### INTRODUCTION

ZT-031 (also known as Ostabolin-C™) is a novel PTH analog that is designed to improve peptide delivery through the nasal mucosa for improved pharmacodynamics. The study aimed at evaluating the nasal absorption properties of ZT-031 in preclinical species.

### METHODS

**Study Design and Materials:**

- **Animals:**
  - Groups of 10 adult female Sprague Dawley rats were administered ZT-031 (10, 75, 125, 250) µg/kg by (SC) injection (75 µg/kg).
  - Groups of 5 male New Zealand white rabbits (Ramona, CA) were administered 100 µL IN instillations to both nares (50 µL per nare) under mild anesthesia.

- **Injection:**
  - ZT-031 was administered in 10 mM Sodium Acetate buffer, 0.1% EDTA at pH 5.0 with 0.18% DDM.

- **Sample Collection:**
  - Blood samples (1 mL) were drawn over a three hour time period at 0, 5, 10, 15, 25, 60 and 120 minutes following IN administration and collected in lithium/heparin anticoagulant-treated tubes and centrifuged immediately for plasma collection.

- **Analysis:**
  - The plasma concentration-time data were used to determine the pharmacokinetic parameters.

- **Statistical Analysis:**
  - Good systemic exposures were observed in all species with relative bioavailability in primates compared to IN dosing at the same dose without DDM.

### RESULTS

**Plasma Concentration-Time Data:**

The plasma concentration-time data were used to determine the pharmacokinetic parameters. The plasma concentration-time data for ZT-031 in rats, rabbits, and monkeys are shown in the figure. The Table shows the pharmacokinetic parameters for ZT-031 in rats, rabbits, and monkeys.

**DISCUSSION AND CONCLUSIONS:**

Based on the above, formulations of PTH analogs with DDM at 0.18% seem appropriate for human clinical trials, pending the results of preclinical toxicology studies.

**REFERENCES:**


### CONCLUSIONS: ZT-031 IN PK IN RATS

- **Dose-Proportional Exposure:**
  - Good systemic exposure of ZT-031 was achieved following IN dosing with dose proportional AUC and Cmax.
  - Tmax was rapid, within 15 minutes of dosing.

- **Good Systemic Exposure:**
  - Good systemic exposures were observed at all doses with relative bioavailability in primates compared to IN dosing at the same dose without DDM.

- **Compliance:**
  - The t½ in the presence of 0.18% DDM is increased longer (71% in the absence of DDM).

**Peptide therapeutics are typically administered via subcutaneous (SC) injection, which may limit their utility.**

**Like most peptide and protein drugs, ZT-031 is delivered by subcutaneous (SC) injection in all species**