

Supplementary Material

Endocannabinoid Modulation using Monoacylglycerol Lipase Inhibition in Tourette Syndrome: A phase 1 Randomized, Placebo-controlled Study

Kirsten R. Müller-Vahl¹, Carolin Fremer¹, Chan Beals², Jelena Ivkovic³, Henrik Loft³ and Christoph Schindler⁴

- 1) Department of Psychiatry, Social Psychiatry and Psychotherapy, Hannover Medical School, Hannover, Germany
- 2) Abide Therapeutics, San Diego, CA, USA
- 3) H. Lundbeck A/S, Valby, Denmark
- 4) Clinical Research Center Core Facility, Hannover Medical School, Hannover, Germany.

Mueller-Vahl.Kirsten@mh-hannover.de

Description of the Time Weighted Analysis (TWA) model.

Efficacy endpoints were analyzed using a mixed model repeated measures (MMRM)-model including all time points. Details of the model structure are given below.

The model provides treatment estimates at each of the time points M4 (4 h), M8 (8 h), and M12 (12 h) and is also used to calculate the Time Weighted Average (TWA) using the following trapezoidal formula:

$$TWA = ((4 - 0) * \frac{M0 + M4}{2} + (8 - 4) * \frac{M4 + M8}{2} + (12 - 8) * \frac{M8 + M12}{2}) / 12 = 0.3333 * M4 + 0.3333 * M8 + 0.1667 * M12$$

Supplemental Table e1 Group mean plasma parameters following 40 mg oral administration of Lu AG06466 in the fasted state (Part A) in 19 participants

	T_{max} (h)	C_{max} (ng/mL)	AUC₀₋₈ (h*ng/mL)	AUC_{last} (h*ng/mL)
Mean	2.14	59.5	269	393
SD	1.03	23.6	97.4	149
CV%	48.0	39.7	36.2	37.8
Min	1.13	25.2	121	164
Median	1.68	59.7	227	343
Max	3.97	107	439	629
Geometric Mean	1.94	55.0	253	366
CV% Geometric Mean	46.6	43.6	38.3	40.4

C_{max} = maximum plasma concentration; AUC₀₋₈ = area under the plasma concentration versus time curve from time 0 to 8 hours; AUC_{last} = area under the plasma concentration versus time curve from time 0 to last timepoint; CV = coefficient of variation; h = hour; max = maximum; min = minimum; SD = standard deviation; T_{max} = time to maximum plasma concentration.

Supplemental Table e2 Group mean plasma parameters following 20 mg oral administration of Lu AG06466 after a high-fat meal (Part B) in seven participants

	T_{max} (h)	C_{max} (ng/mL)	AUC₀₋₈ (h*ng/mL)	AUC_{last} (h*ng/mL)
Mean	5.71	89.8	344	751
SD	2.93	40.7	99.4	306
CV%	51.2	45.3	28.9	40.8
Min	2.00	36.7	242	415
Median	8.00	79.9	334	697
Max	8.00	161	532	1330
Geometric Mean	4.88	81.8	333	704
CV% Geometric Mean	73.8	51.3	27.9	39.7

C_{max} = maximum plasma concentration; AUC₀₋₈ = area under the plasma concentration versus time curve from time 0 to 8 hours; AUC_{last} = area under the plasma concentration versus time curve from time 0 to last timepoint; CV = coefficient of variation; h = hour; max = maximum; min = minimum; SD = standard deviation; T_{max} = time to maximum plasma concentration.