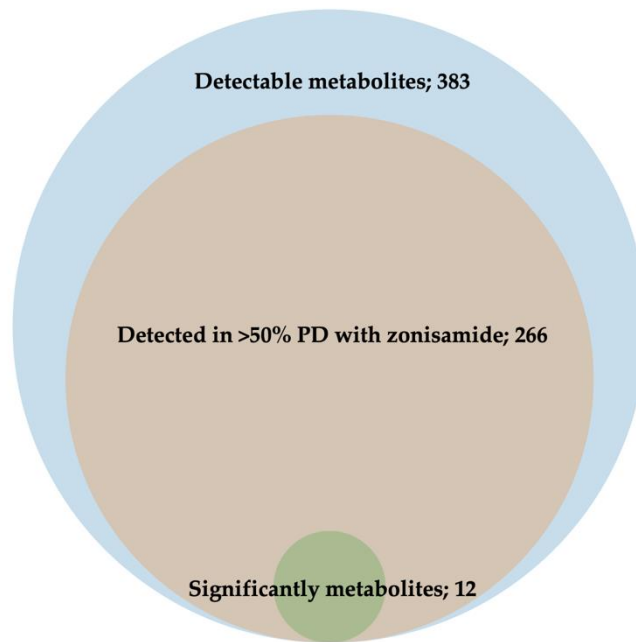1 # Supplementary materials:

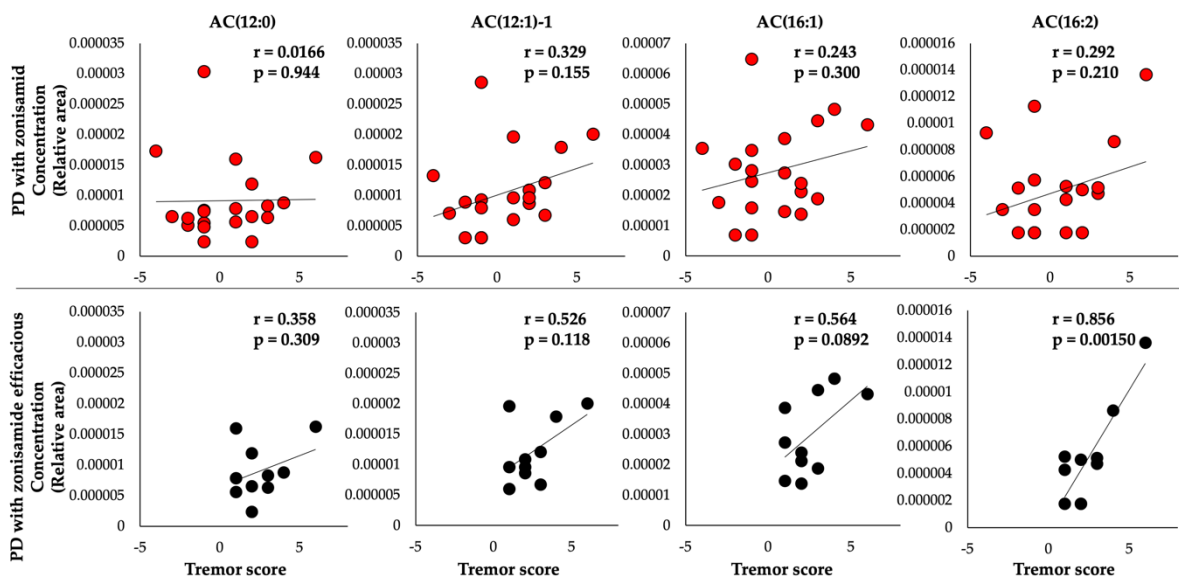2 # Zonisamide administration improves fatty acid β-
3 # oxidation in Parkinson's disease.

4 **Shin-Ichi Ueno [1], Shinji Saiki [1,*], Motoki Fujimaki [1], Haruka Takeshige-Amano [1], Taku Hatano [1],**
5 **Genko Oyama [1], Kei-Ichi Ishikawa [1,2], Akihiro Yamaguchi [2], Wado Akamatsu [2] and Nobutaka**
6 **Hattori [1,*]**

7 **Supplementary Figure 1.** Venn diagram showing the number of metabolites common to the
8 experimental groups

9

10 **Supplementary Figure 2.** Association of LCACs and tremor scores of UPDRS-III in motor
11 amelioration of Parkinson's disease with zonisamide. Red indicates a correlation of tremor scores and
12 LCACs in PD with zonisamide, while black indicates a correlation of tremor scores and LCACs in PD
13 with efficacious zonisamide. Abbreviations: LCACs: long-chain acylcarnitines, PD: Parkinson's
14 disease, UPDRS: Unified Parkinson's Disease Rating Scale. *p*-Value obtained by Spearman's rank
15 correlation coeffecient.

16 **Supplementary Table 1.** Top 10 metabolites as factor loadings by partial least squares analysis.

Compound	R	*p*-Value
1-methylnicotinamide	0.467	0.00930
Imidazolelactic acid	0.430	0.0180
XC0088	0.413	0.0230
AC(16:1)	0.402	0.0280
Stigmasterol	0.395	0.0310
XC0016	0.382	0.0370
Paraxanthine	0.381	0.0380
Ornithine	0.376	0.0410
AC(16:2)	0.368	0.0460
AC(12:1)-1	0.359	0.0520

17 Abbreviations: XC0088, XC0016: unidentified metabolites annotated by Human Metabolome Technologies, Inc.
18 AC: acylcarnitine. *p*-Value obtained by partial least squares regression analysis.

19 **Supplementary Table 2.** Long-chain acylcarnitines in Parkinson's disease with or without
20 zonisamide.

Compound, relative area	Ratio of zonisamide (+) to zonisamide (-)	*p*-Value
AC(12:0)	1.73	0.0407
AC(12:1)-1	1.92	0.0405
AC(12:1)-2	1.66	<0.0001
AC(12:1)-3	1.01	0.0113
AC(13:1)-1	1.07	0.0142
AC(13:1)-2	1.25	0.708
AC(14:0)	1.54	0.320
AC(14:1)	1.54	0.708
AC(14:2)-1	1.50	0.179
AC(14:2)-2	-	-
AC(14:3)	-	-

AC(15:0)	1.00	0.912
AC(16:1)	1.75	0.0366
AC(16:2)	1.95	0.0054
AC(18:0)	1.27	0.281
AC(18:1)	1.38	0.165
AC(18:2)-1	1.27	0.165
AC(18:2)-2	-	-
AC(20:0)	-	-
AC(20:1)	1.27	0.322

Abbreviations: AC: acylcarnitine. *p*-Value obtained by Wilcoxon test.

Supplementary Table 3. The influence of zonisamide treatment duration and treatment dosage on the levels of four LCACs.

Dependent variable	AC(12:0)	AC(12:1)-1	AC(16:1)	AC(16:2)
	p-Value	*p*-Value	*p*-Value	*p*-Value
Treatment period	0.982	0.983	0.238	0.291
Zonisamide dosage	0.284	0.0940	0.633	0.937

Abbreviations: LCACs: long-chain acylcarnitines, *p*-Value obtained by multivariable regression analysis.

Supplementary Table 4. Serum skeletal-muscle-associated proteins in Parkinson's disease with or without zonisamide.

	Zonisamide (-)	Zonisamide (+)	*p*-Value
Creatine kinase [IU/L] **Mean (SD) [N.A.]**	223 (237)	104 (40.2) [2]	0.0798
Aldolase [IU/L] **Mean (SD) [N.A.]**	4.49 (0.881)	3.68 (0.738) [2]	0.0344
Creatinine [mg/dl] **Mean (SD)**	0.653 (0.141)	0.725 (0.256)	0.565
HbA1c [%, NGSP] **Mean (SD)**	5.80 (0.258)	5.82 (0.474)	0.673

Abbreviations: IU/L: international unit per liter, SD: standard deviation, NGSP: National Glycohemoglobin Standardization Program. *p*-Value obtained by Wilcoxon test. N.A. = not available