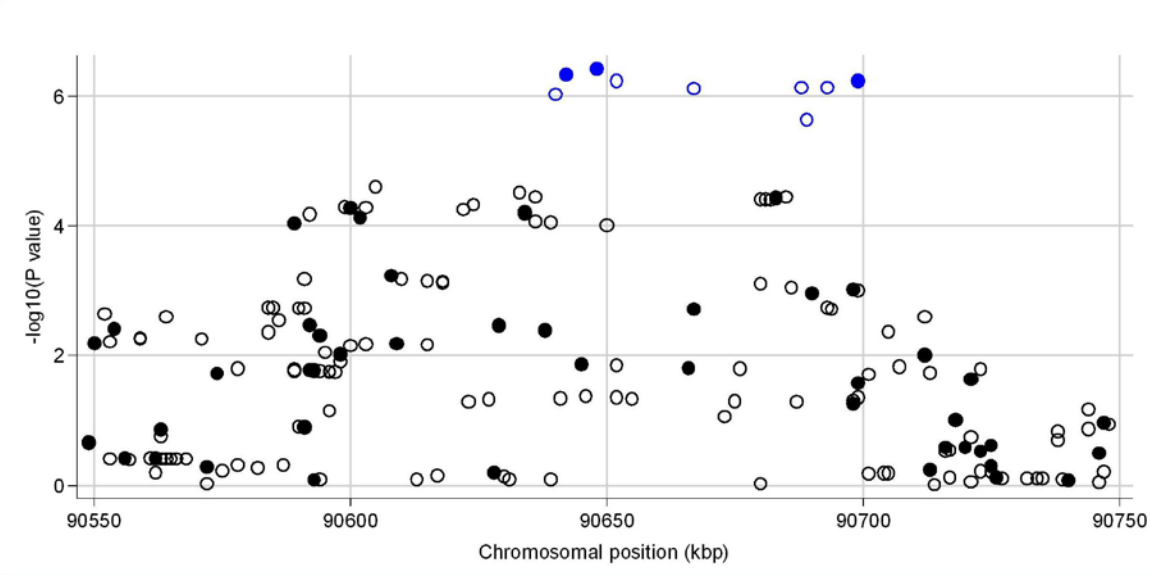

Table S5: Genotyped and imputed SNPs within the associated region on chromosome 1 showing suggestive associations with response to antidepressants ($p < 5 \times 10^{-6}$).
The table includes the marker name (SNP), chromosomal location (Position), and minor allele frequency (MAF). Accuracy is an estimate of the r-squared correlation between estimated and true genotypes. Regression coefficients *b* indicate extra percentage improvement for each minor allele, a negative *b* means that carriers of minor alleles had worse outcome.

SNP	Position	MAF	Accuracy	*b*	p	Imputed
rs10218464	90639568	0.33	0.98	-8.00	9.47E-07	Yes
rs6701608	90641816	0.31	1.00	-8.24	4.66E-07	No
rs2136093	90648480	0.31	1.00	-8.29	3.82E-07	No
rs1472887	90652192	0.31	1.00	-8.17	5.85E-07	Yes
rs7522605	90667128	0.31	1.00	-8.10	7.72E-07	Yes
rs1027854	90688216	0.31	1.00	-8.12	7.55E-07	Yes
rs1337576	90688656	0.29	1.00	-7.95	2.35E-06	Yes
rs506368	90692608	0.31	1.00	-8.13	7.49E-07	Yes
rs2136094	90698568	0.26	1.00	-8.83	5.86E-07	No

Figure S6: Chromosome 10 associated region and response to antidepressants in the whole sample. Negative decadic logarithm of the uncorrected probability of false positive (p values) is plotted against chromosomal location of genotyped (full circles) and imputed (empty circles) SNP markers. P-values smaller than 5x10-6 (suggestive significant) are in blue. The graph covers 200kbp upstream and downstream from the three associated genotyped markers.

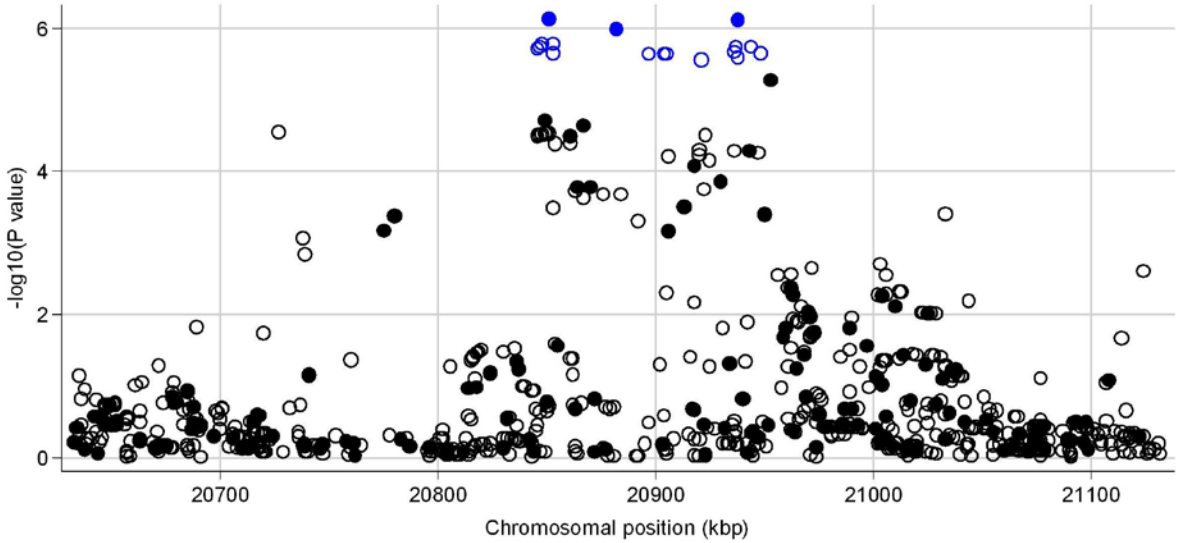

Table S4: Genotyped and imputed SNPs within the associated region on chromosome 10 showing suggestive associations with response to antidepressants ($p < 5 \times 10^{-6}$). The table includes the marker name (SNP), chromosomal location (Position), and minor allele frequency (MAF). Accuracy is an estimate of the r-squared correlation between estimated and true genotypes. Regression coefficients *b* indicate extra percentage improvement for each minor allele, a negative *b* means that carriers of minor alleles had worse outcome.

SNP	Position	MAF	Accuracy	*b*	p	Imputed
rs16920587	20846406	0.06	0.97	-15.48	1.98E-06	Yes
rs16920589	20846536	0.06	0.98	-15.46	1.85E-06	Yes
rs7910350	20848396	0.06	0.99	-15.42	1.68E-06	Yes
rs16920624	20850532	0.07	1.00	-16.04	7.37E-07	No
rs1339653	20853068	0.06	0.99	-15.46	1.65E-06	Yes
rs1339654	20853462	0.06	1.00	-15.25	2.26E-06	Yes
rs7081156	20882036	0.06	1.00	-15.90	1.01E-06	No
rs11595329	20897224	0.06	1.00	-15.22	2.33E-06	Yes
rs12247444	20904498	0.06	1.00	-15.22	2.33E-06	Yes
rs11819199	20905164	0.06	1.00	-15.22	2.33E-06	Yes
rs11594336	20920502	0.07	0.99	-15.04	2.76E-06	Yes
rs16920700	20935812	0.07	1.00	-15.06	2.14E-06	Yes
rs11598280	20937260	0.07	1.00	-15.11	1.85E-06	Yes
rs11598341	20937548	0.07	0.99	-14.87	2.51E-06	Yes
rs11598854	20937908	0.07	1.00	-15.84	7.67E-07	No
rs11593835	20944160	0.07	1.00	-15.11	1.85E-06	Yes
rs2359537	20947672	0.07	1.00	-15.03	2.27E-06	Yes

Figure S7: Interleukin 11 gene and the adjacent chromosome 19 region and response to escitalopram. Negative decadic logarithm of the uncorrected probability of false positive (p values) is plotted against chromosomal location of genotyped (full circles) and imputed (empty circles) SNP markers. P-values smaller than 5x10-6 (suggestive significant) are in blue. The graph covers 100kbp upstream and downstream from the strongest associated genotyped marker (rs1126757).

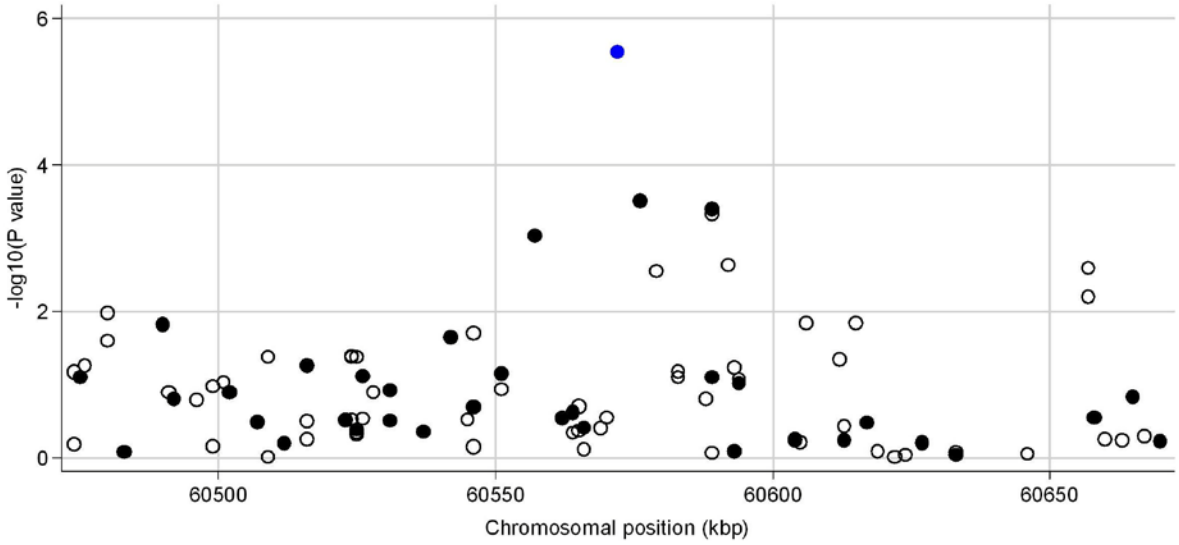

Table S5: Genotyped and imputed SNPs within the IL11 gene region on chromosome 19showing suggestive associations with response to antidepressants ($p < 5 \times 10^{-6}$). The table includes the marker name (SNP), chromosomal location (Position), and minor allele frequency (MAF). Accuracy is an estimate of the r-squared correlation between estimated and true genotypes. Regression coefficients *b* indicate extra percentage improvement for each minor allele, a negative *b* means that carriers of minor alleles had worse outcome.

Snp	position	maf	rsqr1	*b*	p	imputed
rs1126757	60571684	0.48	1.00	10.39	2.83E-06	No

No imputed SNP reached $p < 5 \times 10^{-6}$

Figure S9: Uronyl sulfotransferase (*UST*) gene and the adjacent chromosome 6 region and response to nortriptyline. Negative decadic logarithm of the uncorrected probability of false positive (p values) is plotted against chromosomal location of genotyped (full circles) and imputed (empty circles) SNP markers. P-values smaller than $5x10^{-6}$ (suggestive significant) are in blue. P-values smaller than $5x10^{-8}$ (genome-wide significant) are in red. The graph covers 100kbp upstream and downstream from the strongest associated genotyped marker (rs2500535).

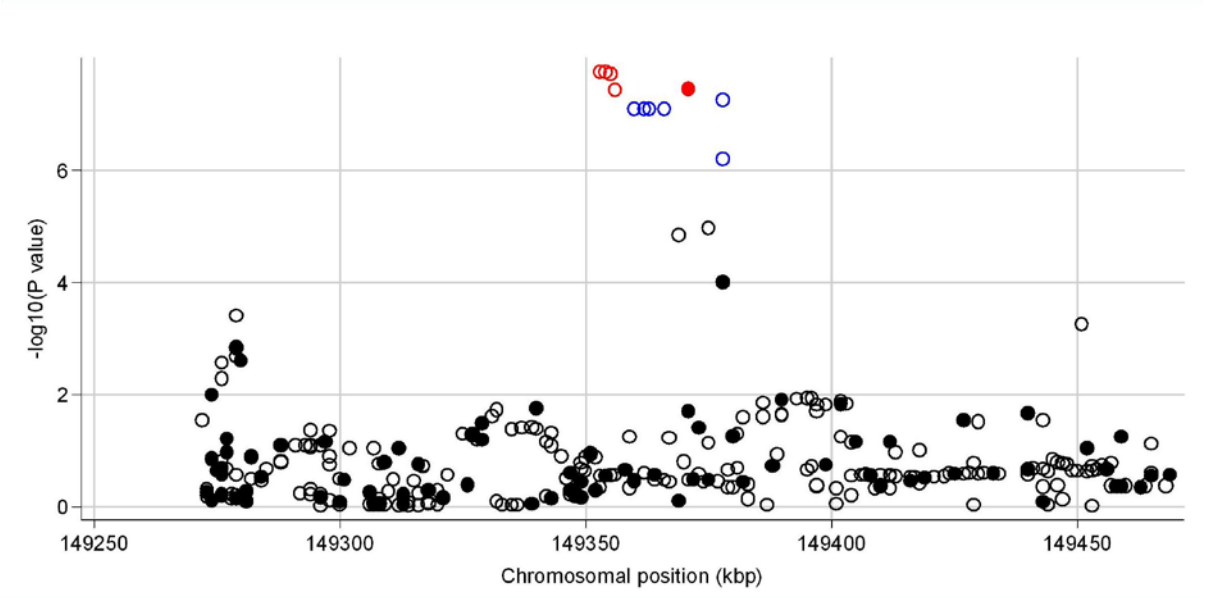

Table S6: Genotyped and imputed SNPs within the UST gene region on chromosome 6 showing suggestive or genome-wide significant associations with response to nortriptyline ($p < 5 \times 10^{-6}$). The table includes the marker name (SNP), chromosomal location (Position), and minor allele frequency (MAF). Accuracy is an estimate of the r-squared correlation between estimated and true genotypes. Regression coefficients *b* indicate extra percentage improvement for each minor allele, a negative *b* means that carriers of minor alleles had worse outcome.

SNP	Position	MAF	Accuracy	*b*	p	Imputed
rs2486404	149353296	0.05	0.90	-30.68	1.73E-08	Yes
rs2500525	149354032	0.05	0.90	-30.65	1.74E-08	Yes
rs2486403	149354848	0.05	0.90	-30.37	1.88E-08	Yes
rs2486402	149355984	0.05	0.93	-28.48	3.70E-08	Yes
rs2486398	149360496	0.06	1.00	-26.63	7.91E-08	Yes
rs2500530	149361984	0.06	1.00	-26.62	7.95E-08	Yes
rs2486397	149362368	0.06	1.00	-26.62	7.97E-08	Yes
rs2486396	149363440	0.06	1.00	-26.61	7.99E-08	Yes
rs2486390	149365888	0.06	1.00	-26.60	8.05E-08	Yes
rs2500535	149370960	0.06	1.00	-27.04	3.56E-08	No
rs2486416	149377696	0.06	0.99	-26.83	5.59E-08	Yes
rs2486415	149377872	0.04	1.00	-26.66	6.25E-07	Yes

Figure S10: Genotyped and imputed SNPs within the RGL gene and adjacent region on chromosome 1 and response to nortriptyline. Negative decadic logarithm of the uncorrected probability of false positive (p values) is plotted against chromosomal location of genotyped (full circles) and imputed (empty circles) SNP markers. P-values smaller than 5x10-6 (suggestive significant) are in blue. The graph covers 100kbp upstream and downstream from the strongest associated genotyped marker (rs4651156).

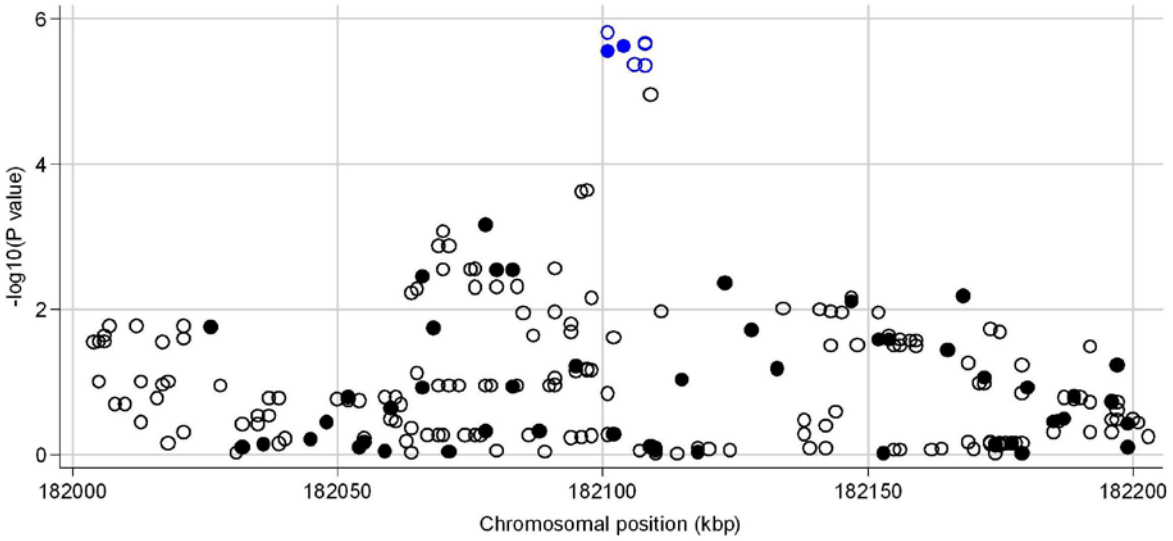

Table S7: Genotyped and imputed SNPs within the RGL gene and adjacent region on chromosome 1 showing suggestive associations with response to nortriptyline ($p < 5 \times 10^{-6}$). The table includes the marker name (SNP), chromosomal location (Position), and minor allele frequency (MAF). Accuracy is an estimate of the r-squared correlation between estimated and true genotypes. Regression coefficients *b* indicate extra percentage improvement for each minor allele, a negative *b* means that carriers of minor alleles had worse outcome.

SNP	Position	MAF	Accuracy	*b*	p	Imputed
rs9425322	182100688	0.17	1.00	-14.97	2.76E-06	No
rs9425323	182100896	0.18	0.99	-15.23	1.53E-06	Yes
rs4651156	182103648	0.29	1.00	-12.63	2.39E-06	No
rs9425326	182105632	0.29	0.96	-12.54	4.22E-06	Yes
rs9425616	182107728	0.17	0.92	-15.52	2.21E-06	Yes
rs9425617	182108400	0.17	0.86	-16.24	2.14E-06	Yes
rs10797917	182108416	0.28	0.85	-13.31	4.34E-06	Yes

Figure S11: Genotyped and imputed SNPs within the *SLC27A1* gene and adjacent region on chromosome 19: genotype-drug interaction. Negative decadic logarithm of the uncorrected probability of false positive (p values) is plotted against chromosomal location of genotyped (full circles) and imputed (empty circles) SNP markers. P-values smaller than 5x10-6 (suggestive significant) are in blue. The graph covers 100kbp upstream and downstream from the strongest associated genotyped marker (rs11666579).

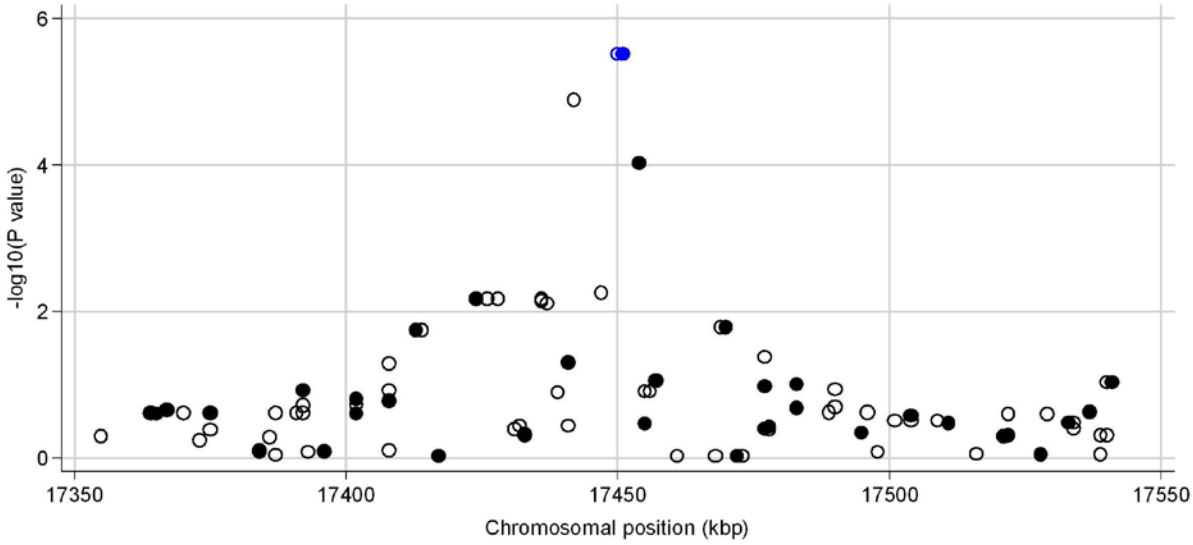

Table S8: Genotyped and imputed SNPs within the *SLC27A1* gene and adjacent region on chromosome 19 showing suggestive genotype-drug interactions ($p < 5 \times 10^{-6}$). The table includes the marker name (SNP), chromosomal location (Position), and minor allele frequency (MAF). Accuracy is an estimate of the r-squared correlation between estimated and true genotypes. Regression coefficients *b* indicate extra percentage improvement for each minor allele with nortriptyline as opposed to escitalopram.

SNP	Position	MAF	Accuracy	*b*	p	Imputed
rs8109783	17449762	0.48	0.99	14.38	3.06E-06	Yes
rs11666579	17451280	0.48	1.00	14.38	3.05E-06	No

Figure S12: Genotyped and imputed SNPs within the identified region on chromosome 18: genotype-drug interaction. Negative decadic logarithm of the uncorrected probability of false positive (p values) is plotted against chromosomal location of genotyped (full circles) and imputed (empty circles) SNP markers. P-values smaller than 5x10-6 (suggestive significant) are in blue. The graph covers 100kbp upstream and downstream from the strongest associated genotyped marker (rs1013696).

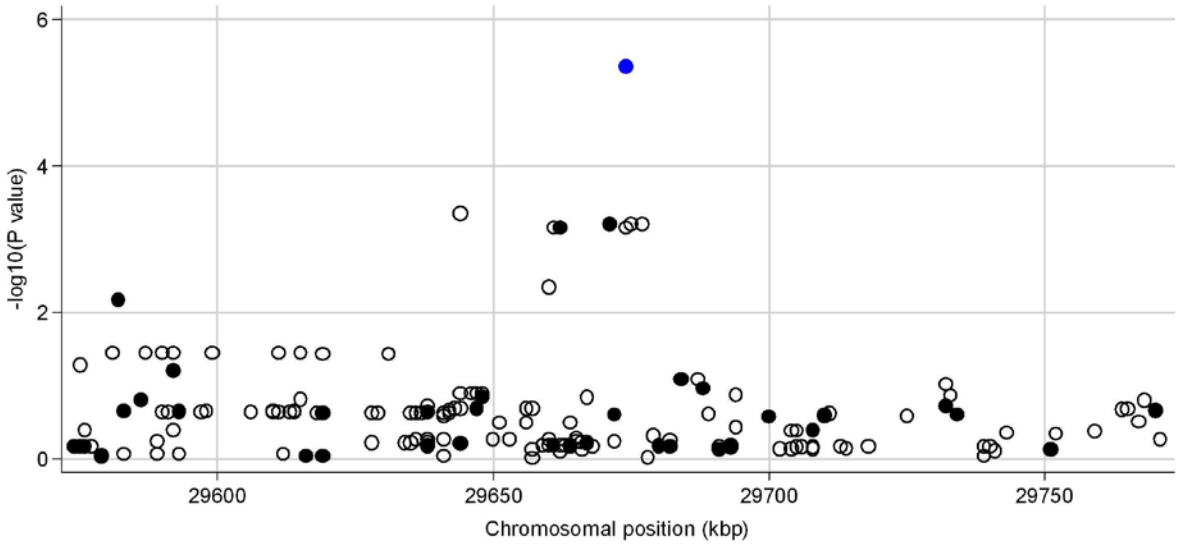

Table S9: Genotyped and imputed SNPs within the identified region on chromosome 18 showing suggestive genotype-drug interactions ($p < 5 \times 10^{-6}$). The table includes the marker name (SNP), chromosomal location (Position), and minor allele frequency (MAF). Accuracy is an estimate of the r-squared correlation between estimated and true genotypes. Regression coefficients *b* indicate extra percentage improvement for each minor allele with nortriptyline as opposed to escitalopram.

SNP	Position	MAF	Accuracy	*b*	p	Imputed
rs1013696	29674008	0.22	1.00	-17.84	4.33E-06	No

No imputed SNP reached $p < 5 \times 10^{-6}$

References

1. Li Y, GR A: Rapid Haplotype Reconstruction and Missing Genotype Inference. Am J Hum Genet 2006; S792290

2. Li Y, Willer CJ, Cristen J, Ding J, Scheet P, Abecasis GR: Markov Model for Rapid Haplotyping and Genotype Imputation in Genome Wide Studies. (unpublished manuscript) 2006;