Figure 1

Table Analyzed	**p-eIF2α/eIF2α 4h WT plac vs WT GBZ10**
Unpaired t test	
P value	0,1328
P value summary	ns
One- or two-tailed P value?	One-tailed
t, df	t=1,530, df=2
Mean WT placebo	0,382
Mean WT GBZ10	0,2629
95% confidence interval	-0,4539 to 0,2157
Table Analyzed	**p-eIF2α/eIF2α 4h 2b5 plac vs 2b5 GBZ10**
Unpaired t test	
P value	0,0763
P value summary	ns
One- or two-tailed P value?	One-tailed
t, df	t=2,257, df=2
Mean 2b5ho placebo	0,2703
Mean 2b5ho GBZ10	0,1806
95% confidence interval	-0,2606 to 0,08128
Table Analyzed	**p-eIF2α/eIF2α 24h WT plac vs WT GBZ10**
Unpaired t test	
P value	0,8267
P value summary	ns
One- or two-tailed P value?	Two-tailed
t, df	t=0,2488, df=2
Mean WT placebo	0,3705
Mean WT GBZ10	0,385
95% confidence interval	-0,2361 to 0,2651
Table Analyzed	**p-eIF2α/eIF2α 24h 2b5 plac vs 2b5 GBZ10**
Unpaired t test	
P value	0,7169
P value summary	ns
One- or two-tailed P value?	Two-tailed
t, df	t=0,4174, df=2
Mean 2b5ho placebo	0,2743
Mean 2b5ho GBZ10	0,2859
95% confidence interval	-0,1081 to 0,1313
Table Analyzed	***Ddit3* 4h WT plac vs WT GBZ10**
Unpaired t test	
P value	0,2993
P value summary	ns
One- or two-tailed P value?	One-tailed
t, df	t=0,6198, df=2
Mean WT placebo	0,01832
Mean WT GBZ10	0,0167
95% confidence interval	-0,01283 to 0,009595
Table Analyzed	***Ddit3* 4h 2b5 plac vs 2b5 GBZ10**
Unpaired t test	
P value	0,0132
P value summary	ns
One- or two-tailed P value?	One-tailed
t, df	t=6,041, df=2
Mean 2b5ho placebo	0,03433
Mean 2b5ho GBZ10	0,02837
95% confidence interval	-0,01020 to -0,001715
Table Analyzed	***Ddit3* 24h WT plac vs WT GBZ10**
Unpaired t test	
P value	0,2585
P value summary	ns
One- or two-tailed P value?	One-tailed
t, df	t=0,7800, df=2
Mean WT placebo	0,01862
Mean WT GBZ10	0,01788
95% confidence interval	-0,004822 to 0,003342
Table Analyzed	***Ddit3* 24h 2b5 plac vs 2b5 GBZ10**
Unpaired t test	
P value	0,0293
P value summary	*
One- or two-tailed P value?	One-tailed
t, df	t=3,946, df=2
Mean 2b5ho placebo	0,03492
Mean 2b5ho GBZ10	0,02526
95% confidence interval	-0,02018 to 0,0008721
Table Analyzed	***Trib3* 4h WT plac vs WT GBZ10**
Unpaired t test	
P value	0,1227
P value summary	ns
One- or two-tailed P value?	One-tailed
t, df	t=1,626, df=2
Mean WT placebo	0,00625
Mean WT GBZ10	0,007055
95% confidence interval	-0,001325 to 0,002935
Table Analyzed	***Trib3* 4h 2b5 plac vs 2b5 GBZ10**
Unpaired t test	
P value	0,1106
P value summary	ns
One- or two-tailed P value?	One-tailed
t, df	t=1,756, df=2
Mean 2b5ho placebo	0,07922
Mean 2b5ho GBZ10	0,06332
95% confidence interval	-0,05485 to 0,02306
Table Analyzed	***Trib3* 24h WT plac vs WT GBZ10**
Unpaired t test	
P value	0,4836
P value summary	ns
One- or two-tailed P value?	One-tailed
t, df	t=0,04640, df=2
Mean WT placebo	0,005235
Mean WT GBZ10	0,00517
95% confidence interval	-0,006093 to 0,005963
Table Analyzed	***Trib3* 24h 2b5 plac vs 2b5 GBZ10**
Unpaired t test	
P value	0,0051
P value summary	**
One- or two-tailed P value?	One-tailed
t, df	t=9,853, df=2
Mean 2b5ho placebo	0,05951
Mean 2b5ho GBZ10	0,03938
95% confidence interval	-0,02891 to -0,01134

Table Analyzed	***Gadd34* 4h WT plac vs WT GBZ10**
Unpaired t test	
P value	0,01
P value summary	*
One- or two-tailed P value?	One-tailed
t, df	t=6,960, df=2
Mean WT placebo	0,02111
Mean WT GBZ10	0,02955
95% confidence interval	0,003222 to 0,01366

Table Analyzed	***Gadd34* 4h 2b5 plac vs 2b5 GBZ10**
Unpaired t test	
P value	0,0339
P value summary	*
One- or two-tailed P value?	One-tailed
t, df	t=3,642, df=2
Mean 2b5ho placebo	0,0263
Mean 2b5ho GBZ10	0,0337
95% confidence interval	-0,001342 to 0,01615

Table Analyzed	***Gadd34* 24h WT plac vs WT GBZ10**
Unpaired t test	
P value	0,3501
P value summary	ns
One- or two-tailed P value?	One-tailed
t, df	t=0,4446, df=2
Mean WT placebo	0,0181
Mean WT GBZ10	0,01726
95% confidence interval	-0,009023 to 0,007333

Table Analyzed	***Gadd34* 24h 2b5 plac vs 2b5 GBZ10**
Unpaired t test	
P value	0,0834
P value summary	ns
One- or two-tailed P value?	One-tailed
t, df	t=2,131, df=2
Mean 2b5ho placebo	0,02418
Mean 2b5ho GBZ10	0,02625
95% confidence interval	-0,002110 to 0,006250

Figure 2

Table Analyzed	**p-eIF2α/eIF2α 4h placebo vs S1**
Unpaired t test	
P value	0,0569
P value summary	ns
One- or two-tailed P value?	One-tailed
t, df	t=1,913, df=5
Mean of placebo	0,07091
Mean of S1 4,5	0,04179
95% confidence interval	-0,06824 to 0,01000
Table Analyzed	**p-eIF2α/eIF2α 4h plac vs GBZ4,5**
Unpaired t test	
P value	0,0725
P value summary	ns
One- or two-tailed P value?	One-tailed
t, df	t=1,725, df=5
Mean of placebo	0,07091
Mean of GBZ 4.5	0,04773
95% confidence interval	-0,05771 to 0,01136
Table Analyzed	**p-eIF2α/eIF2α 4h plac vs GBZ10**
Unpaired t test	
P value	0,0391
P value summary	*
One- or two-tailed P value?	One-tailed
t, df	t=2,354, df=4
Mean of placebo	0,07091
Mean of GBZ 10	0,03487
95% confidence interval	-0,07853 to 0,006459
Table Analyzed	**p-eIF2α/eIF2α 24h plac vs S1**
Mann Whitney test	
P value	0,5
Exact or approximate P value?	Exact
P value summary	ns
One- or two-tailed P value?	One-tailed
Sum of ranks in column A,B	12 , 16
Mann-Whitney U	6
Median of placebo	0,05321, n=3
Median of S1 4,5	0,04328, n=4
Difference: Actual	-0,009931
Difference: Hodges-Lehmann	-0,00393
Table Analyzed	**p-eIF2α/eIF2α 24h plac vs GBZ4,5**
Unpaired t test	
P value	0,1794
P value summary	ns
One- or two-tailed P value?	One-tailed
t, df	t=1,010, df=5
Mean of placebo	0,05421
Mean of GBZ 4.5	0,04648
95% confidence interval	-0,02740 to 0,01194
Table Analyzed	**p-eIF2α/eIF2α 24h plac vs GBZ10**
Unpaired t test	
P value	0,2069
P value summary	ns
One- or two-tailed P value?	One-tailed
t, df	t=0,8910, df=5
Mean of placebo	0,05421
Mean of GBZ 10	0,04637
95% confidence interval	-0,03046 to 0,01478

Figure 4, A

Two-way RM ANOVA	Matching: Stacked							
Alpha	0,05							
				WT: n=8				
Table Analyzed	**WT plac vs VWM placebo body weight**			VWM: n=16				
Source of Variation	% of total variation	P value	P value summary	Significant?	Geisser-Greenhouse's epsilon			
Time x Genotype	2,417	<0,0001	****	Yes				
Time	4,867	<0,0001	****	Yes	0,2083			
Genotype	84,45	<0,0001	****	Yes				
Subject	9,008	<0,0001	****	Yes				
Two-way RM ANOVA	Matching: Stacked							
Alpha	0,05							
Table Analyzed	**WT body weight - treatment vs plac**							
Source of Variation	% of total variation	P value	P value summary	Significant?				
Time x Treatment	4,39	<0,0001	****	Yes				
Time	32,68	<0,0001	****	Yes				
Treatment	27,45	0,0004	***	Yes				
Subject	30,42	<0,0001	****	Yes				
Dunnett's multiple comparisons test	Mean Diff,	95,00% CI of diff,	Significant?	Summary	Adjusted P Value			
Placebo-WT vs. Guanabenz 4.5-WT	3,594	1,760 to 5,428	Yes	***	0,0001			
Placebo-WT vs. Sephin1-WT	1,128	-0,7061 to 2,962	No	ns	0,3101			
Placebo-WT vs. Guanabenz 10-WT	1,15	-0,6840 to 2,984	No	ns	0,2957			
Test details	Mean 1	Mean 2	Mean Diff,	SE of diff,	N1	N2	q	DF
Placebo-WT vs. Guanabenz 4.5-WT	25,74	22,14	3,594	0,7385	176	176	4,866	28
Placebo-WT vs. Sephin1-WT	25,74	24,61	1,128	0,7385	176	176	1,527	28
Placebo-WT vs. Guanabenz 10-WT	25,74	24,59	1,15	0,7385	176	176	1,557	28
Two-way RM ANOVA	Matching: Stacked							
Alpha	0,05							
Table Analyzed	**VWM body weight - treatment vs plac**							
Source of Variation	% of total variation	P value	P value summary	Significant?				
Time x Treatment	7,303	<0,0001	****	Yes				
Time	17,57	<0,0001	****	Yes				
Treatment	10,98	0,0119	*	Yes				
Subject	54,26	<0,0001	****	Yes				
Dunnett's multiple comparisons test	Predicted (LS) mean diff,	95,00% CI of diff,	Significant?	Summary	Adjusted P Value			
Placebo-2b42b5 vs. Guanabenz 4.5-2b42b5	-0,7324	-1,594 to 0,1292	No	ns	0,1125			
Placebo-2b42b5 vs. Sephin1-2b42b5	0,4364	-0,4112 to 1,284	No	ns	0,4653			
Placebo-2b42b5 vs. Guanabenz 10--2b42b5	-0,381	-1,229 to 0,4666	No	ns	0,5703			
Test details	Predicted (LS) mean 1	Predicted (LS) mean	Predicted (LS) mean dif	SE of diff,	N1	N2	q	DF
Placebo-2b42b5 vs. Guanabenz 4.5-2b42b5	15,38	16,11	-0,7324	0,3572	352	330	2,051	59
Placebo-2b42b5 vs. Sephin1-2b42b5	15,38	14,94	0,4364	0,3514	352	352	1,242	59
Placebo-2b42b5 vs. Guanabenz 10--2b42b5	15,38	15,76	-0,381	0,3514	352	352	1,084	59

Figure 4, B

Kruskal-Wallis test						
P value	<0,0001					
Exact or approximate P value?	Approximate					
P value summary	****					
Number of groups	4					
Kruskal-Wallis statistic	21,23					
Dunn's multiple comparisons test	Mean rank diff,	Significant?	Summary	Adjusted P Valu	A-?	
placebo vs. guanabenz (4.5mg/kg)	18,33	Yes	**	0,0085	B	guanabenz (4,5mg/kg)
placebo vs. guanabenz (10mg/kg)	10,75	No	ns	0,2251	C	guanabenz (10mg/kg)
placebo vs. sephin1	-7,75	No	ns	0,5981	D	sephin1
Test details	Mean rank 1	Mean rank 2	Mean rank diff,	n1	n2	Z
placebo vs. guanabenz (4.5mg/kg)	37,13	18,8	18,33	16	15	2,985
placebo vs. guanabenz (10mg/kg)	37,13	26,38	10,75	16	16	1,78
placebo vs. sephin1	37,13	44,88	-7,75	16	16	1,283

Figure 4, C

Table Analyzed	**WT-VWM placebo slips on BB**							
Unpaired t test with Welch's correction								
P value	<0,0001							
P value summary	****							
One- or two-tailed P value?	One-tailed							
Welch-corrected t, df	t=6,788, df=15,63							
Mean WT placebo	0,5							
Mean VWM placebo	9,375							
95% confidence interval	6,098 to 11,65							
Table Analyzed	**WT treatment, slips on BB**							
Kruskal-Wallis test								
P value	0,1546							
Exact or approximate P value?	Approximate							
P value summary	ns							
Number of groups	4							
Kruskal-Wallis statistic	5,247							
Dunn's multiple comparisons test	Mean rank diff,	Significant?	Summary	Adjusted P Valu	A-?			
placebo vs. sephin1	-0,625	No	ns	>0,9999	B	sephin1		
placebo vs. Gbz 10 mg/kg	5,813	No	ns	0,3758	C	Gbz 10 mg/kg		
placebo vs. 2b4he2b5ho - gbz (d4.5)	5,813	No	ns	0,3758	D	2b4he2b5ho - gbz (d4,5)		
Table Analyzed	**VWM treatment, slips on BB**							
Welch's ANOVA test								
W (DFn, DFd)	31,78 (3,000, 25,91)							
P value	<0,0001							
P value summary	****							
Dunnett's T3 multiple comparisons test	Mean Diff,	95,00% CI of diff,	Significant?	Summary	Adjusted P Value	A-?		
placebo vs. sephin1	-1,492	-7,076 to 4,092	No	ns	0,833	B	sephin1	
placebo vs. Gbz 10 mg/kg	6	1,728 to 10,27	Yes	**	0,0015	C	Gbz 10 mg/kg	
placebo vs. 2b4he2b5ho - gbz (d4.5)	8,775	4,862 to 12,69	Yes	****	<0,0001	D	2b4he2b5ho - gbz (d4,5)	
Test details	Mean 1	Mean 2	Mean Diff,	SE of diff,	n1	n2	t	DF
placebo vs. sephin1	9,375	10,87	-1,492	1,973	16	15	0,7561	28,1
placebo vs. Gbz 10 mg/kg	9,375	3,375	6	1,491	16	16	4,024	23,9
placebo vs. 2b4he2b5ho - gbz (d4.5)	9,375	0,6	8,775	1,308	16	15	6,71	15,7

Figure 5

Table Analyzed	**WT-VWM placebo**							
Nested t test								
P value	0,0003							
P value summary	***							
One- or two-tailed P value?	Two-tailed							
t, df	t=8,958, df=5							
F, DFn, Dfd	80,24, 1, 5							
Mean of WT	10,4							
Mean of VWM	37,45							
95% confidence interval	-34,81 to -19,29							
Random effects	SD	Variance						
Variation within subcolumns	6,428	41,32						
Variation among subcolumn means	2,002	4,008						
Table Analyzed	**WT treatment effect**							
ANOVA summary								
F	3,881							
P value	0,1474							
P value summary	ns							
ANOVA table	SS	DF	MS	F (DFn, DFd)	P value			
Treatment (between columns)	55,22	3	18,41	F (3, 3) = 3,881	P=0,1474			
Residual (within columns)	14,23	3	4,743					
Total	69,45	6						
Table Analyzed	**VWM treatment effect**							
Nested one-way ANOVA								
P value	0,0056							
P value summary	**							
F, DFn, Dfd	7,349, 3, 11							
Random effects	SD	Variance						
Variation within subcolumns	7,074	50,04						
Variation among subcolumn means	1,933	3,737						
Dunnett's multiple comparisons test	Mean Diff,	95,00% CI of diff,	Significant?	Summary	Adjusted P Value			
placebo vs. S1	-3,804	-12,17 to 4,565	No	ns	0,5057			
placebo vs. GBZ W10	-2,426	-8,956 to 4,103	No	ns	0,6483			
placebo vs. GBZ D4.5	8,617	1,530 to 15,70	Yes	*	0,0179			
Test details	Mean 1	Mean 2	Mean Diff,	SE of diff,	N1	N2	q	DF
placebo vs. S1	37,42	41,23	-3,804	3,046	27	10	1,249	11
placebo vs. GBZ W10	37,42	39,85	-2,426	2,377	27	24	1,021	11
placebo vs. GBZ D4.5	37,42	28,8	8,617	2,58	27	18	3,34	11

Figure 6

Table Analyzed	**WT VWM placebo -weighed mean**							
Unpaired t test								
P value	0,0009							
P value summary	***							
One- or two-tailed P value?	Two-tailed							
t, df	t=6,028, df=6							
Table Analyzed	**WT (caudal&cranial) ratio**							
ANOVA summary								
F	0,6863							
P value	0,5852							
P value summary	ns							
ANOVA table	SS	DF	MS	F (DFn, DFd)	P value			
Treatment (between columns)	3,82	3	1,273	F (3, 8) = 0,686	P=0,5852			
Residual (within columns)	14,84	8	1,855					
Total	18,66	11						
Table Analyzed	**VWM (caudal&cranial) ratio weighed mean**							
ANOVA summary								
F	2,44							
P value	0,1021							
P value summary	ns							
ANOVA table	SS	DF	MS	F (DFn, DFd)	P value			
Treatment (between columns)	882,5	3	294,2	F (3, 16) = 2,44	P=0,1021			
Residual (within columns)	1929	16	120,6					
Total	2812	19						
Table Analyzed	**VWM- cranial weighed average**							
Data sets analyzed	A-D							
ANOVA summary								
F	1,459							
P value	0,263							
P value summary	ns							
ANOVA table	SS	DF	MS	F (DFn, DFd)	P value			
Treatment (between columns)	478,9	3	159,6	F (3, 16) = 1,45	P=0,2630			
Residual (within columns)	1750	16	109,4					
Total	2229	19						
Table Analyzed	**VWM- caudal weighed average**							
ANOVA summary								
F	3,439							
P value	0,0421							
P value summary	*							
Dunnett's multiple comparisons test	Mean Diff,	95,00% CI of diff,	Below threshold?	Summary	Adjusted P Value	A-?		
placebo vs. GBZ D4.5	24,73	2,405 to 47,06	Yes	*	0,0288	B	GBZ D4,5	
placebo vs. GBZ W 10	17,11	-5,217 to 39,43	No	ns	0,1535	C	GBZ W 10	
placebo vs. S1 D4.5	4,87	-17,46 to 27,20	No	ns	0,8956	D	S1 D4,5	
Test details	Mean 1	Mean 2	Mean Diff,	SE of diff,	n1	n2	q	DF
placebo vs. GBZ D4.5	45,53	20,8	24,73	8,611	5	5	2,872	16
placebo vs. GBZ W 10	45,53	28,43	17,11	8,611	5	5	1,987	16
placebo vs. S1 D4.5	45,53	40,66	4,87	8,611	5	5	0,5655	16
ANOVA table	SS	DF	MS	F (DFn, DFd)	P value			
Treatment (between columns)	1913	3	637,6	F (3, 16) = 3,43	P=0,0421			
Residual (within columns)	2966	16	185,4					
Total	4879	19						
Table Analyzed	**WT - cranial weighed average**							
ANOVA summary								
F	1,148							
P value	0,3872							
P value summary	ns							
Dunnett's multiple comparisons test	Mean Diff,	95,00% CI of diff,	Below threshold?	Summary	Adjusted P Value	A-?		
placebo vs. GBZ D4.5	-0,52	-4,101 to 3,061	No	ns	0,9517	B	GBZ D4,5	
placebo vs. GBZ W 10	-0,6867	-4,268 to 2,895	No	ns	0,9009	C	GBZ W 10	
placebo vs. S1 D4.5	-2,193	-5,775 to 1,388	No	ns	0,2551	D	S1 D4,5	
Test details	Mean 1	Mean 2	Mean Diff,	SE of diff,	n1	n2	q	DF
placebo vs. GBZ D4.5	0,7133	1,233	-0,52	1,244	3	3	0,4181	8
placebo vs. GBZ W 10	0,7133	1,4	-0,6867	1,244	3	3	0,5522	8
placebo vs. S1 D4.5	0,7133	2,907	-2,193	1,244	3	3	1,764	8
ANOVA table	SS	DF	MS	F (DFn, DFd)	P value			
Treatment (between columns)	7,988	3	2,663	F (3, 8) = 1,148	P=0,3872			
Residual (within columns)	18,56	8	2,32					
Total	26,55	11						
Table Analyzed	**WT- caudal weighed average**							
ANOVA summary								
F	0,481							
P value	0,7045							
P value summary	ns							
Dunnett's multiple comparisons test	Mean Diff,	95,00% CI of diff,	Below threshold?	Summary	Adjusted P Value	A-?		
placebo vs. GBZ D4.5	-0,34	-4,774 to 4,094	No	ns	0,992	B	GBZ D4,5	
placebo vs. GBZ W 10	-1,71	-6,144 to 2,724	No	ns	0,5753	C	GBZ W 10	
placebo vs. S1 D4.5	-0,9933	-5,428 to 3,441	No	ns	0,8559	D	S1 D4,5	
Test details	Mean 1	Mean 2	Mean Diff,	SE of diff,	n1	n2	q	DF
placebo vs. GBZ D4.5	1,527	1,867	-0,34	1,54	3	3	0,2208	8
placebo vs. GBZ W 10	1,527	3,237	-1,71	1,54	3	3	1,11	8
placebo vs. S1 D4.5	1,527	2,52	-0,9933	1,54	3	3	0,6451	8
ANOVA table	SS	DF	MS	F (DFn, DFd)	P value			
Treatment (between columns)	5,133	3	1,711	F (3, 8) = 0,481	P=0,7045			
Residual (within columns)	28,45	8	3,557					
Total	33,59	11						

Figure 8

Table Analyzed	**Genotype-plc Ratio p-eIF2a**							
Mann Whitney test								
P value	0,0357							
Exact or approximate P value?	Exact							
P value summary	*							
One- or two-tailed P value?	One-tailed							
Sum of ranks in column A,B	15 , 21							
Mann-Whitney U	0							
Difference between medians								
Median of WT	0,06963, n=2							
Median of VWM	0,02652, n=6							
Difference: Actual	-0,04311							
Difference: Hodges-Lehmann	-0,04268							
Table Analyzed	**WT treatment effect Ratio p-eIF2a**							
ANOVA summary								
F	6,306							
P value	0,0375							
P value summary	*							
Dunnett's multiple comparisons test	Mean Diff,	95,00% CI of diff,	Below threshold?	Summary	Adjusted P Value	A-?		
Plc vs. dGBZ4.5	0,01967	-0,008833 to 0,04817	No	ns	0,1581	B	dGBZ4,5	
Plc vs. wGBZ10	0,02435	-0,004155 to 0,05285	No	ns	0,0847	C	wGBZ10	
Plc vs. S1	-0,004856	-0,03087 to 0,02116	No	ns	0,8681	D	S1	
Test details	Mean 1	Mean 2	Mean Diff,	SE of diff,	n1	n2	q	DF
Plc vs. dGBZ4.5	0,06963	0,04996	0,01967	0,008695	2	2	2,262	5
Plc vs. wGBZ10	0,06963	0,04528	0,02435	0,008695	2	2	2,8	5
Plc vs. S1	0,06963	0,07448	-0,004856	0,007937	2	3	0,6118	5
ANOVA table	SS	DF	MS	F (DFn, DFd)	P value			
Treatment (between columns)	0,00143	3	0,0004768	F (3, 5) = 6,306	P=0,0375			
Residual (within columns)	0,000378	5	7,56E-05					
Total	0,001808	8						
Table Analyzed	**VWM treatment effect ratio p-eIF2a**							
Kruskal-Wallis test								
P value	0,0207							
Exact or approximate P value?	Approximate							
P value summary	*							
Number of groups	4							
Kruskal-Wallis statistic	9,762							
Dunn's multiple comparisons test	Mean rank diff,	Significant?	Summary	Adjusted P Valu	A-?			
Plc vs. dGBZ4.5	9,833	Yes	*	0,0361	B	dGBZ4,5		
Plc vs. wGBZ10	9	No	ns	0,0646	C	wGBZ10		
Plc vs. S1	11,13	Yes	*	0,0201	D	S1		
Test details	Mean rank 1	Mean rank 2	Mean rank diff,	n1	n2	Z		
Plc vs. dGBZ4.5	19,33	9,5	9,833	6	6	2,511		
Plc vs. wGBZ10	19,33	10,33	9	6	6	2,298		
Plc vs. S1	19,33	8,2	11,13	6	5	2,711		
Table Analyzed	**WT-VWM placebo *Ddit3***							
Unpaired t test								
P value	<0,0001							
P value summary	****							
Significantly different (P < 0.05)?	Yes							
One- or two-tailed P value?	One-tailed							
t, df	t=9,345, df=6							
Mean WT	0,06455							
Mean VWM	0,2682							
95% confidence interval	0,1503 to 0,2570							
Table Analyzed	**WT treatment effects *Ddit3***							
ANOVA summary								
F	0,7992							
P value	0,5452							
P value summary	ns							
ANOVA table	SS	DF						
Treatment (between columns)	0,00008096	3						
Residual (within columns)	0,0001688	5						
Total	0,0002498	8						
Table Analyzed	**VWM treatment effects *Ddit3***							
ANOVA summary								
F	5,461							
P value	0,0076							
P value summary	**							
ANOVA table	SS	DF	Significant?	Summary	Adjusted P Value	A-?		
Treatment (between columns)	0,02498	3	No	ns	0,9999	B	Seph1 4,5 mg/kg	
Residual (within columns)	0,02744	18	Yes	**	0,0098	C	Gbz 10 mg/kg	
Total	0,05242	21	Yes	*	0,0458	D	Gbz 4,5 mg/kg	
Dunnett's multiple comparisons test	Mean Diff,	95,00% CI of diff,	0,001583	0,0252	6	4	0,06282	18
Placebo vs. Seph1 4,5 mg/kg	0,001583	-0,06322 to 0,06639	0,07542	0,02254	6	6	3,346	18
Placebo vs. Gbz 10 mg/kg	0,07542	0,01745 to 0,1334	0,05895	0,02254	6	6	2,615	18
Placebo vs. Gbz 4,5 mg/kg	0,05895	0,0009859 to 0,1169						
Test details	Mean 1	Mean 2						
Placebo vs. Seph1 4,5 mg/kg	0,2682	0,2666						
Placebo vs. Gbz 10 mg/kg	0,2682	0,1928						
Placebo vs. Gbz 4,5 mg/kg	0,2682	0,2092						
Table Analyzed	**WT-VWM placebo *Trib3***							
Unpaired t test								
P value	<0,0001							
P value summary	****							
One- or two-tailed P value?	One-tailed							
t, df	t=13,18, df=6							
Mean WT	0,0092							
Mean VWM	0,3998							
95% confidence interval	0,3181 to 0,4630							
Table Analyzed	**WT treatment effects *Trib3***							
ANOVA summary								
F	0,9784							
P value	0,4727							
P value summary	ns							
ANOVA table	SS	DF						
Treatment (between columns)	0,000006076	3						
Residual (within columns)	0,00001035	5						
Total	0,00001643	8						

Table Analyzed	**VWM treatment effects *Trib3***							
Welch's ANOVA test								
W (DFn, DFd)	5,409 (3,000, 8,400)							
P value	0,0233							
P value summary	*							
Dunnett's T3 multiple comparisons test	Mean Diff,	95,00% CI of diff,	Significant?	Summary	Adjusted P Value	A-?		
Placebo vs. Seph1 4,5 mg/kg	0,03603	-0,3444 to 0,4165	No	ns	0,924	B	Seph1 4,5 mg/kg	
Placebo vs. Gbz 10 mg/kg	0,07842	0,0004601 to 0,1564	Yes	*	0,0242	C	Gbz 10 mg/kg	
Placebo vs. Gbz 4,5 mg/kg	0,1123	0,01575 to 0,2089	Yes	*	0,0109	D	Gbz 4,5 mg/kg	
Test details	Mean 1	Mean 2	Mean Diff,	SE of diff,	n1	n2	t	DF
Placebo vs. Seph1 4,5 mg/kg	0,3998	0,3637	0,03603	0,06648	6	4	0,5419	3,38
Placebo vs. Gbz 10 mg/kg	0,3998	0,3213	0,07842	0,02403	6	6	3,263	9,92
Placebo vs. Gbz 4,5 mg/kg	0,3998	0,2874	0,1123	0,02905	6	6	3,867	8,76
Table Analyzed	**WT-VWM placebo Gadd34**							
Unpaired t test								
P value	<0,0001							
P value summary	****							
One- or two-tailed P value?	One-tailed							
t, df	t=11,41, df=6							
Mean WT	0,0873							
Mean VWM	0,2447							
95% confidence interval	0,1236 to 0,1911							
Table Analyzed	**WT treatment effects Gadd34**							
ANOVA summary								
F	3,998							
P value	0,085							
P value summary	ns							
ANOVA table	SS	DF						
Treatment (between columns)	0,0009824	3						
Residual (within columns)	0,0004096	5						
Total	0,001392	8						
Table Analyzed	**VWM treatment effects Gadd34**							
ANOVA summary								
F	1,52							
P value	0,2434							
P value summary	ns							
ANOVA table	SS	DF						
Treatment (between columns)	0,009111	3						
Residual (within columns)	0,03596	18						
Total	0,04508	21						

Figure 9

Table Analyzed	**min α2 CHOP, without ER stress**							
ANOVA summary								
F	1,343							
P value	0,3086							
P value summary	ns							
ANOVA table	SS	DF	MS	F (DFn, DFd)	P value			
Treatment (between columns)	0,04447	2	0,02224	F (2, 9) = 1,343	P=0,3086			
Residual (within columns)	0,149	9	0,01655					
Total	0,1934	11						
Table Analyzed	**plus α2 CHOP, without ER stress**							
ANOVA summary								
F	1,039							
P value	0,3926							
P value summary	ns							
ANOVA table	SS	DF	MS	F (DFn, DFd)	P value			
Treatment (between columns)	0,009861	2	0,00493	F (2, 9) = 1,039	P=0,3926			
Residual (within columns)	0,04271	9	0,004745					
Total	0,05257	11						
Table Analyzed	**min α2 CHOP, ER stress**							
Mann Whitney test								
P value	0,0011							
Exact or approximate P value?	Exact							
P value summary	**							
One- or two-tailed P value?	One-tailed							
Sum of ranks in column A,E	21 , 57							
Mann-Whitney U	0							
Median of DMSO	0,07936, n=6							
Median of TG	1,414, n=6							
Difference: Actual	1,334							
Difference: Hodges-Lehmann	1,343							
Table Analyzed	**min α2 CHOP, ER stress**							
ANOVA summary								
F	4,735							
P value	0,0255							
P value summary	*							
ANOVA table	SS	DF	MS	F (DFn, DFd)	P value			
Treatment (between columns)	2,968	2	1,484	F (2, 15) = 4,73	P=0,0255			
Residual (within columns)	4,702	15	0,3135					
Total	7,67	17						
Dunnett's multiple comparisons test	Mean Diff,	95,00% CI of diff,	Below threshold?	Summary	Adjusted P Value	E-?		
TG 0,33µM vs. TG + S1	0,856	0,06751 to 1,644	Yes	*	0,0334	F	TG + S1	
TG 0,33µM vs. TG + GBZ	0,8667	0,07823 to 1,655	Yes	*	0,0313	G	TG + GBZ	
Test details	Mean 1	Mean 2	Mean Diff,	SE of diff,	n1	n2	q	DF
TG 0,33µM vs. TG + S1	1,367	0,5107	0,856	0,3232	6	6	2,648	15
TG 0,33µM vs. TG + GBZ	1,367	0,5	0,8667	0,3232	6	6	2,681	15
Table Analyzed	**plus α2 CHOP, ER stress**							
Unpaired t test								
P value	0,0063							
P value summary	**							
One- or two-tailed P value?	One-tailed							
t, df	t=3,031, df=10							
Mean of DMSO	0,1349							
Mean of TG	0,5198							
95% confidence interval	0,1020 to 0,6678							
Table Analyzed	**plus α2 CHOP, ER stress**							
Kruskal-Wallis test								
P value	0,0327							
Exact or approximate P value?	Exact							
P value summary	*							
Number of groups	3							
Kruskal-Wallis statistic	6,468							
Dunn's multiple comparisons test	Mean rank diff,	Significant?	Summary	Adjusted P Valu	E-?			
TG 0,33µM vs. TG + S1	6,333	No	ns	0,0798	F	TG + S1		
TG 0,33µM vs. TG + GBZ	7,167	Yes	*	0,0401	G	TG + GBZ		
Test details	Mean rank 1	Mean rank 2	Mean rank diff,	n1	n2	Z		
TG 0,33µM vs. TG + S1	14	7,667	6,333	6	6	2,055		
TG 0,33µM vs. TG + GBZ	14	6,833	7,167	6	6	2,325		
Table Analyzed	**min α2 Trib3, without ER stress**							
ANOVA summary								
F	0,7322							
P value	0,5074							
P value summary	ns							
ANOVA table	SS	DF	MS	F (DFn, DFd)	P value			
Treatment (between columns)	0,1282	2	0,0641	F (2, 9) = 0,732	P=0,5074			
Residual (within columns)	0,7879	9	0,08755					
Total	0,9161	11						
Table Analyzed	**plus α2 Trib3, without ER stress**							
ANOVA summary								
F	0,7063							
P value	0,5189							
P value summary	ns							
ANOVA table	SS	DF	MS	F (DFn, DFd)	P value			
Treatment (between columns)	0,07069	2	0,03535	F (2, 9) = 0,706	P=0,5189			
Residual (within columns)	0,4504	9	0,05004					
Total	0,5211	11						
Table Analyzed	**min α2 Trib3, ER stress**							
Unpaired t test with Welch's correction								
P value	<0,0001							
P value summary	****							
One- or two-tailed P value?	One-tailed							
Welch-corrected t, df	t=12,45, df=5,435							
Mean of DMSO	0,3776							
Mean of TG	2,666							
95% confidence interval	1,827 to 2,750							
Table Analyzed	**min α2 Trib3, ER stress**							
ANOVA summary								
F	4,894							
P value	0,0231							
P value summary	*							
ANOVA table	SS	DF	MS	F (DFn, DFd)	P value			
Treatment (between columns)	3,531	2	1,766	F (2, 15) = 4,89	P=0,0231			
Residual (within columns)	5,412	15	0,3608					
Total	8,944	17						
Dunnett's multiple comparisons test	Mean Diff,	95,00% CI of diff,	Below threshold?	Summary	Adjusted P Value	E-?		
TG 0,33µM vs. TG + S1	1,076	0,2303 to 1,922	Yes	*	0,0135	F	TG + S1	
TG 0,33µM vs. TG + GBZ	0,6567	-0,1892 to 1,503	No	ns	0,1357	G	TG + GBZ	
Test details	Mean 1	Mean 2	Mean Diff,	SE of diff,	n1	n2	q	DF
TG 0,33µM vs. TG + S1	2,666	1,59	1,076	0,3468	6	6	3,103	15
TG 0,33µM vs. TG + GBZ	2,666	2,009	0,6567	0,3468	6	6	1,894	15

Table Analyzed	**plus α2 Trib3, ER stress**
Unpaired t test	
P value	<0,0001
P value summary	****
One- or two-tailed P value?	One-tailed
t, df	t=17,48, df=10
Mean of DMSO	0,4336
Mean of TG	1,727
95% confidence interval	1,128 to 1,458

Table Analyzed	**plus α2 Trib3, ER stress**
ANOVA summary	
F	14,56
P value	0,0003
P value summary	***

ANOVA table	SS	DF	MS	F (DFn, DFd)	P value			
Treatment (between columns)	2,845	2	1,422	F (2, 15) = 14,5(	P=0,0003			
Residual (within columns)	1,466	15	0,0977					
Total	4,31	17						
Dunnett's multiple comparisons test	Mean Diff,	95,00% CI of diff,	Below threshold?	Summary	Adjusted P Value	E-?		
TG 0,33µM vs. TG + S1	0,842	0,4018 to 1,282	Yes	***	0,0006	F	TG + S1	
TG 0,33µM vs. TG + GBZ	0,8447	0,4045 to 1,285	Yes	***	0,0006	G	TG + GBZ	
Test details	Mean 1	Mean 2	Mean Diff,	SE of diff,	n1	n2	q	DF
TG 0,33µM vs. TG + S1	1,727	0,8848	0,842	0,1805	6	6	4,666	15
TG 0,33µM vs. TG + GBZ	1,727	0,8821	0,8447	0,1805	6	6	4,68	15

Table Analyzed	**min α2 Gadd34, without ER stress**
Kruskal-Wallis test	
P value	0,3697
Exact or approximate P value?	Exact
P value summary	ns
Number of groups	3
Kruskal-Wallis statistic	2,192

Table Analyzed	**plus α2 Gadd34, without ER stress**
Kruskal-Wallis test	
P value	0,4803
Exact or approximate P value?	Exact
P value summary	ns
Number of groups	3
Kruskal-Wallis statistic	1,654

Table Analyzed	**min α2 Gadd34, ER stress**
Unpaired t test with Welch's correction	
P value	0,0001
P value summary	***
One- or two-tailed P value?	One-tailed
Welch-corrected t, df	t=8,848, df=5,077
Mean of DMSO	0,1013
Mean of TG	1,453
95% confidence interval	0,9606 to 1,742

Table Analyzed	**min α2 Gadd34, ER stress**
ANOVA summary	
F	7,718
P value	0,005
P value summary	**

ANOVA table	SS	DF	MS	F (DFn, DFd)	P value			
Treatment (between columns)	1,568	2	0,7838	F (2, 15) = 7,71(	P=0,0050			
Residual (within columns)	1,523	15	0,1016					
Total	3,091	17						
Dunnett's multiple comparisons test	Mean Diff,	95,00% CI of diff,	Below threshold?	Summary	Adjusted P Value	E-?		
TG 0,33µM vs. TG + S1	0,5304	0,08158 to 0,9792	Yes	*	0,021	F	TG + S1	
TG 0,33µM vs. TG + GBZ	0,6905	0,2417 to 1,139	Yes	**	0,0036	G	TG + GBZ	
Test details	Mean 1	Mean 2	Mean Diff,	SE of diff,	n1	n2	q	DF
TG 0,33µM vs. TG + S1	1,453	0,9224	0,5304	0,184	6	6	2,883	15
TG 0,33µM vs. TG + GBZ	1,453	0,7622	0,6905	0,184	6	6	3,753	15

Table Analyzed	**plus α2 Gadd34, ER stress**
Unpaired t test	
P value	<0,0001
P value summary	****
One- or two-tailed P value?	One-tailed
t, df	t=10,24, df=10
Mean of DMSO	0,1186
Mean of TG	0,7364
95% confidence interval	0,4835 to 0,7522

Table Analyzed	**plus α2 Gadd34, ER stress**
ANOVA summary	
F	9,228
P value	0,0024
P value summary	**
R squared	0,5517

ANOVA table	SS	DF	MS	F (DFn, DFd)	P value
Treatment (between columns)	0,2148	2	0,1074	F (2, 15) = 9,22(	P=0,0024
Residual (within columns)	0,1746	15	0,01164		
Total	0,3894	17			

Supp. Fig. 1

Table Analyzed	**WT placebo injection & no injection**
Paired t test	
P value	0,2144
P value summary	ns
One- or two-tailed P value?	Two-tailed
t, df	t=1,570, df=3
Number of pairs	4
Mean of differences (injection - no injection)	1,108
SD of differences	1,412
95% confidence interval	-1,138 to 3,355

Table Analyzed	**WT S1 injection & no injection**
Paired t test	
P value	0,2809
P value summary	ns
One- or two-tailed P value?	Two-tailed
t, df	t=1,312, df=3
Number of pairs	4
Mean of differences (injection - no injection)	-1,362
SD of differences	2,076
95% confidence interval	-4,666 to 1,942

Table Analyzed	**WT GBZ10 injection & no injection**
Paired t test	
P value	0,0264
P value summary	*
One- or two-tailed P value?	One-tailed
t, df	t=3,112, df=3
Number of pairs	4
Mean of differences (injection - no injection)	133,9
SD of differences	86,03
95% confidence interval	-3,035 to 270,8

Table Analyzed	**WT GBZ4,5 injection & no injection**
Paired t test	
P value	0,0059
P value summary	**
One- or two-tailed P value?	One-tailed
t, df	t=5,493, df=3
Number of pairs	4
Mean of differences (injection - no injection)	174,8
SD of differences	63,64
95% confidence interval	73,51 to 276,0

Table Analyzed	**VWM placebo injection & no injection**
Paired t test	
P value	0,2472
P value summary	ns
One- or two-tailed P value?	Two-tailed
t, df	t=1,433, df=3
Number of pairs	4
Mean of differences (injection - no injection)	2,304
SD of differences	3,215
95% confidence interval	-2,811 to 7,419

Table Analyzed	**VWM S1 injection & no injection**
Paired t test	
P value	0,6195
P value summary	ns
One- or two-tailed P value?	Two-tailed
t, df	t=0,5518, df=3
Number of pairs	4
Mean of differences (injection - no injection)	0,9126
SD of differences	3,307
95% confidence interval	-4,350 to 6,175

Table Analyzed	**VWM GBZ10 injection & no injection**
Paired t test	
P value	0,003
P value summary	**
One- or two-tailed P value?	One-tailed
t, df	t=7,030, df=3
Number of pairs	4
Mean of differences (injection - no injection)	152
SD of differences	43,25
95% confidence interval	83,21 to 220,9

Table Analyzed	**VWM GBZ4,5 injection & no injection**
Paired t test	
P value	0,0129
P value summary	*
One- or two-tailed P value?	One-tailed
t, df	t=4,124, df=3
Number of pairs	4
Mean of differences (injection - no injection)	151,9
SD of differences	73,67
95% confidence interval	34,69 to 269,1

Table Analyzed	**WT gbz 10 inj, 1 vs 3**
Paired t test	
P value	0,9073
P value summary	ns
One- or two-tailed P value?	Two-tailed
t, df	t=0,1266, df=3
Number of pairs	4
Mean of differences (inj 3 - inj 1)	-8,835
SD of differences	139,6
95% confidence interval	-230,9 to 213,3

Table Analyzed	**WT gbz 10 inj, 1 vs 4**
Wilcoxon matched-pairs signed rank test	
P value	0,875
Exact or approximate P value?	Exact
P value summary	ns
One- or two-tailed P value?	Two-tailed
Sum of positive, negative ranks	4,000 , -6,000
Sum of signed ranks (W)	-2
Number of pairs	4
Number of ties (ignored)	0
Median	-82,74

Table Analyzed	**WT gbz 4,5 inj, 1 vs 3**
Paired t test	
P value	0,0049
P value summary	**
One- or two-tailed P value?	One-tailed
t, df	t=5,893, df=3
Number of pairs	4
Mean of differences (inj 3 - inj 1)	-131,3
SD of differences	44,57
95% confidence interval	-202,2 to -60,41

Table Analyzed	**WT gbz 4,5 inj, 1 vs 4**
Paired t test	
P value	0,0095
P value summary	**
One- or two-tailed P value?	One-tailed
t, df	t=4,632, df=3
Number of pairs	4
Mean of differences (inj 4 - inj 1)	-103,6
SD of differences	44,72
95% confidence interval	-174,7 to -32,41

Table Analyzed	**VWM GBZ 10 inj, 1 vs 3**
Paired t test	
P value	0,3876
P value summary	ns
One- or two-tailed P value?	Two-tailed
t, df	t=1,008, df=3
Number of pairs	4
Mean of differences (inj 3 - inj 1)	14,53
SD of differences	28,83
95% confidence interval	-31,34 to 60,41

Table Analyzed	**VWM GBZ 10 inj, 1 vs 4**
Paired t test	
P value	0,4089
P value summary	ns
One- or two-tailed P value?	Two-tailed
t, df	t=0,9576, df=3
Number of pairs	4
Mean of differences (inj 4 - inj 1)	-37,36
SD of differences	78,04
95% confidence interval	-161,5 to 86,81

Table Analyzed	**VWM GBZ 4,5 inj, 1 vs 3**
Paired t test	
P value	0,0271
P value summary	*
One- or two-tailed P value?	One-tailed
t, df	t=3,080, df=3
Number of pairs	4
Mean of differences (inj 3 - inj 1)	-126,3
SD of differences	82
95% confidence interval	-256,7 to 4,209

Table Analyzed	**VWM GBZ 4,5 inj, 1 vs 4**
Paired t test	
P value	0,0083
P value summary	**
One- or two-tailed P value?	One-tailed
t, df	t=4,856, df=3
Number of pairs	4
Mean of differences (inj 4 - inj 1)	-85,68
SD of differences	35,29
95% confidence interval	-141,8 to -29,52

Table Analyzed	**AUC WT hypothermia GBZ treatments**
ANOVA summary	
F	0,8004
P value	0,4787
P value summary	ns

ANOVA table	SS	DF	MS	F (DFn, DFd)	P value
Treatment (between columns)	12260	2	6130	F (2, 9) = 0,800	P=0,4787
Residual (within columns)	68928	9	7659		
Total	81187	11			

Tukey's multiple comparisons test	Mean Diff,	95,00% CI of diff,	Below threshold?	Summary	Adjusted P Value
WT Gbz10 vs. WT Gbz4,5	-42,66	-215,4 to 130,1	No	ns	0,7754

Test details	Mean 1	Mean 2	Mean Diff,	SE of diff,	n1	n2	q	DF
WT Gbz10 vs. WT Gbz4,5	137,9	180,6	-42,66	61,88	4	4	0,9748	9

Table Analyzed	**AUC VWM hypothermia GBZ treatments**
ANOVA summary	
F	1,246
P value	0,3329
P value summary	ns

ANOVA table	SS	DF	MS	F (DFn, DFd)	P value
Treatment (between columns)	13317	2	6658	F (2, 9) = 1,246	P=0,3329
Residual (within columns)	48094	9	5344		
Total	61411	11			

Tukey's multiple comparisons test	Mean Diff,	95,00% CI of diff,	Below threshold?	Summary	Adjusted P Value			
Mut Gbz10 vs. Mut Gbz4,5	2,53	-141,8 to 146,9	No	ns	0,9987	B	S1 4,5	

Test details	Mean 1	Mean 2	Mean Diff,	SE of diff,	n1	n2	q	DF
Mut Gbz10 vs. Mut Gbz4,5	155,8	153,2	2,53	51,69	4	4	0,06922	9

Supp. Fig. 4

Table Analyzed	***Ddit3* 24H**				
ANOVA summary					
F	5,817				
P value	0,0239				
P value summary	*				
ANOVA table	SS	DF	MS	F (DFn, DFd)	P value
Treatment (between columns)	0,003682	2	0,001841	F (2, 9) = 5,817	P=0,0239
Residual (within columns)	0,002849	9	0,0003165		
Total	0,006531	11			
Dunnett's multiple comparisons test	Mean Diff,	95,00% CI of diff,	Below threshold?	Summary	Adjusted P Value
placebo vs. S1 4.5	-0,007189	-0,04007 to 0,02570	No	ns	0,7963
placebo vs. GBZ 4.5	0,03304	0,0001548 to 0,0659	Yes	*	0,049
Test details	Mean 1	Mean 2	Mean Diff,	SE of diff,	n1
placebo vs. S1 4.5	0,07	0,07719	-0,007189	0,01258	4
placebo vs. GBZ 4.5	0,07	0,03696	0,03304	0,01258	4
Table Analyzed	***Trib3* 24H**				
ANOVA summary					
F	9,211				
P value	0,0066				
P value summary	**				
ANOVA table	SS	DF	MS	F (DFn, DFd)	P value
Treatment (between columns)	0,01494	2	0,007471	F (2, 9) = 9,211	P=0,0066
Residual (within columns)	0,0073	9	0,0008111		
Total	0,02224	11			
Dunnett's multiple comparisons test	Mean Diff,	95,00% CI of diff,	Below threshold?	Summary	Adjusted P Value
placebo vs. S1 4.5	-0,006128	-0,05877 to 0,04652	No	ns	0,9352
placebo vs. GBZ 4.5	0,0716	0,01896 to 0,1242	Yes	*	0,0113
Test details	Mean 1	Mean 2	Mean Diff,	SE of diff,	n1
placebo vs. S1 4.5	0,1153	0,1215	-0,006128	0,02014	4
placebo vs. GBZ 4.5	0,1153	0,04374	0,0716	0,02014	4
Table Analyzed	***Gadd34* 24H**				
ANOVA summary					
F	0,2901				
P value	0,755				
P value summary	ns				
ANOVA table	SS	DF	MS	F (DFn, DFd)	P value
Treatment (between columns)	0,0005901	2	0,000295	F (2, 9) = 0,290	P=0,7550
Residual (within columns)	0,009154	9	0,001017		
Total	0,009744	11			

Supp. Fig. 5

Table Analyzed	**ADRA2A2**							
Unpaired t test								
P value	0,0022							
P value summary	**							
One- or two-tailed P value?	One-tailed							
t, df	t=15,09, df=2							
Mean of - α2	0,00135							
Mean of + α2	124,6							
95% confidence interval	89,07 to 160,1							
Table Analyzed	**min α2 XBP1s/u, without ER stress**							
ANOVA summary								
F	0,8886							
P value	0,4444							
P value summary	ns							
ANOVA table	SS	DF	MS	F (DFn, DFd)	P value			
Treatment (between columns)	0,01802	2	0,009009	F (2, 9) = 0,888(	P=0,4444			
Residual (within columns)	0,09125	9	0,01014					
Total	0,1093	11						
Table Analyzed	**plus α2 XBP1s/u, without ER stress**							
Kruskal-Wallis test								
P value	0,941							
Exact or approximate P value?	Exact							
Do the medians vary signif. (P < 0.05)?	No							
Number of groups	3							
Kruskal-Wallis statistic	0,1538							
Table Analyzed	**min α2 XBP1s/u, ER stress**							
Mann Whitney test								
P value	0,0011							
Exact or approximate P value?	Exact							
P value summary	**							
One- or two-tailed P value?	One-tailed							
Sum of ranks in column A,E	21 , 57							
Mann-Whitney U	0							
Median of DMSO	0,9441, n=6							
Median of TG	13,78, n=6							
Difference: Actual	12,83							
Difference: Hodges-Lehmann	12,77							
Table Analyzed	**min α2 XBP1s/u, ER stress**							
ANOVA summary								
F	4,532							
P value	0,0289							
P value summary	*							
ANOVA table	SS	DF	MS	F (DFn, DFd)	P value			
Treatment (between columns)	106	2	52,98	F (2, 15) = 4,53	P=0,0289			
Residual (within columns)	175,4	15	11,69					
Total	281,3	17						
Dunnett's multiple comparisons test	Mean Diff,	95,00% CI of diff,	Below threshold?	Summary	Adjusted P Value	E-?		
TG 0,33µM vs. TG + S1	5,595	0,7794 to 10,41	Yes	*	0,0232	F	TG + S1	
TG 0,33µM vs. TG + GBZ	4,533	-0,2819 to 9,349	No	ns	0,0655	G	TG + GBZ	
Test details	Mean 1	Mean 2	Mean Diff,	SE of diff,	n1	n2	q	DF
TG 0,33µM vs. TG + S1	13,83	8,235	5,595	1,974	6	6	2,834	15
TG 0,33µM vs. TG + GBZ	13,83	9,296	4,533	1,974	6	6	2,297	15
Table Analyzed	**plus α2 XBP1s/u, ER stress**							
Mann Whitney test								
P value	0,0022							
Exact or approximate P value?	Exact							
P value summary	**							
One- or two-tailed P value?	One-tailed							
Sum of ranks in column A,E	21 , 45							
Mann-Whitney U	0							
Median of DMSO	1,085, n=6							
Median of TG	13,79, n=5							
Difference: Actual	12,71							
Difference: Hodges-Lehmann	12,58							
Table Analyzed	**plus α2 XBP1s/u, ER stress**							
ANOVA summary								
F	19,35							
P value	0,0001							
P value summary	***							
ANOVA table	SS	DF	MS	F (DFn, DFd)	P value			
Treatment (between columns)	238,8	2	119,4	F (2, 13) = 19,3	P=0,0001			
Residual (within columns)	80,22	13	6,171					
Total	319	15						
Dunnett's multiple comparisons test	Mean Diff,	95,00% CI of diff,	Below threshold?	Summary	Adjusted P Value	E-?		
TG 0,33µM vs. TG + S1	9,509	5,622 to 13,40	Yes	****	<0,0001	F	TG + S1	
TG 0,33µM vs. TG + GBZ	6,596	2,875 to 10,32	Yes	**	0,0014	G	TG + GBZ	
Test details	Mean 1	Mean 2	Mean Diff,	SE of diff,	n1	n2	q	DF
TG 0,33µM vs. TG + S1	13,78	4,27	9,509	1,571	5	5	6,052	13
TG 0,33µM vs. TG + GBZ	13,78	7,182	6,596	1,504	5	6	4,385	13

Supp. Data CatWalk WT-VWM placebo

Catetegory	Parameter	Paws	Analysis	VWM placebo vs WT placebo
RUN CHARACTERIZATION	Duration (s)	All	p < 0.0001 (KW)	0 (↑)
	Cadence (steps/s)	All	p < 0.0001 (KW)	0 (↓)
	Average speed (cm/s)	All	p < 0.0001 (KW)	0 (↓)
	Number of steps (#)	All	p < 0.0001 (KW)	0 (↑)
	Maximum variation (%)	All	p = 0.416 (KW)	-
INTERLIMB COORDINATION	Base of support (cm)	FP	p < 0.0001 (AN)	0.984
		HP	p = 0.279 (KW)	
	Stride length (cm)	FP	p < 0.0001 (KW)	0 (↓)
		HP	p < 0.0001 (KW)	0 (↓)
	Step sequence - Regularity index (%)	All	p < 0.0001 (KW)	0.006 (↓)
	Support Lateral (%)	All	p < 0.0001 (KW)	0 (↑)
	Support Single (%)	All	p = 0.001 (KW)	0.001 (↑)
	Support Girdle (%)	All	p < 0.0001 (KW)	0 (↑)
	Support Diagonal (%)	All	p < 0.0001 (KW)	0 (↓)
	Support Three (%)	All	p < 0.0001 (KW)	0.009 (↑)
	Support Four (%)	All	p = 0.023 (KW)	0.787
TEMPORAL	Stand (s)	FP	p < 0.0001 (AN, LOG10)	0 (↑)
		HP	p < 0.0001 (KW)	0.002 (↑)
	Swing (s)	FP	p < 0.0001 (KW)	0.001 (↑)
		HP	p < 0.0001 (KW)	0 (↑)
	Step cycle (s)	FP	p < 0.0001 (AN)	0 (↑)
		HP	p < 0.0001 (KW)	0 (↑)
	Duty cycle (s)	FP	p < 0.0001 (AN)	0.001 (↑)
		HP	p = 0.048 (KW)	0.697
	Single stance (s)	FP	p < 0.0001 (KW)	0.004 (↑)
		HP	p < 0.0001 (KW)	0 (↑)
	Initial dual stance (s)	FP	p < 0.0001 (KW)	0.004 (↑)
		HP	p < 0.0001 (KW)	0.061
	Terminal dual stance (s)	FP	p < 0.0001 (KW)	0.003 (↑)
		HP	p < 0.0001 (KW)	0.052
	Max intensity At (%)	FP	p < 0.0001 (KW)	0 (↑)
		HP	p < 0.0001 (KW)	0 (↓)
	Max contact At (%)	FP	p < 0.0001 (AN)	0.011 (↑)
		HP	p = 0.001 (AN)	0.702
KINETIC	Stand Index	FP	p < 0.0001 (KW)	0.452
		HP	p < 0.0001 (KW)	0.001 (↑)
	Swing speed (cm/s)	FP	p < 0.0001 (KW)	0 (↓)
		HP	p < 0.0001 (KW)	0 (↓)
	Body speed (cm/s)	FP	p < 0.0001 (KW)	0 (↓)
		HP	p < 0.0001 (KW)	0 (↓)
	Body speed variation (cm/s)	FP	p = 0.169 (KW)	-
		HP	p = 0.195 (KW)	-
SPATIAL	Print length (cm)	FP	p < 0.0001 (KW)	0 (↓)
		HP	p < 0.0001 (KW)	0 (↓)
	Print width (cm)	FP	p < 0.0001 (KW)	0 (↓)
		HP	p < 0.0001 (AN)	0 (↓)
	Print area (cm^2)	FP	p < 0.0001 (KW)	0 (↓)
		HP	p < 0.0001 (AN)	0 (↓)
	Max contact area (cm^2)	FP	p < 0.0001 (KW)	0 (↓)
		HP	p < 0.0001 (AN, LOG10)	0 (↓)
	Max contact max intensity (AU)	FP	p < 0.0001 (KW)	0 (↓)
		HP	p < 0.0001 (KW)	0 (↓)
	Max contact mean intensity (AU)	FP	p < 0.0001 (KW)	0 (↓)
		HP	p < 0.0001 (KW)	0.016 (↓)
	Max intensity (AU)	FP	p < 0.0001 (KW)	0 (↓)
		HP	p < 0.0001 (KW)	0 (↓)
	Mean intensity (AU)	FP	p < 0.0001 (KW)	0 (↓)
		HP	p < 0.0001 (KW)	0.009 (↓)
	Min intensity (AU)	FP	p = 0.587 (AN, LOG10)	-
		HP	p = 0.287 (KW)	-

Supp. Data CatWalk VWM treatment

Catetegory	Parameter	Paws	Analysis	VWM S1 D4.5 vs VWM placebo	VWM GBZ W10 vs VWM placebo	VWM GBZ D4.5 vs VWM placebo	VWM GBZ D4.5 vs WT D4.5
RUN CHARACTERIZATION	Duration (s)	All	p < 0.0001 (KW)	0.086	0 (↓)	0 (↓)	0.013 (↑)
	Cadence (steps/s)	All	p < 0.0001 (KW)	0.254	0.026 (↑)	0 (↑)	0.04 (↓)
	Average speed (cm/s)	All	p < 0.0001 (KW)	0.086	0 (↑)	0 (↑)	0.016 (↓)
	Number of steps (#)	All	p < 0.0001 (KW)	0.024 (↑)	0.008 (↓)	0 (↓)	0.002 (↑)
INTERLIMB COORDINATION	Stride length (cm)	FP	p < 0.0001 (KW)	0.021 (↓)	0 (↑)	0 (↑)	0 (↓)
		HP	p < 0.0001 (KW)	0.21	0 (↑)	0 (↑)	0.001 (↓)
	Step sequence - Regularity index (%)	All	p < 0.0001 (KW)	0.228	0.001 (↑)	0 (↑)	0.286
	Support Lateral (%)	All	p < 0.0001 (KW)	0.616	0.008 (↓)	0.001 (↓)	0.636
	Support Single (%)	All	p = 0.001 (KW)	0.21	0.11	0.006 (↓)	0.949
	Support Girdle (%)	All	p < 0.0001 (KW)	0.838	0.005 (↓)	0 (↓)	0.383
	Support Diagonal (%)	All	p < 0.0001 (KW)	0.023 (↓)	0.001 (↑)	0 (↑)	0.007 (↓)
	Support Three (%)	All	p < 0.0001 (KW)	0.119	0.035 (↓)	0.003 (↓)	0.004 (↑)
TEMPORAL	Stand (s)	FP	p < 0.0001 (AN, LOG10)	0.715	0.861	0 (↓)	0.738
		HP	p < 0.0001 (KW)	0.047 (↑)	0.043 (↓)	0 (↓)	0.019 (↑)
	Swing (s)	FP	p < 0.0001 (KW)	0.897	0.035 (↑)	0.829	0.028 (↑)
		HP	p < 0.0001 (KW)	0.616	0.002 (↓)	0 (↓)	0.681
	Step cycle (s)	FP	p < 0.0001 (AN)	0.294	1	0 (↓)	0.276
		HP	p < 0.0001 (KW)	0.086	0.001 (↓)	0 (↓)	0.023 (↑)
	Duty cycle (s)	FP	p < 0.0001 (AN)	0.809	0.011 (↓)	0 (↓)	0.901
	Single stance (s)	FP	p < 0.0001 (KW)	0.515	0.004 (↑)	0.984	0.019 (↑)
		HP	p < 0.0001 (KW)	0.724	0.004 (↓)	0 (↓)	0.636
	Initial dual stance (s)	FP	p < 0.0001 (KW)	0.073	0.067	0 (↓)	0.028 (↑)
	Terminal dual stance (s)	FP	p < 0.0001 (KW)	0.119	0.011 (↓)	0 (↓)	0.19
	Max intensity At (%)	FP	p < 0.0001 (KW)	0.879	0.21	0 (↓)	0.169
		HP	p < 0.0001 (KW)	0.094	0.16	0.012 (↑)	0.392
	Max contact At (%)	FP	p < 0.0001 (AN)	0.964	0.93	0.977	0.067
KINETIC	Stand Index	HP	p < 0.0001 (KW)	0.21	0.003 (↓)	0 (↓)	0.023 (↑)
	Swing speed (cm/s)	FP	p < 0.0001 (KW)	0.119	0.002 (↑)	0 (↑)	0.008 (↓)
		HP	p < 0.0001 (KW)	0.867	0.003 (↑)	0 (↑)	0.028 (↓)
	Body speed (cm/s)	FP	p < 0.0001 (KW)	0.043 (↓)	0 (↑)	0 (↑)	0.016 (↓)
		HP	p < 0.0001 (KW)	0.056	0 (↑)	0 (↑)	0.019 (↓)
SPATIAL	Print length (cm)	FP	p < 0.0001 (KW)	0.838	0.128	0.984	0 (↓)
		HP	p < 0.0001 (KW)	0.11	0.381	0.072	0.548
	Print width (cm)	FP	p < 0.0001 (KW)	0.27	0 (↑)	0 (↑)	0.357
		HP	p < 0.0001 (AN)	0.826	0.994	0.42	0.57
	Print area (cm^2)	FP	p < 0.0001 (KW)	0.287	0.102	0.83	0.003 (↓)
		HP	p < 0.0001 (AN)	0.819	1	0.35	1
	Max contact area (cm^2)	FP	p < 0.0001 (KW)	0.486	0.224	0.77	0.007 (↓)
		HP	p < 0.0001 (AN, LOG10)	0.767	1	0.049 (↑)	1
	Max contact max intensity (AU)	FP	p < 0.0001 (KW)	0.445	0.023 (↑)	0.006 (↑)	0.265
		HP	p < 0.0001 (KW)	0.491	0.149	0 (↑)	0.975
	Max contact mean intensity (AU)	FP	p < 0.0001 (KW)	0.491	0.051	0.045 (↑)	0.238
		HP	p < 0.0001 (KW)	0.616	0.061	0 (↑)	0.265
	Max intensity (AU)	FP	p < 0.0001 (KW)	0.239	0.102	0.072	0.294
		HP	p < 0.0001 (KW)	0.696	0.21	0 (↑)	0.776
	Mean intensity (AU)	FP	p < 0.0001 (KW)	0.323	0.08	0.232	1
		HP	p < 0.0001 (KW)	0.616	0.08	0 (↑)	0.265

Supp. Data CatWalk WT treatment

Catetegory	Parameter	Paws	Analysis	WT S1 D4.5 vs WT placebo	WT GBZ W 10 vs WT placebo	WT GBZ D4.5 vs WT placebo
RUN CHARACTERIZATION	Duration (s)	All	p < 0.0001 (KW)	1	0.574	0.065
	Cadence (steps/s)	All	p < 0.0001 (KW)	0.442	0.721	0.328
	Average speed (cm/s)	All	p < 0.0001 (KW)	0.328	0.959	0.382
	Number of steps (#)	All	p < 0.0001 (KW)	0.958	0.875	0.207
INTERLIMB COORDINATION	Stride length (cm)	FP	p < 0.0001 (KW)	0.959	0.721	0.279
		HP	p < 0.0001 (KW)	0.878	0.505	0.505
	Step sequence - Regularity index (%)	All	p < 0.0001 (KW)	0.916	0.833	0.342
	Support Lateral (%)	All	p < 0.0001 (KW)	0.385	0.161	0.006 (↑)
	Support Single (%)	All	p = 0.001 (KW)	0.701	0.153	0.15
	Support Girdle (%)	All	p < 0.0001 (KW)	0.873	0.155	0.709
	Support Diagonal (%)	All	p < 0.0001 (KW)	0.721	0.878	0.234
	Support Three (%)	All	p < 0.0001 (KW)	0.646	0.959	0.13
	Max contact At (%)	FP	p < 0.0001 (AN)	1	0.921	0.862
TEMPORAL	Stand (s)	FP	p < 0.0001 (AN, LOG10)	0.999	0.993	0.955
		HP	p < 0.0001 (KW)	0.878	0.442	0.234
	Swing (s)	FP	p < 0.0001 (KW)	0.05	0.959	0.279
		HP	p < 0.0001 (KW)	0.038 (↑)	721	0.234
	Step cycle (s)	FP	p < 0.0001 (AN)	0.987	0.996	0.972
		HP	p < 0.0001 (KW)	0.721	0.505	0.279
	Duty cycle (s)	FP	p < 0.0001 (AN)	0.999	0.992	0.35
	Single stance (s)	FP	p < 0.0001 (KW)	0.065	0.574	0.789
		HP	p < 0.0001 (KW)	0.028 (↑)	0.574	0.574
	Initial dual stance (s)	FP	p < 0.0001 (KW)	0.721	0.382	0.105
	Terminal dual stance (s)	FP	p < 0.0001 (KW)	0.645	0.382	0.234
	Max intensity At (%)	FP	p < 0.0001 (KW)	1	0.878	0.007 (↑)
		HP	p < 0.0001 (KW)	0.13	0.574	0.13
	Max contact At (%)	FP	p < 0.0001 (AN)	1	0.921	0.862
KINETIC	Stand index	HP	p < 0.0001 (KW)	0.574	0.279	0.161
	Swing speed (cm/s)	FP	p < 0.0001 (KW)	0.195	0.645	1
		HP	p < 0.0001 (KW)	0.105	0.789	1
	Body speed (cm/s)	FP	p < 0.0001 (KW)	0.442	0.959	0.328
		HP	p < 0.0001 (KW)	0.382	0.959	0.382
SPATIAL	Print length (cm)	FP	p < 0.0001 (KW)	0.574	0.01 (↓)	0 (↓)
		HP	p < 0.0001 (KW)	0.721	0.442	0.001 (↓)
	Print width (cm)	FP	p < 0.0001 (KW)	0.442	0.442	0.279
		HP	p < 0.0001 (AN)	1	0.79	0.001 (↓)
	Print area (cm^2)	FP	p < 0.0001 (KW)	0.195	0.038 (↓)	0 (↓)
		HP	p < 0.0001 (AN)	1	0.958	0.003 (↓)
	Max contact area (cm^2)	FP	p < 0.0001 (KW)	0.195	0.105	0 (↓)
		HP	p < 0.0001 (AN, LOG10)	1	0.871	0.001 (↓)
	Max contact max intensity (AU)	FP	p < 0.0001 (KW)	0.105	0.645	0.001 (↓)
		HP	p < 0.0001 (KW)	1	0.959	0.161
	Max contact mean intensity (AU)	FP	p < 0.0001 (KW)	0.065	0.442	0.002 (↓)
		HP	p < 0.0001 (KW)	0.789	0.789	0.442
	Max intensity (AU)	FP	p < 0.0001 (KW)	0.028 (↓)	0.13	0 (↓)
		HP	p < 0.0001 (KW)	0.878	0.878	0.161
	Mean intensity (AU)	FP	p < 0.0001 (KW)	0.105	0.234	0 (↓)
		HP	p < 0.0001 (KW)	1	0.878	0.234