Vulnerability of *DHCR7^{+/-}* mutation carriers to aripiprazole and trazodone exposure

^a Zeljka Korade, ^bThiago C. Genaro-Mattos, ^bKeri A. Tallman, ^bWei Liu, ^cKrassimira A. Garbett, ^dKatalin Koczok, ^dIstvan Balogh, ^eKaroly Mirnics, and ^bNed A. Porter*



Supplemental Figure S1. Aripiprazole (ARI) or trazodone (TRZ) alter residual cholesterol biosynthesis. Six *DHCR7*-HET, four CTR HF and two fibroblasts having a *DHCR7* variation of unknown significance (VUS) ere cultured in the presence of 500 nM 3¹³C-Lan and different concentrations of ARI or TRZ. A and B graphs show the 3¹³C-derived 7-DHC and 3¹³C-derived cholesterol where 7-DHC is normalized to cholesterol for the six *DHCR7*-HET, the four CTR and the individual data for the VUS#1 and VUS#2 cells. The genotyping for each cell is presented in Figure 2 in the manuscript. Stars above bars show p values <0.01 and represents the difference between control and heterozygous samples.

				/-L	HC level	_		
		HETEROZYGO	US				CONTR	OL
Sample	DMSO	ARI 10	ARI 25	ARI 50	Sample	DMSO	ARI 10	ARI 25
verage	284.5	1961.7	3679.9	5049.4	average	81.8	633.3	1549.9
dev	155.1	451.5	444.0	672.9	stdev	38.3	253.4	530.0
SEM	36.6	106.4	104.6	158.6	SEM	11.0	73.2	153.0
							CONT	
		HETEROZYGO				-	CONTR	
Sample	DMSO	1RZ 10	1RZ 25	1RZ 50	Sample	DMSO	TRZ 10	1RZ 25
average	380.8	1069.6	2370.3	4194.1	average	179.1	328.3	673.4
stdev	204.4	557.1	586.7	684.3	stdev	61.3	81.7	143.7
SEM	48.2	131.3	138.3	161.3	SEM	17.7	23.6	41.5
				Chole	esterol level			
		HETEROZYGO	US				CONTR	OL
Sample	DMSO	ARI 10	ARI 25	ARI 50	Sample	DMSO	ARI 10	ARI 25
average	18356.8	16086.7	14307.2	13385.3	average	23669.0	20891.9	20077.6
stdev	2154.9	2408.5	1773.3	2226.0	stdev	6151.5	4085.1	3483.7
SEM	507.9	567.7	418.0	524.7	SEM	1775.8	1179.3	1005.7
		HETEROZYGO	US				CONTR	
Sample	DMSO	TRZ 10	TRZ 25	TRZ 50	Sample	DMSO	TRZ 10	TRZ 25
average	18983.1	17929.5	16165.0	14695.3	average	22457.6	21645.2	20198.5
stdev	2192.6	3008.3	2599.6	1928.3	stdev	4803.5	3935.9	3161.9
SEM	516.8	709.1	612.7	454.5	SEM	1386.6	1136.2	912.8
			110	8-D	HC level	_		
Sample	DMSO	HETEROZYGO	ARI 25	ARI 50	Sample	DMSO	CONTR ARI 10	ARI 25
average	350 5	500 10	689.0	8365	average	246.6	A11 5	776 7
stdev	149.8	197.8	244.4	321 4	stday	177 2	235.5	351 /
SEM	25.2	152.0 45.1	57.6	75.8	SFM	51 2	68.0	101 4
		HETEROZYGO	US				CONTR	OL
Sample	DMSO	TRZ 10	TRZ 25	TRZ 50	Sample	DMSO	TRZ 10	TRZ 25
average	433.0	631.0	879.1	986.5	average	374.1	630.3	807.9
-		189.6	300.8	277.5	stdev	142.7	241.0	294.1
stdev	171.7		70.9	65.4	SEM	41.2	69.6	84.9
stdev SEM	40.5	44./						
stdev SEM	40.5	44.7		Desm	osterol level			
stdev SEM	40.5	HETEROZYGO	US	Desm	osterol level		CONTR	OL
stdev SEM Sample	171.7 40.5 DMSO	HETEROZYGO ARI 10	US ARI 25	Desm	osterol level	DMSO	CONTR ARI 10	OL ARI 25
stdev SEM Sample average	171.7 40.5 DMSO 284.9	HETEROZYGO ARI 10 228.2	US ARI 25 224.3	Desm ARI 50 233.7	osterol level Sample average	DMSO 441.4	CONTR ARI 10 315.3	OL ARI 25 245.3
stdev SEM Sample average stdev	171.7 40.5 DMSO 284.9 125.0	HETEROZYGO ARI 10 228.2 171.1	US ARI 25 224.3 158.2	Desm ARI 50 233.7 169.5	osterol level Sample average stdev	DMSO 441.4 185.9	CONTR ARI 10 315.3 187.6	OL ARI 25 245.3 67.0
stdev SEM Sample average stdev SEM	171.7 40.5 DMSO 284.9 125.0 29.5	HETEROZYGO ARI 10 228.2 171.1 40.3	US ARI 25 224.3 158.2 37.3	Desm ARI 50 233.7 169.5 40.0	osterol level Sample average stdev SEM	DMSO 441.4 185.9 53.7	CONTR ARI 10 315.3 187.6 54.1	OL ARI 25 245.3 67.0 19.3
stdev SEM Sample average stdev SEM	171.7 40.5 DMSO 284.9 125.0 29.5	HETEROZYGO ARI 10 228.2 171.1 40.3	US ARI 25 224.3 158.2 37.3	Desm ARI 50 233.7 169.5 40.0	osterol level Sample average stdev SEM	DMSO 441.4 185.9 53.7	CONTR ARI 10 315.3 187.6 54.1	ARI 25 245.3 67.0 19.3
stdev SEM Sample average stdev SEM	1/1.7 40.5 DMSO 284.9 125.0 29.5	HETEROZYGO ARI 10 228.2 171.1 40.3 HETEROZYGO TRZ 10	US ARI 25 224.3 158.2 37.3 US TRZ 25	Desm ARI 50 233.7 169.5 40.0	osterol level Sample average stdev SEM	DMSO 441.4 185.9 53.7	CONTR ARI 10 315.3 187.6 54.1	OL ARI 25 245.3 67.0 19.3 OL TRZ 25
stdev SEM Sample average stdev SEM Sample average	1/1.7 40.5 DMSO 284.9 125.0 29.5	HETEROZYGO ARI 10 228.2 171.1 40.3 HETEROZYGO TRZ 10 261.8	US ARI 25 224.3 158.2 37.3 US TRZ 25 237.4	Desm ARI 50 233.7 169.5 40.0 TRZ 50 234.9	osterol level Sample average stdev SEM	DMSO 441.4 185.9 53.7 DMSO 437.2	CONTR ARI 10 315.3 187.6 54.1 TRZ 10 334 1	OL ARI 25 245.3 67.0 19.3 OL TRZ 25 276 °
stdev SEM Sample average stdev SEM Sample average	1/1.7 40.5 DMSO 284.9 125.0 29.5 DMSO 29.1 1835	HETEROZYGO ARI 10 228.2 171.1 40.3 HETEROZYGO TRZ 10 261.8 19.2 1	US ARI 25 224.3 158.2 37.3 US TRZ 25 237.4 199.9	Desm ARI 50 233.7 169.5 40.0 TRZ 50 234.9 182.9	osterol level Sample average stdev SEM Sample average	DMSO 441.4 185.9 53.7 DMSO 437.3 112.9	CONTR ARI 10 315.3 187.6 54.1 TRZ 10 334.1 101.0	OL ARI 25 245.3 67.0 19.3 OL TRZ 25 276.8 10.3 0
stdev SEM Sample average stdev SEM Sample average stdev SEM	1/1.7 40.5 DMSO 284.9 125.0 29.5 DMSO 292.1 182.5 43.0	HETEROZYGO ARI 10 228.2 171.1 40.3 HETEROZYGO TRZ 10 261.8 193.1 45.5	US ARI 25 224.3 158.2 37.3 US TRZ 25 237.4 198.8 46.9	Desm ARI 50 233.7 169.5 40.0 TRZ 50 234.9 182.8 43.1	osterol level Sample average stdev SEM	DMSO 441.4 185.9 53.7 DMSO 437.3 112.8 32.6	CONTR ARI 10 315.3 187.6 54.1 TRZ 10 334.1 101.0 29.2	COL ARI 25 245.3 67.0 19.3 COL TRZ 25 276.8 103.0 29
stdev SEM Sample average stdev SEM Sample average stdev SEM	1/1./ 40.5 DMSO 284.9 125.0 29.5 DMSO 29.2 125.0 29.5 DMSO 29.2 125.0 29.5 29.1 182.5 43.0	HETEROZYGO ARI 10 228.2 171.1 40.3 HETEROZYGO TRZ 10 261.8 193.1 45.5	US ARI 25 224.3 158.2 37.3 TRZ 25 237.4 198.8 46.9	Desm ARI 50 233.7 169.5 40.0 7RZ 50 234.9 182.8 43.1	osterol level Sample average stdev SEM Sample average stdev SEM	DMSO 441.4 185.9 53.7 DMSO 437.3 112.8 32.6	CONTR ARI 10 315.3 187.6 54.1 TRZ 10 334.1 101.0 29.2	OL ARI 25 245.3 67.0 19.3 COL TRZ 25 276.8 103.0 29.7
stdev SEM Sample average stdev SEM Sample average stdev SEM	171.7 40.5 DMSO 284.9 125.0 29.5 DMSO 292.1 182.5 43.0	HETEROZYGO ARI 10 228.2 171.1 40.3 HETEROZYGO TRZ 10 261.8 193.1 45.5	US ARI 25 224.3 158.2 37.3 US TRZ 25 237.4 198.8 46.9	Desm <i>ARI 50</i> 233.7 169.5 40.0 <i>TRZ 50</i> 234.9 182.8 43.1 Lano	osterol level Sample average stdev SEM Sample average stdev SEM sterol level	DMSO 441.4 185.9 53.7 DMSO 437.3 112.8 32.6	CONTR ARI 10 315.3 187.6 54.1 TRZ 10 334.1 101.0 29.2	OL ARI 25 245.3 67.0 19.3 OL TRZ 25 276.8 103.0 29.7
stdev SEM Sample average stdev SEM Sample average stdev SEM	171.7 40.5 DMSO 284.9 125.0 29.5 DMSO 292.1 182.5 43.0	HETEROZYGO ARI 10 228.2 171.1 40.3 HETEROZYGO 7RZ 10 261.8 193.1 45.5 HETEROZYGO	US ARI 25 224.3 158.2 37.3 US TRZ 25 237.4 198.8 46.9 US	Desm <i>ARI 50</i> 233.7 169.5 40.0 <i>TRZ 50</i> 234.9 182.8 43.1 Lano	osterol level Sample average SEM Sample average stdev SEM sterol level	DMSO 441.4 185.9 53.7 DMSO 437.3 112.8 32.6	CONTR ARI 10 315.3 187.6 54.1 TRZ 10 334.1 101.0 29.2 CONTR	COL ARI 25 245.3 67.0 19.3 COL TRZ 25 276.8 103.0 29.7 COL
stdev SEM Sample average stdev SEM Sample average stdev SEM Sample	171.7 40.5 DMSO 284.9 125.0 29.5 DMSO 292.1 182.5 43.0	HETEROZYGO ARI 10 228.2 171.1 40.3 HETEROZYGO 7RZ 10 261.8 193.1 45.5 HETEROZYGO ARI 10	US 224.3 158.2 37.3 TRZ 25 237.4 198.8 46.9 US ARI 25	Desm ARI 50 233.7 169.5 40.0 7RZ 50 234.9 182.8 43.1 Lanco ARI 50	osterol level Sample stdev SEM Sample average stdev SEM sterol level Sample	DMSO 441.4 185.9 53.7 DMSO 437.3 112.8 32.6	CONTR ARI 10 315.3 187.6 54.1 7RZ 10 334.1 101.0 29.2 CONTR ARI 10	COL ARI 25 245.3 67.0 19.3 COL TRZ 25 276.8 103.0 29.7 COL ARI 25
stdev SEM Sample average stdev SEM Sample average SEM SEM	171.7 40.5 DMSO 284.9 125.0 29.5 DMSO 292.1 182.5 43.0 DMSO 56.2	HETEROZYGO ARI 10 228.2 171.1 40.3 HETEROZYGO TRZ 10 261.8 193.1 45.5 HETEROZYGO ARI 10 40.3	US ARI 25 224.3 158.2 37.3 US TRZ 25 237.4 198.8 46.9 US ARI 25 48.1	Desm ARI 50 233.7 169.5 40.0 7RZ 50 234.9 182.8 43.1 Lano ARI 50 30.4	osterol level Sample average stdev SEM Sample average stdev SEM sterol level Sample average	DMSO 441.4 185.9 53.7 DMSO 437.3 112.8 32.6 DMSO DMSO 63.4	CONTR ARI 10 315.3 187.6 54.1 7RZ 10 334.1 101.0 29.2 CONTR ARI 10 54.9	COL 7RZ 25 245.3 67.2 19.3 07.2 7RZ 25 276.8 103.0 29.7 COL ARI 25 56.2
stdev SEM Sample average stdev SEM Sample average stdev SEM Sample average stdev	1/1./ 40.5 DMSO 284.9 125.0 29.5 DMSO 292.1 182.5 43.0 DMSO 56.2 32.5 43.0	44.7 HETEROZYGO ARI 10 228.2 171.1 40.3 HETEROZYGO TRZ 10 261.8 193.1 45.5 HETEROZYGO ARI 10 40.3 28.5	US ARI 25 224.3 158.2 37.3 TRZ 25 237.4 198.8 46.9 US ARI 25 48.1 28.9 48.1 28.9 48.1 28.9 48.1 28.9 48.1 28.9 48.1 48.9 48.1 48.2 48.1 48.2 48.1 48.2 48.1 48.2 48.1 48.2 48.1 48.2 48.1 48.2	Desm ARI 50 233.7 169.5 40.0 17RZ 50 234.9 182.8 43.1 ARI 50 30.4 18.8 0 30.4 18.8 19.8	osterol level Sample average stdev SEM Sample average stdev SEM sterol level Sample average stdev	DMSO 441.4 185.9 53.7 DMSO 437.3 112.8 32.6 DMSO 63.4 51.7	CONTR ARI 10 315.3 187.6 54.1 TRZ 10 334.1 101.0 29.2 CONTR ARI 10 54.9 50.3 107.6 54.9 50.3 107.6 54.9 50.3 107.6 54.9 50.3 107.6 54.9 50.3 107.6 54.9 50.3 107.6 54.9 50.3 107.6 54.9 50.3 107.6 54.9 50.3 107.6 54.9 50.3 107.6 54.9 50.3 107.6 54.9 50.3 107.6 54.9 5	OL ARI 25 245.3 67.0 19.3 OL TRZ 25 276.8 103.0 29.7 OL ARI 25 56.2 44.1 42.5 20.
stdev SEM Sample average stdev SEM Sample average stdev SEM Sample average stdev SEM	171.7 40.5 DMSO 284.9 125.0 29.5 DMSO 29.5 A3.0 DMSO 56.2 32.5 7.7	44.7 HETEROZYGO ARI 10 228.2 171.1 40.3 HETEROZYGO TRZ 10 261.8 193.1 45.5 HETEROZYGO ARI 10 40.3 261.8 193.1 45.5 HETEROZYGO ARI 10 40.3 28.5 6.7	US ARI 25 224.3 158.2 37.3 US TRZ 25 237.4 198.8 46.9 US ARI 25 48.1 28.9 6.8	Desm ARI 50 233.7 169.5 40.0 7RZ 50 234.9 182.8 43.1 Lanco ARI 50 30.4 18.8 4.4	osterol level Sample stdev SEM Sample average stdev SEM sterol level Sample average stdev SEM	DMSO 441.4 185.9 53.7 DMSO 437.3 112.8 32.6 DMSO 63.4 51.7 14.9	CONTR ARI 10 315.3 187.6 54.1 TRZ 10 334.1 101.0 29.2 CONTR ARI 10 54.9 50.3 14.5	OL ARI 25 245.3 67.0 19.3 OL TRZ 25 276.8 103.0 29.7 OL ARI 25 56.2 44.1 12.7
stdev SEM Sample average stdev SEM Sample average stdev SEM Sample average stdev SEM	171.7 40.5 DMSO 284.9 125.0 29.5 DMSO 292.1 182.5 43.0 DMSO 56.2 32.5 7.7	HETEROZYGO ARI 10 228.2 171.1 40.3 HETEROZYGO 7RZ 10 261.8 193.1 45.5 HETEROZYGO ARI 10 40.3 28.5 6.7	US 224.3 158.2 37.3 TRZ 25 237.4 198.8 46.9 US ARI 25 48.1 28.9 6.8	Desm ARI 50 233.7 169.5 40.0 40.0 TRZ 50 234.9 182.8 43.1 Lanco ARI 50 30.4 18.8 4.4	osterol level Sample average stdev SEM Sample average stdev SEM sterol level Sample average stdev SEM	DMSO 441.4 185.9 53.7 DMSO 437.3 112.8 32.6 DMSO 63.4 51.7 14.9	CONTR ARI 10 315.3 187.6 54.1 TRZ 10 334.1 101.0 29.2 CONTR ARI 10 54.9 50.3 14.5	OL ARI 25 245.3 67.2 19.3 07.2 276.8 103.0 29.7 COL ARI 25 56.2 56.2 44.1 12.7
stdev SEM Sample average stdev SEM Sample average stdev SEM Sample average stdev SEM	171.7 40.5 DMSO 284.9 125.0 29.5 DMSO 29.5 DMSO 29.1 182.5 43.0 DMSO 56.2 32.5 7.7 DMCC	HETEROZYGO ARI 10 228.2 171.1 40.3 HETEROZYGO 7RZ 10 261.8 193.1 45.5 HETEROZYGO ARI 10 40.3 28.5 6.7 HETEROZYGO TRZ 10	US ARI 25 224.3 158.2 37.3 TRZ 25 237.4 198.8 46.9 US ARI 25 48.1 28.9 6.8 US	Desm ARI 50 233.7 169.5 40.0 7RZ 50 234.9 182.8 43.1 Lano ARI 50 30.4 18.8 4.4	osterol level Sample average stdev SEM Sample average stdev SEM sterol level Sample average stdev SEM	DMSO 441.4 185.9 53.7 DMSO 437.3 112.8 32.6 DMSO 63.4 51.7 14.9	CONTR ARI 10 315.3 187.6 54.1 TRZ 10 334.1 101.0 29.2 CONTR ARI 10 54.9 50.3 14.5 CONTR	OL ARI 25 245.3 67.0 19.3 OL TRZ 25 276.8 103.0 29.7 OL ARI 25 56.2 44.1 12.7 OL
stdev SEM Sample average stdev SEM Sample average stdev SEM Sample average stdev SEM	1/1.7 40.5 DMSO 284.9 125.0 29.5 DMSO 292.1 182.5 43.0 DMSO 56.2 32.5 7.7	44.7 HETEROZYGO ARI 10 228.2 171.1 40.3 HETEROZYGO TRZ 10 261.8 193.1 45.5 HETEROZYGO ARI 10 40.3 28.5 6.7 HETEROZYGO TRZ 10 C1.2	US ARI 25 224.3 158.2 37.3 US TRZ 25 237.4 198.8 46.9 US ARI 25 48.1 28.9 6.8 US TRZ 25 (S 29.2 199.6	Desm ARI 50 233.7 169.5 40.0 7RZ 50 234.9 182.8 43.1 Kanon ARI 50 30.4 18.8 4.4 7RZ 50 30.4 18.8 4.4	osterol level Sample average stdev SEM Sample average stdev SEM Semple average stdev SEM	DMSO 441.4 185.9 53.7 DMSO 437.3 112.8 32.6 DMSO 63.4 51.7 14.9 DMSO	CONTR ARI 10 315.3 187.6 54.1 TRZ 10 334.1 101.0 29.2 CONTR ARI 10 54.9 50.3 14.5 CONTR TRZ 10 CONTR TRZ 10 CONTR TRZ 10 CONTR C	OL ARI 25 245.3 67.0 19.3 60L TRZ 25 276.8 103.0 29.7 COL ARI 25 56.2 44.1 12.7 COL TRZ 25 56.2 44.1 12.7 COL TRZ 25 56.2 44.1 12.7 COL
stdev SEM Sample average stdev SEM Sample average stdev SEM Sample average stdev SEM	1/1.7 40.5 DMSO 284.9 125.0 29.5 DMSO 292.1 182.5 43.0 DMSO 56.2 32.5 7.7 DMSO 56.2 32.5 7.7	44.7 HETEROZYGO ARI 10 228.2 171.1 40.3 HETEROZYGO TRZ 10 261.8 193.1 45.5 HETEROZYGO ARI 10 40.3 28.5 6.7 HETEROZYGO TRZ 10 61.1 24.6	US 224.3 158.2 37.3 TRZ 25 237.4 198.8 46.9 US ARI 25 48.1 28.9 6.8 US TRZ 25 6.8 US	Desm ARI 50 233.7 169.5 40.0 7RZ 50 234.9 182.8 43.1 Lance ARI 50 30.4 18.8 4.4 7RZ 50 55.4 76.6	osterol level Sample average SEM Sample average stdev SEM Sterol level Sample average stdev SEM	DMSO 441.4 185.9 53.7 DMSO 437.3 112.8 32.6 DMSO 63.4 51.7 14.9 DMSO 69.3 20.6	CONTF ARI 10 315.3 187.6 54.1 7RZ 10 334.1 101.0 29.2 CONTF ARI 10 54.9 50.3 14.5 CONTF TRZ 10 67.4 22 C	OL ARI 25 245.3 67.0 19.3 OL TRZ 25 276.8 103.0 29.7 OL ARI 25 56.2 44.1 12.7 OL TRZ 25 56.2 44.1 12.7 OL

Supplemental Table S1A (Companion to Figure 4). Sterol levels, reported as ng/million cells.

Supplemental Table S1B. (Companion to Figure 4). Significance of sterol levels differences.

ARI 10 I.79E-16 1.87E-07 I.87E-07 5.43E-10 I.25E-05 4.57E-05 9.48E-05 (significance ARI 10 2.35E-03 5.29E-03 2.06E-01 4.00E-04 4.00E-04 4.00E-04 6.55E-01 6.58E-03 9.48E-03	ARI 25 2.41E-26 2.66E-09 1.76E-12 TRZ 25 2.32E-10 1.60E-10 evalues) ARI 25 5.40E-07 9.23E-02 1.87E-06 1.27E-03 1.87E-01 6.81E-04	ARI 50 1.07E-2: 2.90E-1: 1.02E-0: TR2 50 4.29E-2: 8.50E-1: 6.55E-1: ARI 50 7.85E-0: 2.61E-0: 7.85E-0: 4.33E-0: 1.91E-0: 2.19E-0:
1.79E-16 1.87E-07 5.43E-10 7.15E-05 4.57E-05 9.48E-05 (significance 4.00E-04 7.2.06E-01 4.00E-04 7.2.06E-01 6.68E-03 9.48E-05 0.55E-01 6.68E-03 0.55E-01 0.55E-0	2.41E-26 2.66E-09 1.76E-12 TRZ 25 2.69E-15 2.23E-10 1.60E-10 1.60E-10 XRI 25 5.40E-07 9.23E-02 1.87E-06 TRZ 25 1.27E-03 1.87E-01 6.81E-04	1.07E-2 2.90E-1 1.02E-0 TRZ 50 4.29E-2 8.50E-1 6.55E-1 7.85E-0 7.85E-0 5.26E-0 5.26E-0 5.26E-0 7.85E-0 5.26E-0 1.91E-0 2.19E-0
1.87E-07 5.43E-10 7.15E-05 4.57E-05 9.48E-05 (significance <i>ARI 10</i> 5.29E-03 2.06E-01 4.00E-04 7.210 2.38E-01 6.65E-03 9.668E-03 9.668E-03	2.66E-09 1.76E-12 TRZ 25 2.69E-15 2.23E-10 1.60E-10 2.23E-10 4.60E-10 2.23E-10 3.40E-07 9.23E-02 1.87E-06 TRZ 25 1.27E-03 1.87E-01 6.81E-04	2.90E-1: 1.02E-0: TR2 50 4.29E-2: 8.50E-1: 6.55E-1: ARI 50 7.85E-0: 2.61E-0: 7.85E-0: 4.33E-0: 1.91E-0: 2.19E-0:
5,43E-10 TRZ 10 2,15E-05 9,48E-05 (significance AR/ 10 5,29E-03 2,06E-01 4,00E-04 4,00E-04 4,00E-04 7RZ 10 2,38E-01 6,68E-03 e,65E-0	1.76E-12 TRZ 25 2.69E-15 2.23E-10 1.60E-10 2.23E-10 1.60E-10 2.23E-10 1.60E-10 2.23E-02 1.87E-06 1.27E-03 1.87E-01 6.81E-04	1.02E-0 TR2 50 4.29E-2; 8.50E-1; 6.55E-1; 6.55E-1; 6.55E-1; 7.85E-0; 2.61E-0; 5.26E-0; TR2 50 4.33E-0; 1.91E-0; 2.19E-0;
TRZ 10 2.15E-05 2.15E-05 4.57E-05 9.48E-05 9.48E-05 (significance v. 4.87E-05) 9.06E-01 4.00E-04 4.00E-04 4.00E-04 4.00E-04 6.55E-01 6.68E-03 gnificance v. 4.8E-03 9.06E-01	Arr 2 25 2.69E-15 2.23E-10 1.60E-10 Arr 25 5.40E-07 9.23E-02 1.87E-06 1.87E-01 6.81E-04	ARI 50 ARI 50 7.85E-0: 2.61E-0. 5.26E-0: 7.85E-0: 7.85E-0: 2.61E-0. 5.26E-0: 7.85E-0: 7.85E-0: 2.61E-0. 7.85E-0: 2.61E-0.
2.15E-05 4.57E-05 9.48E-05 (significance ARI 10 5.29E-03 2.06E-01 4.00E-04 TRZ 10 2.38E-01 6.58E-03 gnificance v.	2.69E-15 2.23E-10 1.60E-10 ARI 25 5.40E-07 9.23E-02 1.87E-06 TRZ 25 1.27E-03 1.87E-01 6.81E-04	4.29E-2: 8.50E-1 6.55E-1 7.85E-0 2.61E-0 7.85E-0 7.95E
4.57E-05 9.48E-05 (significance ARI 10 5.29E-03 2.06E-01 4.00E-04 7RZ 10 2.38E-01 6.68E-03 (significance v.	2.23E-10 1.60E-10 2 values) ARI 25 5.40E-07 9.23E-02 1.87E-06 TRZ 25 1.27E-03 1.87E-01 6.81E-04	8.50E-1- 6.55E-1: 7.85E-0: 2.61E-0: 5.26E-0: 7.85E-0: 2.61E-0: 7.85E-0: 2.61E-0: 7.85E-0: 2.19E-0:
9.48E-05 (significance ARI 10 5.29E-03 2.06E-01 4.00E-04 7RZ 10 2.38E-01 6.55E-01 6.65E-03 8 gnificance v	1.60E-10 ARI 25 5.40E-07 9.23E-02 1.87E-06 TRZ 25 1.27E-03 1.87E-01 6.81E-04	6.55E-1: ARI 50 7.85E-00 2.61E-00 5.26E-00 5.26E-00 7.85E-00 2.19E-00 2.19E-00
(significance ARI 10 5.29E-03 2.06E-01 4.00E-04 7RZ 10 2.38E-01 6.55E-01 6.68E-03 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9	ARI 25 ARI 25 5.40E-07 9.23E-02 1.87E-06 6 TRZ 25 1.27E-03 1.87E-01 6.81E-04	ARI 50 7.85E-02 2.61E-02 5.26E-02 TRZ 50 4.33E-02 1.91E-02 2.19E-02
(significance ARI 10 5.29E-03 2.06E-01 4.00E-04 TRZ 10 2.38E-01 6.55E-01 6.68E-03 6.68E-03	arrial arrial ARI 25 5.40E-07 5.40E-07 9.23E-02 1.87E-06 1.27E-03 1.87E-01 6.81E-04	ARI 50 7.85E-0: 2.61E-0: 5.26E-0: TRZ 50 4.33E-0: 1.91E-0 2.19E-0:
ARI 10 ARI 10 5.29E-03 2.06E-01 4.00E-04 TRZ 10 2.38E-01 6.55E-01 6.68E-03 Gamma and a state of the stat	ARI 25 ARI 25 5.40E-07 9.23E-02 1.87E-06 TRZ 25 1.27E-03 1.87E-01 6.81E-04	ARI 50 7.85E-00 2.61E-00 5.26E-00 TRZ 50 4.33E-00 1.91E-00 2.19E-00
5.29E-03 2.06E-01 4.00E-04 7RZ 10 2.38E-01 6.55E-01 6.68E-03	5.40E-07 9.23E-02 1.87E-06 TRZ 25 1.27E-03 1.87E-01 6.81E-04	7.85E-02 2.61E-02 5.26E-02 5.26E-02 7 <i>RZ 50</i> 4.33E-02 1.91E-02 2.19E-02
2.06E-01 4.00E-04 TRZ 10 2.38E-01 6.55E-01 6.68E-03 ignificance vi API 10	9.23E-02 1.87E-06 TRZ 25 1.27E-03 1.87E-01 6.81E-04	2.61E-02 5.26E-02 7RZ 50 4.33E-02 1.91E-02 2.19E-02
4.00E-04 TRZ 10 2.38E-01 6.55E-01 6.68E-03 ignificance vi API 10	1.87E-06 TRZ 25 1.27E-03 1.87E-01 6.81E-04	5.26E-0 TRZ 50 4.33E-0 1.91E-0 2.19E-0
TRZ 10 2.38E-01 6.55E-01 6.68E-03	TRZ 25 1.27E-03 1.87E-01 6.81E-04	TRZ 50 4.33E-0° 1.91E-0° 2.19E-0°
2.38E-01 6.55E-01 6.68E-03	1.27E-03 1.87E-01 6.81E-04	4.33E-0 1.91E-0 2.19E-0
6.55E-01 6.68E-03	1.27E-03 1.87E-01 6.81E-04	4.33E-0 1.91E-0 2.19E-0
6.68E-03	6.81E-04	2.19E-0
ignificance v	0.01E-04	2.176-03
gnificance v		
ignificance v		
API 10	alues)	
ANI 10 I	ARI 25	ARI 50
1.68E-03	2.49E-05	2.07E-0
6.56F-02	3.51F-04	1.35E-0
7.65E-02	7.34F-01	9.66F-0
TRZ 10	TRZ 25	TRZ 50
2.38E-03	4.29F-06	2.51E-0
4.46F-03	1.40F-04	2.12E-0
9.93E-01	5.27E-01	3.62E-0
	•	
(significance	values)	
ARI 10	ARI 25	ARI 50
1.26E-01	4.33E-01	6.13E-0
6.87E-01	7.16E-01	3.48E-0
	5.49E-01	6.88E-0
3.17E-01		
3.17E-01	TRZ 25	TRZ 50
3.17E-01 TRZ 10 7.21E-01	TRZ 25 9.44E-01	TRZ 50 3.11E-01
3.17E-01 TRZ 10 7.21E-01 8.41E-01	TRZ 25 9.44E-01 2.73E-01	TRZ 50 3.11E-03 1.32E-03
	1.68E-03 6.56E-02 7.65E-02 7.65E-02 7.72 7.72 7.72 7.72 7.72 9.93E-01 (significance ARI 10 1.26E-01 6.87E-01 6.37E-01	1.68E-03 2.49E-05 6.56E-02 3.51E-04 7.65E-02 7.34E-01 7.82 0 7.83E-03 4.29E-06 4.46E-03 1.40E-04 9.93E-01 5.27E-01 (significance values) ARI 10 ARI 25 1.26E-01 4.33E-01 6.87E-01 7.16E-01 6.37E-01 5.49E-01

Supplemental Table S2A (Companion to Figure 5). ¹³C-labeled Sterol levels, reported as ng/million cells; 13C 8-DHC could not be determined because of overlapping MS fragments with isotopic internal standards.

OPPOSE CONTROL Sample DMSO AN 25						/	-DHC lev	vel					
Note Note <th< td=""><td></td><td></td><td></td><td>HETEROZYG</td><td>ious</td><td></td><td></td><td></td><td></td><td>CONTR</td><td>ROL</td><td></td></th<>				HETEROZYG	ious					CONTR	ROL		
Normality Normality <t< th=""><th>5</th><th>Sample</th><th>DMSO</th><th>ARI 10</th><th>ARI 25</th><th>ARI 50</th><th></th><th>Sample</th><th>DMSO</th><th>ARI 10</th><th>ARI 25</th><th>ARI 50</th></t<>	5	Sample	DMSO	ARI 10	ARI 25	ARI 50		Sample	DMSO	ARI 10	ARI 25	ARI 50	
Note Description Note	õ	avorago	14.9	251.0	621.0	91/1 2		avorago	14.0	AN 10	209.1	625	
Bite JJJJ JJJJJ JJJJJ JJJJJ JJJJJ JJJJJ JJJJJ JJJJJJ JJJJJJ JJJJJJJJJJJJJJJJJJJJJJJJJJJJJJJJJJJJ	₹.	average	44.8	351.0	651.9	914.5		average	14.0	94.5	508.1	625.	
SEM 7.9 37.7 47.3 55.0 SEM 4.4 15.6 32.2 4 Semple 0.450 172.10 172.25 172.20	Ī	stdev	33.3	159.8	200.5	233.4		stdev	15.2	54.2	111.7	161.	
Normalia	ļ,	SEM	7.9	37.7	47.3	55.0		SEM	4.4	15.6	32.2	46	
Description NETEROXYCOUS TWD 1782 J0 1782 J0 1	٩												
Digginary bit is the set of the	¥			HETEROZYG	ious					CONTR	ROL		
Document Description Provide the second state of	ō	Sample	DMSO	TRZ 10	TRZ 25	TRZ 50		Sample	DMSO	TRZ 10	TRZ 25	TRZ 50	
Stder 72.9 170.2 197.4 180.9 stder 20.3 4.5.0 100.7.7 177.5 SEM 172.2 40.1 46.5 42.6 SEM 5.9 13.0 29.1 4 Semple DMS0. API 20 API 25 API 50 SEM 5.9 13.0 29.1 4 Sample DMS0. API 25 API 50 Sample DMS0. API 25 API 50 Sample DMS0. API 25 API 50 Sample DMS0. TRE 20 YEGUS Sample DMS0. TRE 20 YEE 20 Y	6	average	89.8	274.6	566.4	856.5		average	41.5	87.8	192.6	430	
Description Description SEM 2.5.9 3.3.0 2.9.1 4.4 Semple 0.050 3.0.0 2.9.1 4.4 Semple 0.050 3.0.0 2.9.1 4.4 Semple 0.050 3.0.0 2.9.1 4.4 Semple 0.050 7.7.2 0.0.1 2.9.1 4.4 Semple 0.050 1.0.1 3.0.1 2.0.1 1.0.1 Semple 0.050 1.0.2 3.0.1 1.0.1 3.0.1 1.0.1 Semple 0.0450 1.0.2 3.6 1.0.2 3.6 1.0.2 Semple 0.0450 1.0.2 3.6 1.0.2 3.6 1.0.2 Semple 0.0450 1.02.3 1.0.2.5 1.0.2 3.6 1.0.2 Semple 0.0450 1.02.3 1.0.2.6 1.0.2.6 1.0.2.6 1.0.2.6 Semple 0.0450 1.02.3 1.0.2.6 1.0.2.7 1.0.2.7 3.6.6 5 Sem	A	stdev	72.9	170.2	197.4	180.9		stdev	20.3	45.0	100.7	170	
Description Description Control Control Sample DMSO ATT 10 ART 25 ART 90 swerage 833.6 611.8 403.9 288.6 123.6 <td>۲</td> <td>SEM</td> <td>17.2</td> <td>40.1</td> <td>46.5</td> <td>42.6</td> <td></td> <td>SEM</td> <td>5.9</td> <td>13.0</td> <td>29.1</td> <td>40</td>	۲	SEM	17.2	40.1	46.5	42.6		SEM	5.9	13.0	29.1	40	
Cholesterol level Sample DMSO ARI 10 ARI 25 NET 47.3 37.3 21.0 23.6 Sample DMSO TR2.8 (18.10 marks) SEM CONTROL Sample DMSO TR2.10 (18.10 marks) SEM Sample DMSO ARI 10 (18.10 marks) SEM Sample DMSO TR2.10 (18.25		02111	1/12	10.1	10.5	12.0		02111	5.5	15.0	2512		
CONTROL CONTROL Sample DMSO RR 10 AR1 25 AR1 2						Ch	lestero	امريما					
Normalian OMSO ARI 20 ARI 25 ARI 20 Somple DMSO ARI 25 ARI 25 </td <td></td> <td></td> <td></td> <td>HETEROZYG</td> <td>ious</td> <td>Circ</td> <td>nestero</td> <td></td> <td></td> <td>CONTR</td> <td>ROL</td> <td></td>				HETEROZYG	ious	Circ	nestero			CONTR	ROL		
December Interfage 833.6 (2006) 611.8 (2006) 403.9 (2006) 288.8 (2006) interfage 77.8 (2006) 77.2 (2006) 77.3 (2006) 77.3 (2007) 77.2 (2007) 77.2 (2007) 77.2 (2007) 77.2 (2007) 77.2 (2007) 77.2 (2007) 77.2 (2007) 77.2 (2007) 77.2 (2007) 77.2 (2007) </td <td>Ľ</td> <td>Sample</td> <td>DMSO</td> <td>ARI 10</td> <td>ARI 25</td> <td>ARI 50</td> <td></td> <td>Sample</td> <td>DMSO</td> <td>ARI 10</td> <td>ARI 25</td> <td>ARI 50</td>	Ľ	Sample	DMSO	ARI 10	ARI 25	ARI 50		Sample	DMSO	ARI 10	ARI 25	ARI 50	
Normalize State 200.6 158.1 89.1 100.1 SEM 200.6 158.1 89.1 100.1 State 248.6 193.0 211.6 155 SEM 271.8 35.7 61.1 4 Sample DMSO TR2 10 TR2 50 SEM 1093.6 1093.6 1093.6 1083.7 1025.0 186.1 655.7 474.5 1093.6 103.7 125.0 186.1 105.3 1093.6 1083.7 126.9 188 166.7 105.3 92.6 82.3 SEM 54.7 474.3 36.6 5 SEM 39.3 24.8 21.8 19.4 SEM 54.7 472.3 36.6 5 Semple DMSO ARI 10 ARI 25 ARI 25 38.6 58.9 5 18.1 20.5 13.1 12.6 13.1 12.6 13.1 13.1 13.1 13.1 13.1 13.1 13.1 13.1 13.1 13.1 <	2 Z	average	853.6	611.8	403.9	288.8		average	872.8	788.0	723.6	521	
SEM JOUG JOUG <thj< td=""><td>RA RA</td><td>stdey</td><td>200.6</td><td>158.1</td><td>89.1</td><td>100.1</td><td></td><td>stdev</td><td>248.6</td><td>193.0</td><td>211.6</td><td>159</td></thj<>	RA RA	stdey	200.6	158.1	89.1	100.1		stdev	248.6	193.0	211.6	159	
Description Provide Description Provide Description Sample DMSO TRZ 10 TRZ 25 TRZ 50 average 1208.1 1093.6 1050.4 860 Sample DMSO TRZ 10 TRZ 25 TRZ 50 average 1208.1 1093.6 1050.4 860 Sample DMSO TRZ 10 TRZ 25 TRZ 50 average 1208.1 1093.6 1050.4 860 Stew 39.3 24.8 21.8 19.4 Stew 54.7 47.3 36.6 5 Sample DMSO ARI 20 ARI 25 ARI 50 average 1208.1 1093.6 1050.4 860 Sample DMSO ARI 20 ARI 20 ARI 20 average 1208.5 5 5 5 5 5 5 5 107.0 107.0 107.0 107.0 107.0 107.0 107.0 107.0 107.0 107.0 107.0 107.0 107.0 107.0		SEM	47.2	27.2	21.0	200.1		SEM	71.0	200.0	£11.0 £1.1	1.75	
Dogo HETEROZYGOUS average CONTROL 1053 Sample 2005 D/MSO TRZ 20 TRZ 25 TRZ 50 average Sample 2005 D/MSO TRZ 21 TRZ 25 TTZ 25 TRZ 25 TTZ 25 TRZ 25 TTZ 25 <thtz 25<="" th=""> TTZ 25</thtz>	ARIF	SEIVI	47.5	57.5	21.0	25.0		SEIVI	/1.8	55.7	01.1	40	
Sample DMSO TR2 10 TR2 25 TR2 50 sterage 1095.5 884.1 658.7 474.5 sterage 1095.5 884.1 658.7 474.5 sterage 1095.5 884.1 658.7 474.5 sterage 1208.1 1093.6 1093.6 1050.4 866 sterage 139.3 24.8 21.8 19.4 1093.6 1050.4 866 SEM 39.3 24.8 21.8 19.4 109.5 56.6 5 Sample DMSO RRI 50 serage 120.7 107.5 120.7 120.8 120.8 120.8 120.9 <t< td=""><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></t<>													
Dimple DMSO TR2 10 TR2 25 TR2 50 average 1045.5 884.1 658.7 474.3 stdev 166.7 105.3 92.6 82.3 SEM 39.3 24.8 21.8 19.4 SEM 39.3 24.8 21.8 19.4 SEM 39.3 24.8 21.8 19.4 SEM 55.7 474.3 36.6 5 SEM 39.3 24.8 21.8 19.4 55.0 Semple DMSO 77.2 77.3 36.6 5 Sample DMSO 77.2 77.3 36.6 5 Sample DMSO 77.2 77.3 36.6 5 stdev 76.7 87.1 107.3 73.8 5 5 stdev 76.7 87.1 107.3 73.8 5 5 5 stdev 75.2 66.3 136.1 36.5 13 5 <td< td=""><td>ž</td><td></td><td></td><td>HETEROZYG</td><td>IOUS</td><td></td><td></td><td></td><td></td><td>CONTR</td><td>ROL</td><td></td></td<>	ž			HETEROZYG	IOUS					CONTR	ROL		
Decreage 1095.5 884.1 658.7 474.5 average 1208.1 1093.6 0303.4 866 SEM 39.3 24.8 21.8 19.4 SEM 54.7 47.3 36.6 5 SEM 39.3 24.8 21.8 19.4 SEM 54.7 47.3 36.6 5 SEM 54.7 47.3 36.6 5 7 3 5	3	Sample	DMSO	TRZ 10	TRZ 25	TRZ 50		Sample	DMSO	TRZ 10	TRZ 25	TRZ 50	
Sem Idev 165.7 105.3 92.6 82.3 SEM 39.3 24.8 21.8 19.4 SEM 189.6 163.7 126.9 185 SEM 39.3 24.8 21.8 19.4 SEM 54.7 47.3 36.6 5 SEM 39.3 24.8 21.8 19.4 SEM 54.7 47.3 36.6 5 Sem Desmosterol level Control Control Sem Control Sem Ari 20 Ari 25 Ari 50 Sem 12.5 10.7.3 13.6.3 stdev 13.6.1 13.6.1 stdev 13.1 20.5 25.3 17.4 Sem 19.4 25.4 17.0 1 Sample DMSO R2 10 TR2 50 Sem 13.1 20.5 25.3 17.4 Sem 13.2 44.5 13.7 14.6 13.2 44.5 13.2 44.5 14.6 13.2 44.5 14.6 13.2 44.5 14.6 <td>0</td> <td>average</td> <td>1045.5</td> <td>884.1</td> <td>658.7</td> <td>474.5</td> <td></td> <td>average</td> <td>1208.1</td> <td>1093.6</td> <td>1050.4</td> <td>860</td>	0	average	1045.5	884.1	658.7	474.5		average	1208.1	1093.6	1050.4	860	
SEM 39.3 24.8 21.8 19.4 SEM 54.7 47.3 36.6 5 SEM 39.3 24.8 21.8 19.4 SEM 54.7 47.3 36.6 5 Sample METEROZYGOUS CONTROL Sample CONTROL Sample ARI 25 ARI 50 average 174.5 21.3.7 159.3 132.3 sterv 76.7 87.1 107.3 73.8 SEM 19.4 25.4 17.0 1 sterv 76.7 87.1 107.3 73.8 SEM 19.4 25.4 17.0 1 sterv 76.7 87.1 107.3 73.8 SEM 19.4 25.4 17.0 1 sterv 76.7 77.2 77.2 57.2 4 10.4 123.9 1 19.4 15.2 19.3 10.2 1 stervarage 13.1.3 136.2 114.4 123.9 13.2 1 10.0 1 </td <td>3</td> <td>stdev</td> <td>166.7</td> <td>105.3</td> <td>92.6</td> <td>82.3</td> <td></td> <td>stdev</td> <td>189.6</td> <td>163.7</td> <td>126.9</td> <td>185</td>	3	stdev	166.7	105.3	92.6	82.3		stdev	189.6	163.7	126.9	185	
Desmosterol level Sample DMSO ARI 20 ARI 25 ARI 50 stdev 76.7 174.5 213.7 159.3 13.3 stdev 76.7 177.3 73.8 52.7 66.7 136.0 55.7 stdev 52.6 68.3 42.3 55.7 52.7 66.7 35.2 4 METEROZYGOUS Sample DMSO TR2 10 TR2 25 TR2 50 average 13.3 13.6 13.4 123.9 13.4 13.2 13.3 13.4 13.4 13.5 13.4 13.4 13.5 13.4 13.2 13.3 13.6 13.4 13.2 13.3 13.6 13.4 13.2 13.3 13.2 13.3 13.2 13.3 13.2 13.3 13.2 13.3 13.2 13.3 13.2 13.3 13.2 13.3 13.2 13.3 13.2 13.3 13.2 13.3 13.2 13.3 13.2 13.3 13.2 13.3	=	SEM	39.3	24.8	21.8	19.4		SEM	54.7	47.3	36.6	5	
Desmosterol level Sample DMSO ARI 10 ARI 25 ARI 50 average 162.9 151.6 178.6 136.1 stdev 76.7 87.1 107.3 73.8 SEM 18.1 20.5 25.3 17.4 Sample DMSO ARI 10 ARI 25 ARI 50 average 131.3 136.2 114.4 123.9 stdev 52.6 68.3 42.3 55.7 SEM 12.4 16.1 10.0 13.1 Sample DMSO TRZ 10 TRZ 25 TRZ 50 average 180.0 166.9 144.6 155 stdev 52.6 68.3 42.3 55.7 SEM 12.4 16.1 10.0 13.1 Sample DMSO TRZ 10 TRZ 25 TRZ 50 average 180.0 166.9 144.6 155 stdev 52.6 68.3 42.3 55.7 SEM 12.4 16.1 10.0 13.1 Sample DMSO TRZ 10 TRZ 25 TRZ 50 average 180.0 166.9 144.6 155 stdev 52.7 66.7 35.2 4 SEM 15.2 19.3 10.2 1 Sample DMSO TRZ 10 TRZ 25 TRZ 50 average 1208.9 1370.9 1359.2 1376 stdev 50.7 712.4 885.6 483.7 SEM 118.0 167.9 208.7 114.0 Sample DMSO ARI 10 ARI 25 ARI 50 average 1208.9 1370.9 1359.2 1376 stdev 478.9 674.5 551.6 710 Sample DMSO TRZ 10 TRZ 25 TRZ 50 average 1208.9 1370.9 1359.2 1376 stdev 478.9 674.5 551.6 710 SEM 138.3 194.7 159.2 200 METEROZYGOUS Sample DMSO TRZ 10 TRZ 25 TRZ 50 average 1362.1 1343.5 1351.7 1316.4													
Destriction level Sample DMSO ARI 10 ARI 25 ARI 50 average 162.9 151.6 178.6 136.1 stdev 76.7 87.1 107.3 73.8 SEM 18.1 20.5 25.3 17.4 Sample DMSO ARI 10 ARI 25 ARI 50 average 162.9 151.6 178.6 136.1 stdev 76.7 87.1 107.3 73.8 SEM 19.4 25.4 17.0 1 Sample DMSO TRZ 10 TRZ 25 TRZ 50 average 131.3 136.2 114.4 123.9 stdev 52.6 68.3 423.3 55.7 SEM 12.4 16.1 10.0 13.1 Sample DMSO TRZ 10 TRZ 25 TRZ 50 average 180.0 166.9 144.6 155 stdev 52.7 66.7 35.2 4 SEM 15.2 19.3 10.2 1 Lanosterol level Lanosterol level Sample DMSO ARI 10 ARI 25 ARI 50 average 1236.8 1414.0 1516.4 1314.7 stdev 500.7 712.4 885.6 483.7 SEM 118.0 167.9 208.7 114.0 Sample DMSO ARI 10 ARI 25 ARI 50 average 1208.9 1370.9 1359.2 1378 stdev 478.9 674.5 551.6 710 Sem 138.3 194.7 159.2 200 METEROZYGOUS Sample DMSO ARI 10 ARI 25 ARI 50 average 1208.9 1370.9 1359.2 1378 stdev 500.7 712.4 885.6 483.7 SEM 118.0 167.9 208.7 114.0 Sample DMSO ARI 10 ARI 25 ARI 50 average 1208.9 1370.9 1359.2 1378 stdev 478.9 674.5 551.6 710 SEM 138.3 194.7 159.2 200 METEROZYGOUS Sample DMSO 7R2 10 TRZ 25 TRZ 50 average 1362.1 1343.5 1351.7 1316.4													
Sample DMSO ARI 10 ARI 25 ARI 50 average 162.9 151.6 178.6 136.1 stdev 76.7 87.1 107.3 73.8 SEM 18.1 20.5 25.3 17.4 Sample DMSO ARI 20 ARI 50 average 174.5 213.7 159.3 135.5 SEM 18.1 20.5 25.3 17.4 SEM 19.4 25.4 17.0 1 Sample DMSO TRZ 10 TRZ 25 TRZ 50 average 180.0 166.9 144.6 155 stdev 52.6 68.3 42.3 55.7 Sem 15.2 19.3 10.2 1 stdev 52.6 68.3 42.3 55.7 Sem 15.2 19.3 10.2 1 stdev 52.6 68.3 42.3 55.7 Sem 15.2 19.3 10.2 1 stdev 52.6 68.						Dec							
Sample DMSO TRZ 10 TRZ 25 TRZ 50 TRZ 50 <th></th> <th></th> <th></th> <th>HETEROZYG</th> <th>ous</th> <th>Des</th> <th>mostero</th> <th>ol level</th> <th></th> <th>CONTR</th> <th>ROL</th> <th></th>				HETEROZYG	ous	Des	mostero	ol level		CONTR	ROL		
Sectors 121.0 <	<u> </u>	Sample	DM50	HETEROZYG ARI 10	ious Ari 25	Des ARI 50	mostero	ol level	DMSO	CONTR ARI 10	KOL ARI 25	ARI 50	
SEM 18.1 20.5 25.3 17.4 SEM 18.1 20.5 25.3 17.4 SEM 18.1 20.5 25.3 17.4 SEM 19.4 25.4 17.0 1 Semple DMSO TR2 10 TR2 25 TR2 50 average 131.3 136.2 114.4 123.9 stdev 52.6 68.3 42.3 55.7 SEM 12.4 16.1 10.0 13.1 SEM 12.4 16.1 10.0 13.1 SEM 12.4 16.1 10.0 13.1 Semple DMSO ARI 10 ARI 25 ARI 50 average 1236.8 1414.0 1516.4 1314.7 stdev 50.7 712.4 885.6 483.7 SEM 118.0 167.9 208.7 114.0 Semple DMSO 7R2 10 TR2 25 TR2 50 average 138.3	20LE	Sample	DM50	HETEROZYG ARI 10	OUS ARI 25 178 6	Des ARI 50 136 1	mostero	bi level Sample	DMS0 174 5	CONTR ARI 10 2113 7	OL ARI 25 150 3	ARI 50	
Sample DMSO TRZ 10 TRZ 25 TRZ 50 average 131.3 136.2 114.4 123.9 stdev 52.7 66.7 35.2 4 SEM 12.4 16.1 10.0 13.1 SEM 15.2 19.3 10.2 1 Lanosterol level Sample DMSO TRZ 10 TRZ 25 TRZ 50 average 130.0 166.9 144.4 123.9 stdev 52.6 68.3 42.3 55.7 SEM 15.2 19.3 10.2 1 Lanosterol level SEM 15.2 19.3 10.2 1 Lanosterol level Sample DMSO ARI 10 ARI 25 ARI 50 average 120.8 1414.0 1516.4 1314.7 Stdev 500.7 712.4 885.6 483.7 32.4 17.0 1359.2 1376.3 SEM 118.0 167.9 208.7 114.0 38.3 194.7<	KAZULE	Sample	DMSO 162.9	HETEROZYG ARI 10 151.6 297	OUS ARI 25 178.6	Des ARI 50 1367 -	mostero	bi level Sample average trav	DMSO 174.5 671	CONTR ARI 10 213.7	ROL ARI 25 159.3	ARI 50 132	
HETEROZYGOUS Sample CONTROL Sample DMSO TRZ 50 average 131.3 136.2 114.4 123.9 stdev 52.6 68.3 42.3 55.7 SEM 12.4 16.0 166.7 35.2 4 SEM 12.4 16.0 180.0 166.7 35.2 4 SEM 12.4 16.0 136.7 35.7 Sample OMSO ARI 50 average 1236.8 1362.1 1342.5 ARI 50 average 1208.7 1370 377.2 ARI 50 average 1208.7 1378 31370.9 1359.2	PIPRAZOLE	Sample average stdev SEA	DMSO 162.9 76.7	HETEROZYG ARI 10 151.6 87.1 20 5	OUS ARI 25 178.6 107.3 25 2	Des Ari 50 136.1 73.8	mostero	DI Ievel Sample average stdev	DMSO 174.5 67.1 194	CONTR ARI 10 213.7 88.0 25.4	ROL ARI 25 159.3 58.9 170.0	ARI 50 132 53	
Initial colspan="2">Control Sample DMSO TR2 50 average 131.3 136.2 114.4 123.9 stdev 52.6 68.3 42.3 55.7 SEM 12.4 16.1 10.0 136.2 144.6 152.2 SEM 12.4 16.1 10.0 180.0 166.7 35.2 4 Lanosterol level Sem 12.36.8 141.40 136.4 131.7 37.6 CONTROL Sample DMSO ARI 25 RR 250 ARI 25 ARI 25 RR 250 Sample DMSO ARI 25 ARI 50 ARI 25 ARI 25 ARI 50 <th< td=""><td>ARIPIPRAZOLE</td><td>Sample average stdev SEM</td><td>DMSO 162.9 76.7 18.1</td><td>HETEROZYG ARI 10 151.6 87.1 20.5</td><td>OUS ARI 25 178.6 107.3 25.3</td><td>Des ARI 50 136.1 73.8 17.4</td><td>mostero</td><td>Sample Sample average stdev SEM</td><td>DMSO 174.5 67.1 19.4</td><td>CONTR ARI 10 213.7 88.0 25.4</td><td>OL ARI 25 159.3 58.9 17.0</td><td>ARI 50 132 55</td></th<>	ARIPIPRAZOLE	Sample average stdev SEM	DMSO 162.9 76.7 18.1	HETEROZYG ARI 10 151.6 87.1 20.5	OUS ARI 25 178.6 107.3 25.3	Des ARI 50 136.1 73.8 17.4	mostero	Sample Sample average stdev SEM	DMSO 174.5 67.1 19.4	CONTR ARI 10 213.7 88.0 25.4	OL ARI 25 159.3 58.9 17.0	ARI 50 132 55	
Sample DMSD TR2 10 TR2 25 TR2 30 average 131.3 136.2 114.4 123.9 average 180.0 166.7 35.2 4 stdev 52.6 68.3 42.3 55.7 stdev 52.7 66.7 35.2 4 SEM 12.4 16.1 10.0 13.1 SEM 15.2 19.3 10.2 1 SEM 12.4 16.1 10.0 13.1 SEM 15.2 19.3 10.2 1 Semple DMSO ARI 10 ARI 25 ARI 50 average 120.8.9 137.0.9 135.2 14 Semple DMSO ARI 10 ARI 25 ARI 50 average 1208.9 1370.9 1359.2 1376 stdev 500.7 712.4 885.6 483.7 stdev 478.9 674.5 551.6 711 SEM 118.0 167.9 208.7 114.0 SEM 138.3 194.7	E ARIPIPRAZOLE	Sample average stdev SEM	DMSO 162.9 76.7 18.1	HETEROZYG ARI 10 151.6 87.1 20.5	OUS ARI 25 178.6 107.3 25.3	Des ARI 50 136.1 73.8 17.4	mosterc	bi level Sample average stdev SEM	DMSO 174.5 67.1 19.4	CONTE ARI 10 213.7 88.0 25.4	OL ARI 25 159.3 58.9 17.0	ARI 50 132 53	
average 131.3 136.2 114.4 123.9 average 180.0 166.9 144.6 155.7 stdev 52.6 68.3 42.3 55.7 stdev 52.7 66.7 35.2 4 SEM 12.4 16.1 10.0 13.1 SEM 15.2 19.3 10.2 1 Lanosterol level SetM SetM 144.6 155 SetM 12.4 144.6 155 SetM 12.4 144.6 155 Linosterol level SetM 15.2 19.3 10.2 1 ARI 25 ARI 25 ARI 25 ARI 25 SetM 136.0 167.9 137.0 SetM 118.0 167.9 208.7 136.7 <th cols<="" td=""><td></td><td>Sample average stdev SEM</td><td>DMSO 162.9 76.7 18.1</td><td>HETEROZYG ARI 10 151.6 87.1 20.5</td><td>ARI 25 178.6 107.3 25.3</td><td>Des ARI 50 136.1 73.8 17.4</td><td>mostero</td><td>DI level Sample average stdev SEM</td><td>DMSO 174.5 67.1 19.4</td><td>CONTR ARI 10 213.7 88.0 25.4 CONTR</td><td>ROL ARI 25 159.3 58.9 17.0</td><td>ARI 50 132 53 19</td></th>	<td></td> <td>Sample average stdev SEM</td> <td>DMSO 162.9 76.7 18.1</td> <td>HETEROZYG ARI 10 151.6 87.1 20.5</td> <td>ARI 25 178.6 107.3 25.3</td> <td>Des ARI 50 136.1 73.8 17.4</td> <td>mostero</td> <td>DI level Sample average stdev SEM</td> <td>DMSO 174.5 67.1 19.4</td> <td>CONTR ARI 10 213.7 88.0 25.4 CONTR</td> <td>ROL ARI 25 159.3 58.9 17.0</td> <td>ARI 50 132 53 19</td>		Sample average stdev SEM	DMSO 162.9 76.7 18.1	HETEROZYG ARI 10 151.6 87.1 20.5	ARI 25 178.6 107.3 25.3	Des ARI 50 136.1 73.8 17.4	mostero	DI level Sample average stdev SEM	DMSO 174.5 67.1 19.4	CONTR ARI 10 213.7 88.0 25.4 CONTR	ROL ARI 25 159.3 58.9 17.0	ARI 50 132 53 19
Stdev 52.6 68.3 42.3 55.7 stdev 52.7 66.7 35.2 4 SEM 12.4 16.1 10.0 13.1 SEM 15.2 19.3 10.2 1 Lanosterol level SEM CONTROL Semile OM/SO ARI 30 ARI 50 average 1236.8 1414.0 1516.4 1314.7 Sample DM/SO ARI 30 ARI 50 average 1208.9 1370.9 1359.2 1370 SEM 1360.7 712.4 885.6 483.7 SEM 138.3 194.7 159.2 200 HETEROZYGOUS Sample DM/SO 778.26 average 1362.1 1331.3 1346.5 </td <td>DONE AKIPIPKAZOLE</td> <td>Sample average stdev SEM Sample</td> <td>DMSO 162.9 76.7 18.1 DMSO</td> <td>HETEROZYG ARI 10 151.6 87.1 20.5 HETEROZYG TRZ 10</td> <td>OUS ARI 25 178.6 107.3 25.3 OUS TRZ 25</td> <td>Des ARI 50 136.1 73.8 17.4 TRZ 50</td> <td>mosterc</td> <td>Sample Sample average stdev SEM Sample</td> <td>DMSO 174.5 67.1 19.4 DMSO</td> <td>CONTF ARI 10 213.7 88.0 25.4 CONTF TRZ 10</td> <td>ROL ARI 25 159.3 58.9 17.0 ROL TRZ 25</td> <td>ARI 50 132 5: 1! TRZ 50</td>	DONE AKIPIPKAZOLE	Sample average stdev SEM Sample	DMSO 162.9 76.7 18.1 DMSO	HETEROZYG ARI 10 151.6 87.1 20.5 HETEROZYG TRZ 10	OUS ARI 25 178.6 107.3 25.3 OUS TRZ 25	Des ARI 50 136.1 73.8 17.4 TRZ 50	mosterc	Sample Sample average stdev SEM Sample	DMSO 174.5 67.1 19.4 DMSO	CONTF ARI 10 213.7 88.0 25.4 CONTF TRZ 10	ROL ARI 25 159.3 58.9 17.0 ROL TRZ 25	ARI 50 132 5: 1! TRZ 50	
SEM 12.4 16.1 10.0 13.1 SEM 15.2 19.3 10.2 1 Lanosterol level CONTROL Sample DMSO ARI 10 ARI 25 ARI 50 average 123.6 141.0 151.2 19.3 10.2 1 Sample DMSO ARI 10 ARI 25 ARI 50 average 20.87 131.0 Sample DMSO ARI 10 ARI 25 ARI 50 average stdev 500.7 712.4 885.6 483.7 55LM 138.3 194.7 159.2 1372 SEM 118.0 167.9 208.7 114.0 SEM 138.3 194.7 159.2 200 HETEROZYGOUS Sample DMSO 7R2 10 7R2 25 7R2 50 average 1362.1 1335.7 1316.4	2000NE AKINIKAZOLE	Sample average stdev SEM Sample average	DMSO 162.9 76.7 18.1 DMSO 131.3	HETEROZYG ARI 10 151.6 87.1 20.5 HETEROZYG TRZ 10 136.2	ARI 25 178.6 107.3 25.3 7RZ 25 114.4	Des ARI 50 136.1 73.8 17.4 TRZ 50 123.9	mostero	Sample average stdev SEM Sample average	DMSO 174.5 67.1 19.4 DMSO 180.0	CONTR ARI 10 213.7 88.0 25.4 CONTR TRZ 10 166.9	OL ARI 25 159.3 58.9 17.0 ROL 7RZ 25 144.6	ARI 50 1322 55 15 15	
Lanosterol level Sample CONTROL Sample OMSO ARI 50 average 1236.8 1414.0 1516.4 1314.7 stdev 500.7 712.4 885.6 483.7 SEM 118.0 167.9 208.7 114.0 HETEROZYGOUS Sample DMSO TRZ 50 average 1362.1 1343.5 1351.7 1316.4	AKITIYAZOLE	Sample average stdev SEM Sample average stdev	DM50 162.9 76.7 18.1 DM50 131.3 52.6	HETEROZYG ARI 10 151.6 87.1 20.5 HETEROZYG TRZ 10 1366.3	OUS ARI 25 178.6 107.3 25.3 TRZ 25 114.4 42.3	Des ARI 50 136.1 73.8 17.4 TRZ 50 123.9 55.7	mostero	Sample average stdev SEM Sample average stdev	DMSO 174.5 67.1 19.4 DMSO 180.0 52.7	CONTR ARI 10 213.7 88.0 25.4 TRZ 10 166.7	ROL ARI 25 159.3 58.9 17.0 ROL TRZ 25 144.6 33.2	ARI 50 132 5: 1! TRZ 50 153 4(4)	
ONSO ARI 10 ARI 25 ARI 50 Sample DMSO ARI 10 ARI 50 average 1236.8 1414.0 1516.4 1314.7 stdev 500.7 712.4 885.6 483.7 SEM 118.0 167.9 200 METEROZYGOUS Sample DMSO TRZ 50 AMETEROZYGOUS Sample DMSO TRZ 50 Sample DMSO TRZ 50 average 1362.1 1343.5 1351.7 1316.4	TRAZODONE ARIPIPRAZOLE	Sample average stdev SEM Sample average stdev Stdev Stdev	DMSO 162.9 76.7 18.1 DMSO 131.3 52.6 12.4	HETEROZYG ARI 10 151.6 87.1 20.5 HETEROZYG TRZ 10 136.2 68.3 16.1	OUS ARI 25 178.6 107.3 25.3 7RZ 25 114.4 42.3 10.0	Des ARI 50 136.1 73.8 17.4 TRZ 50 123.9 55.7 13.1	mosterc	Sample Sample average stdev SEM Sample average stdev SEM	DMSO 174.5 67.1 19.4 DMSO 180.0 52.7 15.2	CONTF ARI 10 213.7 88.0 25.4 TRZ 10 166.9 66.7 19.3	ARI 25 159.3 58.9 17.0 TRZ 25 144.6 35.2 10.2	ARI 50 132 5: 11 12 15 3 44 11 12	
Sample DMSO ARI 10 ARI 25 ARI 50 average 1236.8 1414.0 1516.4 1314.7 stdev 500.7 712.4 885.6 483.7 Stdev 500.7 712.4 885.6 483.7 Stdev 180.0 167.9 208.7 114.0 K METEROZYGOUS Sample DMSO 774.2 774.5 Sample DMSO 774.5 551.6 716 SEM 118.0 167.9 208.7 114.0 SEM 138.3 194.7 559.2 206 Sample DMSO 782.10 782.25 782.50 782.50 782.50 782.50 782.50 average 1459.20 1476.08 1564.50 1346.3	TRAZODONE ARIPIPRAZOLE	Sample average stdev SEM Sample average stdev SEM	DMSO 162.9 76.7 18.1 DMSO 131.3 52.6 12.4	HETEROZYG ARI 10 151.6 87.1 20.5 HETEROZYG TRZ 10 136.2 68.3 16.1	OUS ARI 25 178.6 107.3 25.3 OUS TRZ 25 114.4 42.3 10.0	Des ARI 50 136.1 73.8 17.4 TRZ 50 123.9 55.7 13.1 Lau	mostero	DI level Sample average stdev SEM Sample average stdev SEM	DMSO 174.5 67.1 19.4 DMSO 180.0 52.7 15.2	CONTR ARI 10 213.7 88.0 25.4 TRZ 10 166.9 66.7 19.3	ARI 25 159.3 58.9 17.0 TRZ 25 144.6 35.2 10.2	ARI 50 1322 5: 11 17 15 35 44 4 4 1	
Average 1236.8 1414.0 1516.4 1314.7 stdev 500.7 712.4 885.6 483.7 SEM 118.0 167.9 208.7 114.0 SEM 118.0 167.9 208.7 114.0 Semple DMSO TRZ 10 TRZ 25 TRZ 50 average 136.1 1314.7 1350.2 1370.9 Sample DMSO TRZ 10 TRZ 25 TRZ 50 average 136.1 1316.4 1316.4	TRACODONE ANIPIPRAZOLE	Sample average stdev SEM Sample average stdev SEM	DMSO 162.9 76.7 18.1 DMSO 131.3 52.6 12.4	HETEROZYG ARI 10 151.6 87.1 20.5 HETEROZYG TRZ 10 136.2 68.3 16.1 HETEROZYG	OUS ARI 25 178.6 107.3 25.3 7RZ 25 114.4 42.3 10.0	Des ARI 50 136.1 73.8 17.4 77.8 17.4 77.7 13.1 13.1	nosterol	Sample Sample average stdev SEM Sample average stdev SEM	DMSO 174.5 67.1 19.4 DMSO 180.0 52.7 15.2	CONTR ARI 10 213.7 88.0 25.4 TRZ 10 166.9 66.7 19.3 CONTR	ARI 25 159.3 58.9 17.0 TRZ 25 144.6 35.2 10.2 10.2	ARI 50 1322 5: 11 17 15 33 44 1 1:	
stdev 500.7 712.4 885.6 483.7 SEM 118.0 167.9 208.7 114.0 SEM 118.0 167.9 208.7 114.0 SEM 138.3 194.7 159.2 206 Sample DMSO TRZ 10 TRZ 25 TRZ 50 average 1362.1 1343.5 1351.7 1316.4	DIE AKIPIPRAZOLE	Sample average stdev SEM Sample average stdev SEM	DMSO 162.9 76.7 18.1 DMSO 131.3 52.6 12.4	HETEROZYG ARI 10 151.6 87.1 20.5 HETEROZYG 7RZ 10 136.2 68.3 16.1 HETEROZYG ARI 10	OUS ARI 25 178.6 107.3 25.3 OUS TRZ 25 114.4 42.3 10.0 OUS ARI 25	Des ARI 50 136.1 73.8 17.4 TRZ 50 123.9 55.7 13.1 Lai ARI 50	mostero	Di level Sample average stdev SEM Sample average stdev SEM Ievel Sample	DMSO 174.5 67.1 19.4 DMSO 180.0 52.7 15.2 DMSO	CONTR ARI 10 213.7 88.0 25.4 CONTR TRZ 10 166.9 66.7 19.3 CONTR ARI 10	OL ARI 25 159.3 58.9 17.0 ROL TRZ 25 144.6 35.2 10.2 OL ARI 25	ARI 50 1322 53 15 15 15 15 3 48 13 13 48 13 13 48 13 13 13 13 13 13 13 14 13 13 14 13 14 14 14 14 14 14 15 15 15 15 15 15 15 15 15 15 15 15 15	
SEM 118.0 167.9 208.7 114.0 SEM 118.0 167.9 208.7 114.0 Sem TRZ 10 TRZ 25 TRZ 50 average 136.1 1343.5 1351.7 1316.4		Sample average stdev SEM Sample average stdev SEM	DMSO 162.9 76.7 18.1 DMSO 131.3 52.6 12.4	HETEROZYG ARI 10 151.6 87.1 20.5 HETEROZYG 7RZ 10 136.2 68.3 16.1 HETEROZYG ARI 10 1414.0	ARI 25 178.6 107.3 25.3 7RZ 25 114.4 42.3 10.0 WS ARI 25 1516.4	Des Ari 50 136.1 73.8 17.4 7RZ 50 123.9 55.7 13.1 Lai ARI 50 1314.7	mostero	Sample average stdev SEM Sample average stdev SEM Ievel Sample average	DMSO 174.5 67.1 19.4 DMSO 180.0 52.7 15.2 DMSO 1208.9	CONTR ARI 10 213.7 88.0 25.4 TRZ 10 166.9 66.7 19.3 CONTR ARI 10 1370.9	ROL ARI 25 159.3 58.9 17.0 ROL 7R2 25 144.6 35.2 10.2 ROL ARI 25 1359.2	ARI 50 1322 15 15 15 15 15 3 4 4 12 15 3 4 4 12 15 3 15 3 15 3 15 15 15 15 15 15 15 15 15 15 15 15 15	
Num 110.0 107.5 206.7 114.0 Servi 136.3 194.7 159.2 206 Num HETEROZYGOUS Sample DMSO TRZ 10 TRZ 25 TRZ 50 Sample DMSO TRZ 25 TRZ 50 average 136.2.1 1343.5 1351.7 1316.4 Sample DMSO TRZ 10 TRZ 25 TRZ 50 average 1459.2.0 1476.08 1564.50 1346.5	RAZOLE ARIPIPRAZOLE ARIPIPRAZOLE	Sample average stdev SEM Sample average stdev SEM Sample average ctdev	DMSO 162.9 76.7 18.1 DMSO 131.3 52.6 12.4 DMSO 1236.8 500.7	HETEROZYG ARI 10 151.6 87.1 20.5 HETEROZYG TRZ 10 136.2 68.3 16.1 HETEROZYG ARI 10 1414.0 712 4	OUS ARI 25 178.6 107.3 25.3 OUS TRZ 25 114.4 42.3 10.0 OUS ARI 25 1516.4 885.6	Des ARI 50 136.1 73.8 17.4 TRZ 50 123.9 55.7 13.1 Kalina Kal	mostero	DI level Sample average stdev SEM Sample average stdev SEM Sample average stdev	DMSO 174.5 67.1 19.4 DMSO 180.0 52.7 15.2 DMSO 1208.9 479.0	CONTR ARI 10 213.7 88.0 25.4 CONTR 7R2 10 166.9 66.7 19.3 CONTR ARI 10 1370.9 674.5	OL ARI 25 159.3 58.9 17.0 OL TRZ 25 144.6 35.2 10.2 OL ARI 25 1359.2 55.1 6	ARI 50 132 5: 153 44 1: 1: 3 44 1: 1: 3 4 8 1: 3 7: 5 1: 5 3 4 5 1: 5 3 4 5 1: 5 5 5 5 5 5 7 7 5 5 5 7 7 7 5 5 5 7 7 7 5 5 7 7 7 7 5 7	
HETEROZYGOUS CONTROL Sample DMSO TRZ 10 TRZ 50 Sample DMSO TRZ 10 TRZ 50 average 1362.1 1343.5 1316.4	VIPRAZOLE TRAZODONE ARIPIPRAZOLE	Sample average stdev SEM Sample average stdev SEM	DMSO 162.9 76.7 18.1 DMSO 131.3 52.6 12.4 DMSO 1236.8 500.7 1126.8 500.7	HETEROZYG ARI 10 151.6 87.1 20.5 HETEROZYG 7RZ 10 136.2 68.3 16.1 HETEROZYG ARI 10 1414.0 712.4	OUS ARI 25 178.6 107.3 25.3 7R2 25 114.4 42.3 10.0 KI 25 1516.4 885.6 200 5	Des 136.1 73.8 17.4 TRZ 50 123.9 55.7 13.1 La ARI 50 1314.7 483.7 1116.	mostero	Sample average stdev SEM Sample average stdev SEM Ievel Sample average stdev Sample average	DMSO 174.5 67.1 19.4 180.0 52.7 15.2 DMSO 1208.9 478.9 1202.9	CONTR ARI 10 213.7 88.0 25.4 TRZ 10 166.9 66.7 19.3 CONTR ARI 10 1370.9 674.5 102.5	ROL ARI 25 159.3 58.9 17.0 ROL TRZ 25 144.6 35.2 10.2 ROL ARI 25 1359.2 551.6 1359.2	ARI 50 1323 5: 11: 7772 50 1533 44 11: 716 716 716 716 717 716 717 717 717 717	
Sample DMSO TR2 10 TR2 55 TR2 50 Sample DMSO TR2 10 TR2 25 TR2 50 average 1362.1 1343.5 1351.7 1316.4 average 1459.20 1476.08 1564.50 1346.5	ARIPIPRAZOLE ARIPIPRAZOLE ARIPIPRAZOLE	Sample average stdev SEM Sample average stdev SEM	DMSO 162.9 76.7 18.1 DMSO 131.3 52.6 12.4 DMSO 1236.8 500.7 118.0	HETEROZYG ARI 10 151.6 87.1 20.5 HETEROZYG 136.2 68.3 16.1 HETEROZYG ARI 10 1414.0 712.4 167.9	OUS ARI 25 178.6 107.3 25.3 OUS TRZ 25 114.4 42.3 10.0 OUS ARI 25 1516.4 885.6 208.7	Des 136.1 73.8 17.4 <i>TRZ 50</i> 123.9 55.7 13.1 <i>Lat</i> <i>ARI 50</i> 1314.7 483.7 114.0	nosterol	DI level Sample average stdev SEM Sample average stdev SEM level average stdev SEM	DMSO 174.5 67.1 19.4 DMSO 180.0 52.7 15.2 DMSO 1208.9 478.9 138.3	CONTR ARI 10 213.7 88.0 25.4 CONTR 7R2 10 166.9 66.7 19.3 CONTR ARI 10 1370.9 674.5 194.7	ROL ARI 25 159.3 58.9 17.0 TRZ 25 144.6 35.2 10.2 ROL ARI 25 1359.2 551.6 159.2	ARI 50 1323 5: 11: 1533 44 4 4 11: 1533 44 4 4 11: 1378 716 206	
Sample DMSO TRZ 10 TRZ 25 TRZ 50 Sample DMSO TRZ 10 TRZ 25 TRZ 50 average 1362.1 1343.5 1351.7 1316.4 average 1459.20 1476.08 1564.50 1346.5	ARIPIPRAZOLE ARIPIPRAZOLE ARIPIPRAZOLE	Sample average stdev SEM Sample average stdev SEM Sample average stdev SEM	DMSO 162.9 76.7 18.1 DMSO 131.3 52.6 12.4 DMSO 1236.8 500.7 118.0	HETEROZYG ARI 10 151.6 87.1 20.5 HETEROZYG 7RZ 10 136.2 68.3 16.1 HETEROZYG ARI 10 1414.0 712.4 167.9	OUS ARI 25 178.6 107.3 25.3 OUS TRZ 25 114.4 42.3 10.0 OUS ARI 25 1516.4 885.6 208.7	Des ARI 50 136.1 73.8 17.4 TRZ 50 123.9 55.7 13.1 Lat ARI 50 1314.7 483.7 114.0	nosterol	DI level Sample average stdev SEM Sample average stdev SEM level Sample average stdev SEM	DMSO 174.5 67.1 19.4 DMSO 180.0 52.7 15.2 DMSO 1208.9 478.9 138.3	CONTR ARI 10 213.7 88.0 25.4 CONTR TR2 10 166.9 66.7 19.3 CONTR ARI 10 1370.9 674.5 194.7	INCL	ARI 50 13235 5: 15 15 15 3 44 1 1 3 7 15 3 44 1 1 3 7 8 7 16 1378 7 16 206	
average 1362.1 1343.5 1351.7 1316.4 average 1459.20 1476.08 1564.50 1346.5	NE ARIPIPRAZOLE ARPIPRAZOLE	Sample average stdev SEM Sample average stdev SEM	DMSO 162.9 76.7 131.3 52.6 1236.8 500.7 118.0	HETEROZYG ARI 10 151.6 87.1 20.5 HETEROZYG 7RZ 10 136.2 68.3 16.1 HETEROZYG ARI 10 1414.0 712.4 167.9	OUS ARI 25 178.6 107.3 25.3 OUS TRZ 25 114.4 42.3 10.0 OUS ARI 25 1516.4 885.6 208.7 OUS	Des ARI 50 136.1 73.8 17.4 TRZ 50 123.9 55.7 13.1 Kari 50 1314.7 483.7 114.0	nosterol	Sample average stdev SEM Sample average stdev SEM Sample average stdev SEM	DMSO 174.5 67.1 19.4 DMSO 180.0 52.7 15.2 DMSO 1208.9 478.9 138.3	CONTR ARI 10 213.7 88.0 25.4 TRZ 10 166.9 66.7 19.3 CONTR ARI 10 1370.9 674.5 194.7	ROL ARI 25 159.3 58.9 17.0 TRZ 25 144.6 35.2 10.2 IOL ARI 25 1359.2 551.6 159.2	ARI 50 1322 55 15 15 7 7 7 7 7 8 7 16 206	
	UUNE ANIFITRAZULE AIRPUDUNE ANIFITRAZULE	Sample average stdev SEM Sample average stdev SEM Sample average stdev SEM	DMSO 162.9 76.7 18.1 DMSO 131.3 52.6 12.4 DMSO 1236.8 500.7 118.0 DMSO	HETEROZYG ARI 10 151.6 87.1 20.5 HETEROZYG TRZ 10 136.2 68.3 16.1 HETEROZYG ARI 10 1414.0 712.4 167.9 HETEROZYG TRZ 10	OUS ARI 25 178.6 107.3 25.3 OUS TRZ 25 114.4 42.3 10.0 OUS ARI 25 1516.4 885.6 208.7 OUS TRZ 25	Des ARI 50 136.1 73.8 17.4 782 50 123.9 55.7 13.1 782 50 782 50	nosterol	bl level Sample average stdev SEM Sample average stdev SEM Sample average stdev SEM	DMSO 174.5 67.1 19.4 DMSO 180.0 52.7 15.2 DMSO 1208.9 478.9 138.3 DMSO	CONTR ARI 10 213.7 88.0 25.4 CONTR TR2 10 166.9 66.7 19.3 CONTR ARI 10 1370.9 674.5 194.7 CONTR TR2 10	OL ARI 25 159.3 58.9 17.0 OL TRZ 25 144.6 35.2 10.2 OL ARI 25 1359.2 551.6 159.2 Sol. TRZ 25	ARI 50 132 53 15 15 15 3 48 48 13 13 716 206	
5 stdev 424.6 351.1 411.7 431.6 stdev 294.04 331.33 480.23 287.4	ANITITIAALULE INALOUUNE ANITITIAALULE	Sample average stdev SEM Sample average stdev SEM Sample average stdev SEM	DMSO 162.9 76.7 18.1 DMSO 131.3 52.6 1236.8 500.7 118.0 DMSO 1362.1	HETEROZYG ARI 10 151.6 87.1 20.5 HETEROZYG 68.3 16.1 HETEROZYG ARI 10 1414.0 712.4 167.9 HETEROZYG TRZ 10 1343.5	OUS ARI 25 178.6 107.3 25.3 OUS TRZ 25 114.4 42.3 10.0 ARI 25 1516.4 885.6 208.7 TRZ 25 1351.7	Des ARI 50 136.1 73.8 17.4 TRZ 50 123.9 55.7 13.1 ARI 50 1314.7 483.7 114.0 TRZ 50 1316.4	nosterol	Sample average stdev SEM Sample average stdev SEM Sample average stdev SEM	DMSO 174.5 67.1 19.4 180.0 52.7 15.2 DMSO 1208.9 478.9 138.3 UMSO 1459.20	CONTR ARI 10 213.7 88.0 25.4 TRZ 10 166.7 19.3 CONTR ARI 10 1370.9 674.5 194.7 1476.08	TRZ 25 159.3 58.9 17.0 TRZ 25 144.6 35.2 10.2 ARI 25 1359.2 551.6 159.2 SOL TRZ 25 1564.50	ARI 50 132 53 153 48 133 48 133 48 133 48 133 48 133 48 134 716 206 1346.3	
	ARPIPAZOUONE ARPIPAZOUE ARPIPAZOUE ARPIPAZOUE	Sample average stdev SEM Sample average stdev SEM Sample average stdev SEM	DMSO 162.9 76.7 181.3 52.6 12.4 DMSO 123.4 DMSO 123.4 DMSO 123.4 DMSO 123.4 DMSO 123.4 DMSO 123.6.7 500.7 118.0	HETEROZYG ARI 10 151.6 87.1 20.5 HETEROZYG TRZ 10 136.2 68.3 16.1 HETEROZYG ARI 10 1414.0 712.4 167.9 HETEROZYG TRZ 10 1343.5 351.1	ARI 25 178.6 107.3 25.3 TRZ 25 114.4 42.3 10.0 ARI 25 1516.4 885.6 208.7 TRZ 25 1351.7 411.7	Des ARI 50 136.1 78.2	nosterol	bl level Sample average stdev SEM Sample average stdev SEM Sample average stdev SEM Sample average stdev SEM	DMSO 174.5 767.1 19.4 DMSO 180.0 52.7 15.2 DMSO 1208.9 478.9 138.3 DMSO 1459.20 294.04	CONTR ARI 10 213.7 23.7 25.4 CONTR TRZ 10 166.9 66.7 19.3 19.3 CONTR ARI 10 1370.9 674.5 194.7 TRZ 10 1476.08 331.33	ROL ARI 25 159.3 58.9 17.0 TRZ 25 144.6 35.2 10.2 ROL ARI 25 1359.2 551.6 159.2 S51.6 159.2 S51.6 480.23	ARI 50 132. 533 153. 153. 48 133 1346.37. 1346.37. 287.8	
	TRAZODONE ARIPIPRAZOLE TRAZODONE ARIPIPRAZOLE	Sample average stdev SEM Sample average stdev SEM Sample average stdev SEM	DMSO 162.9 76.7 18.1 DMSO 131.3 52.6 1236.8 500.7 118.0 DMSO 1362.1 424.6 1204.1	HETEROZYG ARI 10 151.6 87.1 20.5 HETEROZYG 68.3 16.1 HETEROZYG ARI 10 1414.0 712.4 167.9 HETEROZYG TRZ 10 1343.5 351.1 20.5	OUS ARI 25 178.6 107.3 25.3 OUS TRZ 25 114.4 42.3 10.0 ARI 25 1516.4 885.6 208.7 TRZ 25 1351.7 411.7 25.1 20.7 20	Des ARI 50 136.1 73.8 17.4 TRZ 50 123.9 55.7 13.1 ARI 50 1314.7 483.7 1314.7 483.7 1316.4 431.6 1316.4 411.6	nosterol	DI level Sample average stdev SEM Sample average stdev SEM Sample average stdev SEM	DMSO 174.5 67.1 19.4 180.0 52.7 15.2 DMSO 1208.9 478.9 138.3 UMSO 1459.20 29.404 29.404 29.404	CONTR ARI 10 213.7 88.0 25.4 TRZ 10 166.7 19.3 CONTR ARI 10 1370.9 674.5 194.7 TRZ 10 1476.08 331.33 9 c f f c.08	ROL ARI 25 159.3 58.9 17.0 TRZ 25 144.6 33.2 10.2 ARI 25 1359.2 551.6 159.2 TRZ 25 1564.50 480.23 120 c ²	ARI 50 132 53 153 44 137 ARI 50 153 44 137 716 206 1346.3 287.8 292	

Supplemental Table S2B (Companion to Figure 5). Significance of sterol level differences.

ш	13C-7-DHC (significance values)				
TIOZ		ARI 10	ARI 25	ARI 50	
RA	HET ARI vs HET DMSO	2.87E-09	5.00E-14	4.23E-17	
IPI	CNT ARI vs CNT DMSO	5.84E-05	7.36E-09	7.55E-12	
AR	CNT ARI vs HET ARI	1.12E-05	2.25E-05	8.85E-04	
ШŅ		TRZ 10	TRZ 25	TRZ 50	
Ō	HET TRZ vs HET DMSO	1.65E-04	3.23E-11	6.10E-18	
ĄZO	CNT TRZ vs CNT DMSO	3.68E-03	4.17E-05	8.25E-08	
TR	CNT TRZ vs HET ARI	9.43E-04	1.68E-06	5.22E-07	

	13C-Chole	sterol (significa		
SOL		ARI 10	ARI 25	ARI 50
RAZ	HET ARI vs HET DMSO	3.09E-04	3.72E-10	2.06E-12
III	CNT ARI vs CNT DMSO	3.60E-01	1.28E-01	4.43E-04
AR	CNT ARI vs HET ARI	1.06E-02	3.80E-06	3.43E-05
ų		TRZ 10	TRZ 25	TRZ 50
Ō	HET TRZ vs HET DMSO	1.43E-03	4.71E-10	8.95E-15
₽ZO	CNT TRZ vs CNT DMSO	1.28E-01	2.56E-02	1.63E-04
TR	CNT TRZ vs HET ARI	1.98E-04	1.54E-10	1.70E-08

	13C-Lanos	sterol (significar		
GOLE		ARI 10	ARI 25	ARI 50
RAZ	HET ARI vs HET DMSO	3.94E-01	2.52E-01	6.38E-01
alali	CNT ARI vs CNT DMSO	5.05E-01	4.84E-01	5.02E-01
AR	CNT ARI vs HET ARI	8.70E-01	5.89E-01	7.72E-01
щ		TRZ 10	TRZ 25	TRZ 50
Ō	HET TRZ vs HET DMSO	8.87E-01	9.41E-01	7.51E-01
AZO	CNT TRZ vs CNT DMSO	8.96E-01	5.24E-01	3.52E-01
TR	CNT TRZ vs HET ARI	3.09E-01	2.05E-01	8.35E-01

	13C-Desmo	osterol (significance values)			
SOLE		ARI 10	ARI 25	ARI 50	
RAZ	HET ARI vs HET DMSO	6.84E-01	6.16E-01	2.94E-01	
	CNT ARI vs CNT DMSO	2.32E-01	5.62E-01	1.06E-01	
AR	CNT ARI vs HET ARI	6.71E-02	5.76E-01	8.92E-01	
ų		TRZ 10	TRZ 25	TRZ 50	
DO	HET TRZ vs HET DMSO	8.10E-01	2.97E-01	6.87E-01	
AZO	CNT TRZ vs CNT DMSO	5.98E-01	6.55E-02	2.17E-01	
TR/	CNT TRZ vs HET ARI	2.34E-01	5.09E-02	1.40E-01	

SUPPLEMENTARY MATERIALS AND METHODS

Cell Cultures. Human control and *DHCR7*-heterozygous human fibroblasts were established from skin biopsy samples. All fibroblasts were maintained in DMEM supplemented with L-glutamine, 10% fetal bovine serum (FBS; Thermo Scientific HyClone, Logan, UT), and penicillin/streptomycin at 37°C and 5% CO₂ and were used between passages 5 and 15. The experiments were performed with fibroblasts grown in 96-well plates. The cells were plated at 5×10^4 /cm² cells per well in regular medium. After overnight incubation in cell culture incubator, the medium was replaced with DMEM containing 10% delipidated serum, 500 nM 3¹³C-Lan with or without ARI and TRZ at 10, 25 and 50 nM. This medium was changed every two days and the cells were cultured for six days. At the end of experiment, Hoechst dye (10 uL of 40 ng/uL, Molecular Probes) was added to each well and the plates were incubated at 37°C for 30 min. The plates were imaged using an ImageXpress Micro XL (Molecular Devices, Sunnyvale, CA) with 10X objective. After imaging the cells were rinsed two times with PBS (pH 7.4), PBS was removed completely and the plates were frozen at -80°C until analysis. The total number of cells per well was extracted from images and used as a normalizer for sterol values. The whole study was done over the course of two years and we repeated experiments with both ARI and TRZ and different cell lines at least three times. The graphs in the Results section show one example where all twelve fibroblasts (six controls and six DHCR7-HET) were grown simultaneously and all samples processed at the same time. Each biological replicate had three technical replicates. Cultures with and without 13C-lanosterol were processed at the same time. Although DHCR7-HET fibroblasts have different mutations the level of 7-DHC was similar in all of them and the response to pharmaceutical treatment was similar.

Sterol extraction and LC-MS/MS measurements. To each well in the 96-well plate was added the internal standards (10 μ L of stock solution in MeOH: 0.87 nmol d_7 -Chol, 0.033 nmol d_7 -7-DHC, 0.069 nmol d_7 -8-DHC) and MeOH (100 μ L). The plate was gently shaken on an Orbital shaker for 30 min at room temperature to lyse the cells and extract the sterols. The supernatant was transferred to a PTAD- predeposited 96-well plate (0.2 mg per well). The plates were sealed with Easy Pierce Heat Sealing Foil (ThermoScientific AB-1720) and allowed to react for 30 min at room temperature. The sealed plates were kept in -80 °C until LC-MS analysis. The sealed plates were analyzed on an Acquity UPLC system equipped with ANSI-compliant well plate holder. The sterols (10 μ L injection) were analyzed on an UPLC C18 column (1.7 μ m, 2.1 mm × 50 mm) with 100% MeOH (0.1% v/v acetic acid) mobile phase at a flow rate of 550 µL/min and runtime of 1.0 min. A TSQ Quantum Ultra tandem mass spectrometer (ThermoFisher) was used for MS detections, and data were acquired with a Finnigan Xcalibur software package. MS/MS analysis of the PTAD derivatives was acquired in the positive ion mode using atmospheric pressure chemical ionization (APCI) and selected reaction monitoring (SRM). MS parameters were optimized for the 7-DHC-PTAD adduct and were as follows: auxiliary nitrogen gas pressure at 55 psi and sheath gas pressure at 60 psi; discharge current at 22 μ A and vaporizer temperature at 265°C. Collision induced dissociation (CID) was optimized at 12 eV under 1.0 mTorr of argon.

Sterols were analyzed by selective reaction monitoring (SRM) using the following transitions: Chol 369 \rightarrow 369, d_7 -Chol 376 \rightarrow 376, 7-DHC 560 \rightarrow 365, d_7 -7-DHC 567 \rightarrow 372, 8-DHC 558 \rightarrow 363, d_7 -8-DHC 565 \rightarrow 370, Des 592 \rightarrow 560, Lan 634 \rightarrow 602, ¹³C₃-Chol 372 \rightarrow 372, ¹³C₃-7-DHC 563 \rightarrow 368, ¹³C₃-Des 595 \rightarrow 563, and ¹³C₃-Lan 637 \rightarrow 605. ¹³C₃-8-DHC could not be analyzed due to interference from the 7-DHC isotope (m/z 561). The values for Lan and Des were calculated

relative to the d_7 -7-DHC standard using response factors of 0.93 and 1.17, respectively.(Kim *et al*, 2016) Final sterol numbers are reported as nmol/million cells.

Total RNA isolation and quantitative RT-PCR. To obtain sufficient amount of material for total RNA isolation, human fibroblasts were grown in 6-well plates under identical conditions as for lipid extraction (six days in delipidated medium with or without aripiprazole). Total RNA was isolated from cultured human fibroblasts using Trizol (Life Techologies, Rockville, MD). Total RNA (500 ng) from each sample was reverse transcribed to cDNA using a High Capacity cDNA Archive kit (Applied Biosystems, Foster City, CA). Real-time PCR was performed with a StepOnePlusTM (ThermoFisher Scientific) (25 µl reaction volume, 2X SYBR green master mix, and gene specific primers). All samples were run in quadruplicate. qPCR dissociation curve of the amplicons was performed after each qPCR run. Primers used were Dhcr7 (Qiagen QT00074606), EBP (Qiagen QT00087570), Actb (Qiagen QT00095431), RPLP0 (Qiagen QT00075012). Data from the PCRs were analyzed using the comparative cycle number determined as threshold (Ct) method (Kurrasch et al., 2004). Differential expression was calculated as $\Delta\Delta$ Ct relative to expression of either Actb or RPLP0 as normalizers. Actb and RPLP0 expression showed no change regardless of the sample type or treatment. The expression of Dhcr7 and EBP mRNAs did not change in response to aripiprazole treatment. The same response was obtained for either control or heterozygous fibroblasts. $\Delta\Delta Ct$ mean \pm SE for Dhcr7 in Dhcr^{+/-} fibroblasts treated with aripiprazole and compared to untreated cells (Actb normalizer) = 0.130 ± 0.049 ; (RPLP0 normalizer) = 0.102 \pm 0.046; $\Delta\Delta$ Ct mean \pm SE for EBP in Dhcr^{+/-} fibroblasts treated with aripiprazole and compared to untreated cells (Actb normalizer) = -0.010 ± 0.142 ; (RPLP0 normalizer) = -0.038 ± 0.147 . $\Delta\Delta$ Ct mean \pm SE for Dhcr7 in control fibroblasts treated with aripiprazole and compared to untreated cells (Actb normalizer) = 0.172 ± 0.051 ; (RPLP0

normalizer) = 0.105 ± 0.043 ; $\Delta\Delta$ Ct mean \pm SE for EBP in control fibroblasts treated with aripiprazole and compared to untreated cells (Actb normalizer) = 0.091 ± 0.038 ; (RPLP0 normalizer) = 0.024 ± 0.010 .

Kurrasch, D. M., et al., 2004. Quantitative real-time polymerase chain reaction measurement of regulators of G-protein signaling mRNA levels in mouse tissues. Methods Enzymol. 389, 3-15.

Statistical Analyses. Final sterol numbers are reported as nmol/million cells. Levels of 3^{13} C-labeled sterols were calculated using response factors relative to d7-Chol. All calculations of variability, standard deviation (SD), standard error (SE), and t-test were performed in Microsoft Excel or GraphPad Prism. Results were considered statistically significant if they had p<0.01 using two-sample assuming equal variances and two tail distribution.