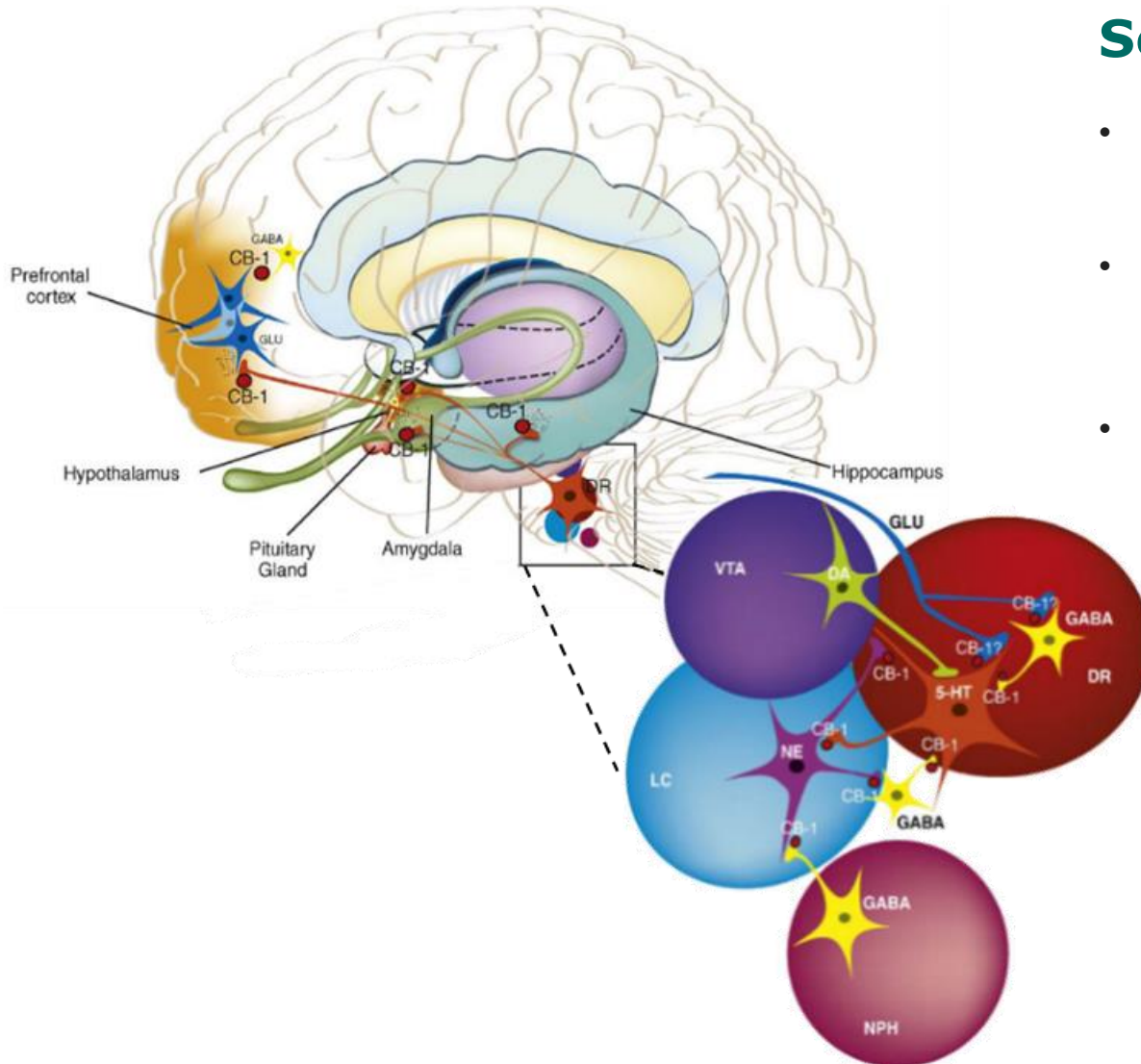




Seltorexant (MIN-202)

A drug in development to treat insomnia and major depressive disorder (MDD) by restoring physiological sleep and controlling brain arousal levels

Rationale for focus on Insomnia and MDD: Targeting circuits in the orexin system that mediate “hyperarousal” in mood disorders



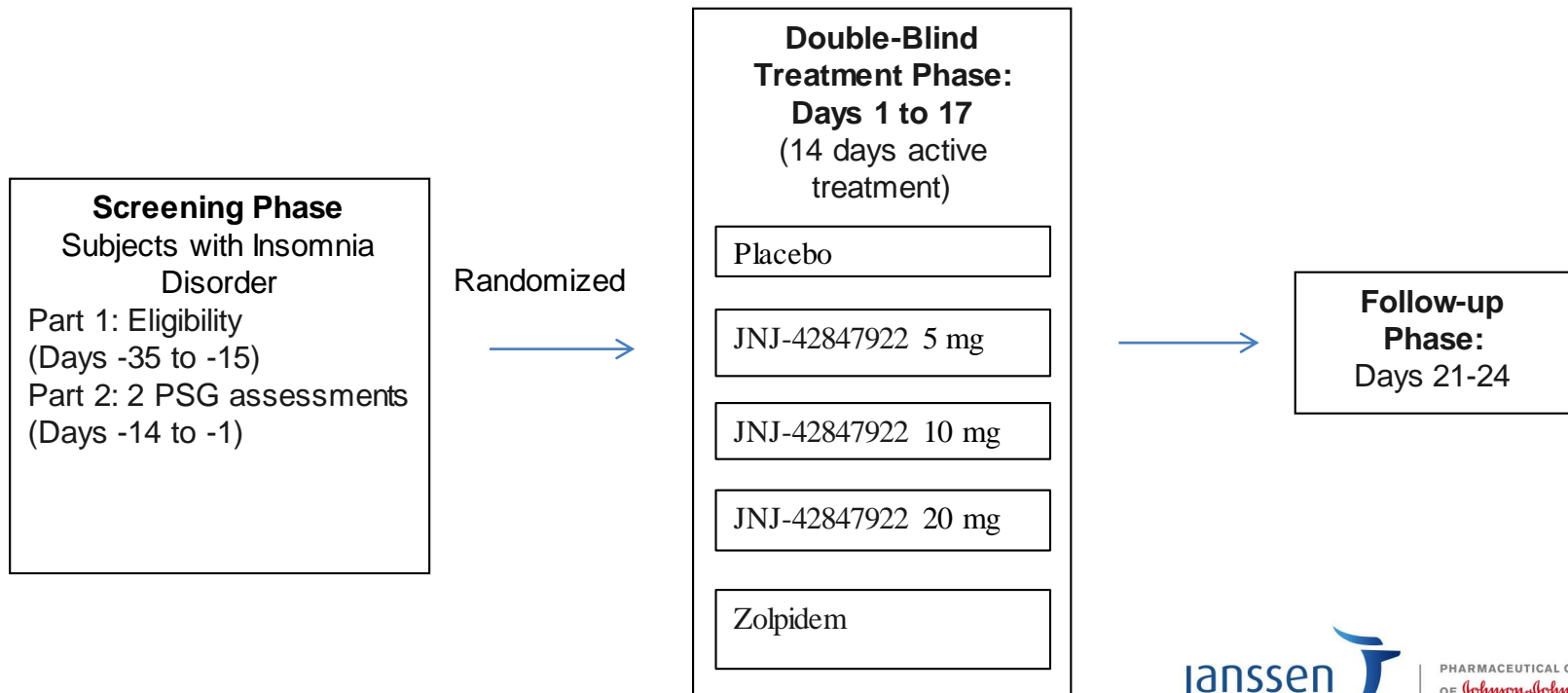
Seltorexant

- Highly selective for Orexin-₂ (relative to Orexin-₁)
- Short Tmax (30 minutes) – produces rapid onset of effect
- Short half-life (2 hours) – minimizes daytime “hangover”

janssen  PHARMACEUTICAL COMPANIES
OF 

 **MINERVA**
NEUROSCIENCES, INC.

A 2-week dose-ranging study evaluating the efficacy and safety of seltorexant 5 mg, 10 mg and 20 mg vs. placebo and active comparator (zolpidem), in both adult (18 to 64 years, inclusive) and elderly (65 to 85 years, inclusive) subjects with insomnia disorder without psychiatric comorbidity.

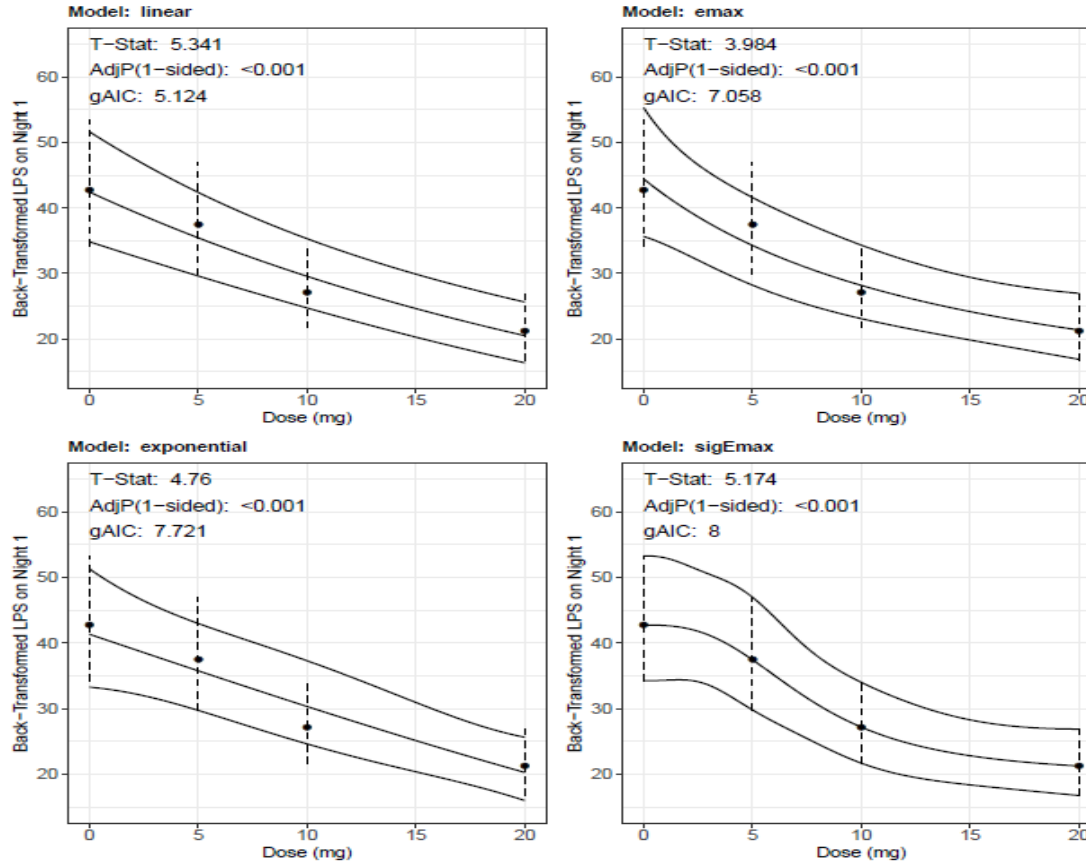


ISM2005 Baseline Sleep Characteristics

Summary of Baseline Insomnia and Illness Status; Full Analysis Set (Study 42847922ISM2005)

	Placebo	Seltorexant				Zolpidem	Total
		5 mg	10 mg	20 mg	Combined		
Analysis set: Full	75	71	74	71	216	73	364
Baseline ISI total score							
N	75	71	74	71	216	73	364
Mean (SD)	19.8 (3.33)	20.5 (3.09)	20.7 (3.42)	20.2 (3.36)	20.5 (3.29)	20.1 (2.88)	20.2 (3.22)
Median	19.0	20.0	20.5	20.0	20.0	20.0	20.0
Range	(12;28)	(13;27)	(13;27)	(12;28)	(12;28)	(13;27)	(12;28)
Baseline LPS (min)							
N	75	71	74	71	216	73	364
Mean (SD)	88.7 (53.41)	85.9 (49.85)	92.0 (57.15)	82.4 (46.88)	86.8 (51.47)	87.9 (54.37)	87.4 (52.33)
Median	72.0	74.8	74.4	70.0	73.4	73.3	73.1
Range	(26;281)	(25;236)	(25;320)	(26;271)	(25;320)	(27;297)	(25;320)
Baseline WASO over first 6 hours (min)							
N	75	71	74	71	216	73	364
Mean (SD)	83.1 (39.01)	72.7 (37.06)	81.6 (48.57)	84.8 (38.60)	79.7 (41.94)	74.5 (37.53)	79.4 (40.48)
Median	76.3	64.8	71.9	83.5	74.9	71.3	74.6
Range	(17;192)	(9;169)	(9;232)	(21;201)	(9;232)	(3;179)	(3;232)

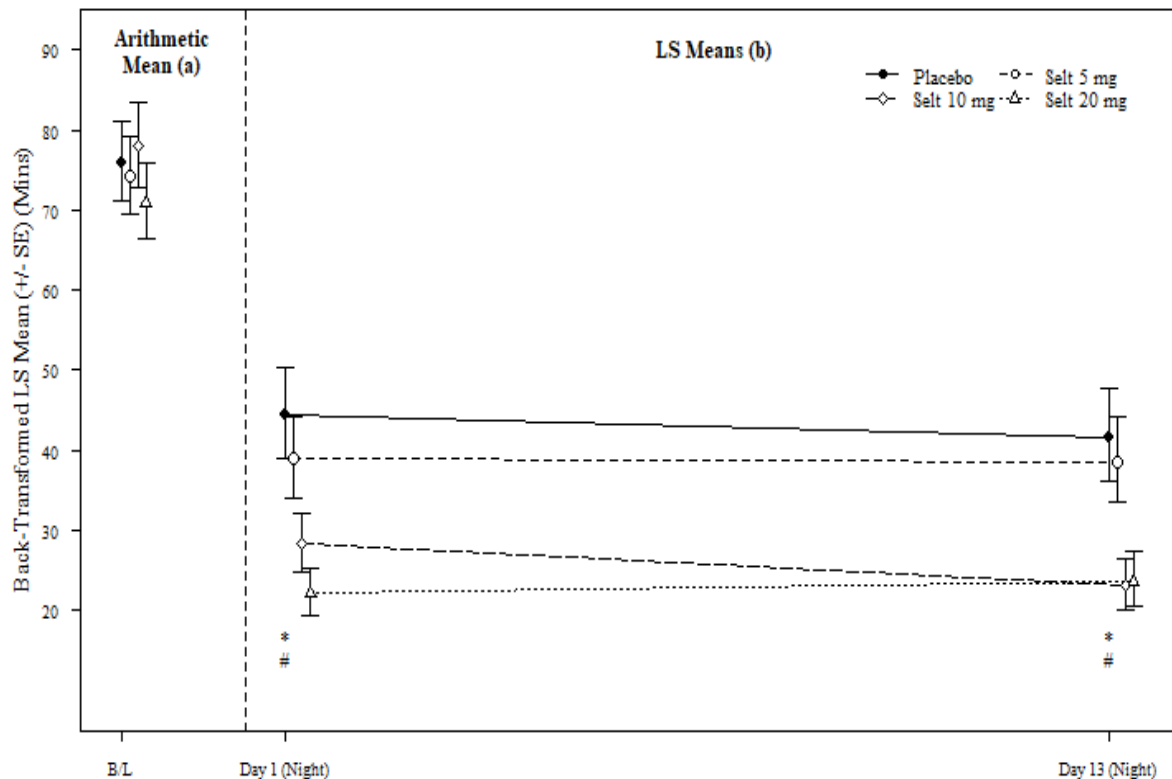
Dose-response testing by MCP-Mod method



- All four pre-specified models showed a significant dose-response relationship in log-transformed LPS at Day 1 (Night) where the adjusted 1-sided p-values were <0.001.
- Linear and sigEmax models showed the best fit for the data with the largest and similar T-statistic (linear: 5.341, sigEmax: 5.174) in these models

Primary Efficacy Endpoint

LPS night 1 compared to placebo



- Significant separation of the 10 mg and 20 mg dose groups from placebo, indicating a 36% and 49% improvement in LPS at night 1
- 43% and 42 % improvement in LPS at night 13 compared to placebo

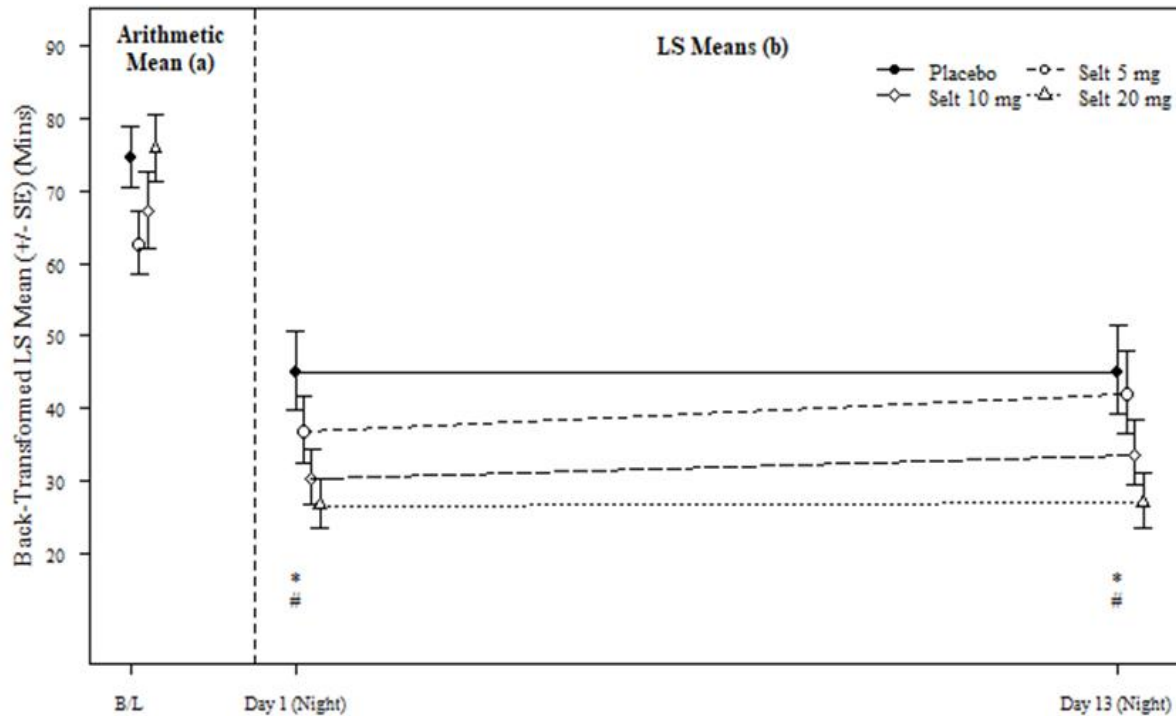
Comparison vs. Placebo (alpha=0.10): + Selt 5 mg; * Selt 10 mg; # Selt 20 mg.

Number of Subjects:

Placebo	75	75	69
Selt 5 mg	71	71	69
Selt 10 mg	74	73	73
Selt 20 mg	71	71	69

Key Secondary Efficacy Endpoint WASO-6 over time (night 1 – night13)

Back-transformed LS means (+/- SE) of WASO-6 over time using MMRM analysis on the log-transformed data.



Comparison vs. Placebo (alpha=0.10): + Selt 5 mg; * Selt 10 mg; # Selt 20 mg.

Number of Subjects:

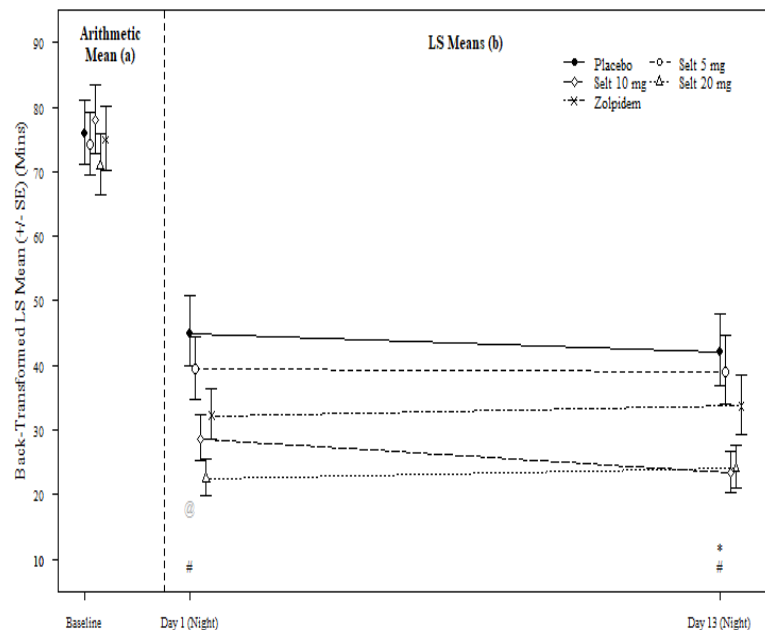
Placebo	75	74	68
Selt 5 mg	71	71	69
Selt 10 mg	74	73	73
Selt 20 mg	71	71	68

- Separation of the 10 mg and 20 mg dose groups from placebo was significant, showing a 32% and 40% improvement in WASO at night 1
- 25% and 40% improvement in WASO at night 13 compared to placebo

Comparison to Zolpidem

LPS & WASO-6 over time (night 1 – night 13)

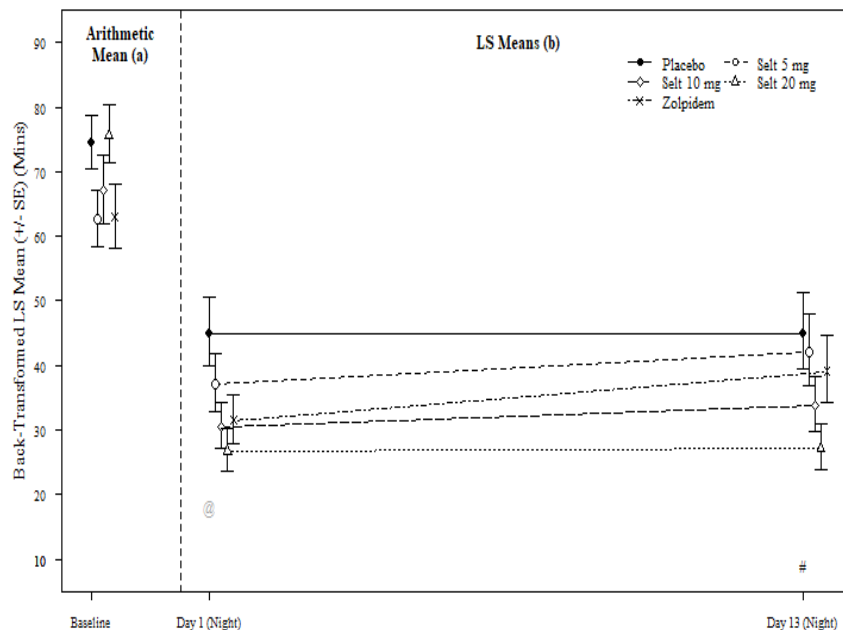
- LPS LS mean over time (no multiplicity adjustment)



Comparison vs. Zolpidem (alpha=0.10): @ Placebo; + Salt 5 mg; * Salt 10 mg; # Salt 20 mg.

Number of Subjects:	Baseline	Day 1 (Night)	Day 13 (Night)
Placebo	75	75	69
Salt 5 mg	71	71	69
Salt 10 mg	74	73	73
Salt 20 mg	71	71	69
Zolpidem	73	73	69

- WASO LS mean over time (no multiplicity adjustment)



Comparison vs. Zolpidem (alpha=0.10): @ Placebo; + Salt 5 mg; * Salt 10 mg; # Salt 20 mg.

Number of Subjects:	Baseline	Day 1 (Night)	Day 13 (Night)
Placebo	75	74	68
Salt 5 mg	71	71	69
Salt 10 mg	74	73	73
Salt 20 mg	71	71	68
Zolpidem	73	73	69

There was a significant separation from zolpidem by the 20 mg dose group at night 1 for LPS, at night 13 for LPS and WASO-6. Similarly, a significant separation from zolpidem was observed for the 10 mg dose at night 13 for LPS.

Conclusion

- Seltorexant met its primary endpoint of demonstrating dose response efficacy (MCP-Mod) in patients with insomnia
- Seltorexant 10 and 20 mg superior to placebo on LPS and WASO-6 at Night 1 and Night 13
- Similar efficacy across subgroups except possibly WASO-6 (better in the elderly than adults)
- Seltorexant well tolerated with overall TEAEs similar to placebo
- Seltorexant shows superior and more sustained efficacy as compared to zolpidem