Improvements with ON-SXB vs placebo were reported for shifts to a lighter stage of sleep (NT1: 6, 7.5, 9 g, all P<0.001; NT2: 6 and 7.5 g, P<0.05; 9 g, P<0.001), NA (NT1: 6 g, P<0.05; 7.5 and 9 g, P<0.01; NT2: 6 g, directional improvement; 7.5 and 9 g, P<0.05), and sleep quality (NT1: 6, 7.5, 9 g, all P<0.001; NT2: 6, 7.5, 9 g, all P<0.05). Significant improvements in ESS and refreshing nature of sleep for ON-SXB vs placebo were reported for NT1 (6, 7.5, 9 g, P≤0.001) with directional improvements observed for the NT2 subgroup.
**Conclusion:** Results of these subgroup efficacy analyses are generally consistent with previously reported REST-ON endpoints and support ON-SXB treatment efficacy in adults with NT1 or NT2.
**Support (If Any):** Avadel Pharmaceuticals

## 0402

### EFFICACY OF FT218, A ONCE-NIGHTLY SODIUM OXYBATE FORMULATION, IN PATIENTS WITH NARCOLEPSY: POST-HOC SENSITIVITY ANALYSES FROM THE REST-ON TRIAL

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**Introduction:** In REST-ON, once-nightly sodium oxybate (ON-SXB; FT218) achieved significant improvement (P<0.001) vs placebo for all coprimary endpoints: Maintenance of Wakefulness test (MWT) mean sleep latency, Clinical Global Impression of Improvement (CGI-I) rating, and weekly number of cataplexy attacks (NCA).
**Methods:** Individuals aged ≥16 years were randomized 1:1 to receive ON-SXB (1 week, 4.5 g; 2 weeks, 6 g; 5 weeks, 7.5 g; 5 weeks, 9 g) or placebo. Post-hoc sensitivity analyses were conducted with methods to handle missing data: completer population; placebo-based multiple imputation (MI) with missing not at random assumption; analysis of covariance (ANCOVA); and tipping point-based MI of worsening values until P>0.05.
**Results:** Completers (ON-SXB, n=69; placebo, n=79) showed significant improvement (P<0.001) with 6, 7.5, and 9 g ON-SXB vs placebo on all coprimary endpoints; with 9-g dose, mean (95% CI) differences vs placebo were 6.0 min (3.3–8.7) on MWT and –6.6 (–9.6 to –3.6) in NCA; 72.3% and 31.6%, respectively (odds ratio [OR], 5.7 [95% CI: 2.8–11.6]), were CGI-I responders. All ON-SXB doses achieved significant improvement (P<0.001) vs placebo on all coprimary endpoints with placebo-based MI and ANCOVA. With placebo-based MI, mean (95% CI) differences vs placebo (9-g dose) were 5.4 min (2.8–8.0) on MWT and –6.4 (–11.3 to –3.7) in NCA; 63.0% and 28.5%, respectively (OR, 4.3 [95% CI: 2.3–8.0]), were CGI-I responders. With ANCOVA, mean (95% CI) differences vs placebo (9-g dose) were 6.0 min (3.6–8.5) on MWT and –6.4 (–9.0 to –3.8) in NCA; CGI-I rating difference was –1.0 (–1.3 to –0.7). With MWT tipping point MI, between-treatment differences lost significance with worsening of 7.0, 5.2, and 4.3 min from baseline for 6, 7.5, and 9 g, respectively (implausible for 7.5- and 9-g doses). When withdrawals from ON-SXB were imputed as "not improved," CGI-I remained significant (all 3 doses, P<0.001). Mean NCA remained significant for all 3 doses vs placebo with worsening trajectories imputed; positive results were not tipped over with plausible values.
**Conclusion:** These results support the robustness of the primary efficacy data for ON-SXB for narcolepsy treatment.
**Support (If Any):** Avadel Pharmaceuticals

## 0403

### EFFICACY OF ONCE-NIGHTLY SODIUM OXYBATE (ON-SXB; FT218) FOR EXCESSIVE DAYTIME SLEEPINESS AND CATAPLEXY: POST-HOC NUMBER NEEDED TO TREAT AND EFFECT SIZE ANALYSES FROM REST-ON

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**Introduction:** FT218 is an investigational, extended-release, once-nightly formulation of sodium oxybate (ON-SXB) for adults with narcolepsy. ON-SXB treatment achieved significant improvement vs placebo (6 g, 7.5 g, and 9 g, all P<0.001) for the coprimary endpoints of mean sleep latency on the Maintenance of Wakefulness test (MWT), Clinical Global Impression of Improvement rating, and number of weekly cataplexy episodes (NCA), and the secondary endpoint Epworth sleepiness scale (ESS) score, in the phase 3 REST-ON trial (NCT02720744). Post-hoc analyses of numbers needed to treat (NNT) and effect sizes were performed to further contextualize the effectiveness of ON-SXB.
**Methods:** Participants in REST-ON (aged ≥16 years with narcolepsy type 1 or 2) were randomized 1:1 to receive ON-SXB (1 week, 4.5 g; 2 weeks, 6 g; 5 weeks, 7.5 g; 5 weeks, 9 g) or placebo. MWT response was defined as ≥5-min increase from baseline in mean sleep latency, ESS response as a score ≤10, and cataplexy response as ≥50% reduction from baseline in mean NCA. Effect sizes were calculated using Cohen's d; NNTs were the inverse of the absolute risk reduction.
**Results:** The modified intent-to-treat population included 190 participants (ON-SXB, n=97 [NT1, n=73]; placebo, n=93 [NT1, n= 72]). For MWT response, all ON-SXB doses (6 g at week 3, 7.5 g at week 8, and 9 g at week 13) had NNTs of 3 and effect sizes of 0.7–0.9. A dose-response effect was seen for ESS response with NNTs ranging from 3 to 6. Effect sizes were between –0.5 to –0.7 for the 3 doses (decreases signifying response). The NNT for cataplexy response was 6 for ON-SXB 6 g and 3 for ON-SXB 7.5 and 9 g; effect sizes were between –0.7 to –0.8.
**Conclusion:** NNT calculations show that 3–6 patients need to be treated with ON-SXB to achieve ≥5 minutes increased sleep latency on the MWT, ESS score ≤10, or a ≥50% reduction in cataplexy. Considering these post-hoc analyses may be useful to clinicians in discussing treatment expectations and provide support for the efficacy of ON-SXB for excessive daytime sleepiness and cataplexy in adults with narcolepsy.NNT calculations show that 3–6 patients need to be treated with ON-SXB to achieve ≥5 minutes increased sleep latency on the MWT, ESS score ≤10, or a ≥50% reduction in cataplexy. Considering these post-hoc analyses may be useful to clinicians in discussing treatment expectations and provide support for the efficacy of ON-SXB for excessive daytime sleepiness and cataplexy in adults with narcolepsy.
**Support (If Any):** Avadel Pharmaceuticals