• At the same daily dose, ADS-4101 exhibited equivalent bioavailability (determined by AUC0-24) to lacosamide IR.

- Known lacosamide IR AEs observed in this study (oral hypoesthesia, dizziness, abnormal dreams, and euphoria), incidences were comparable or lower for 600 mg ADS-4101 versus 400 mg lacosamide IR, and the number of subjects with these AEs were comparable tolerability relative to the approved maximum dose (400 mg) of lacosamide IR tablets, in healthy volunteers.

Objectives
The objective of this Phase 1b study was to evaluate the steadystate pharmacokinetic (PK) profiles of three ascending doses of ADS-4101 compared to three ascending doses of lacosamide IR in 24 healthy volunteers.

Methods
The study was a randomized, multi-dose, open-label, single-center, 2-treament (administered at three dose levels), crossover study in healthy volunteers comparing the PK profiles, safety, and tolerability of ADS-4101 Lacosamide IR formulation to lacosamide IR. The study was designed to allow for comparison of steady-state plasma concentrations during the day when the burden of seizures is highest. This was an open-label, single-center, 2-treament (administered at three dose levels), crossover study in healthy volunteers comparing the PK profiles of three ascending doses of ADS-4101 compared to three ascending doses of lacosamide IR. One formulation (Formulation 2) was selected for further evaluation (see Figure 1). This was an open-label, single-center, 2-treament study, and the following were included: 1) known partial-onset seizures, 2) age ≥ 18 years, 3) body weight of ≥ 50 kg, and 4) baseline lacosamide IR concentration of ≤ 100 mg/L. The study design is shown in Figure 2. Baseline demographic characteristics are presented in Table 1.

Key findings: ADS-4101 exhibited equivalent PK and tolerability to lacosamide IR in healthy volunteers, including the following:

- ADS-4101 exhibited a 1.7-fold increase in average daytime lacosamide concentration and a 1.4-fold increase in average nighttime concentration compared to 600 mg/day lacosamide IR.
- At the 600 mg dose, ADS-4101 provided high and sustained plasma concentrations overnight that peaked the following morning and were sustained throughout the day.
- At the same daily dose, ADS-4101 showed similar PK profiles to lacosamide IR, with comparable tolerability relative to the approved maximum dose (400 mg) of lacosamide IR tablets, in healthy volunteers.
- ADS-4101 was safe and well tolerated across all three doses.

Conclusions
These results support the clinical development of ADS-4101 up to 600 mg/day for partial onset seizures.

References

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