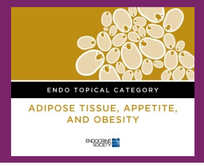
MON-691



Oral Delivery of a Bispecific GLP-1/GLP-2 Receptor Agonist (PG-102) via a Robotic Pill (RT-114) Achieves Bioequivalence to Subcutaneous Injection in Canines

Anvesh Dasari[1], Arvinder Dhalla[1], Leonard Fung[1], Mir Hashim[1], Kyle Horlen[1], Kristina Kaminskaya[1], Heather Kennedy[1], Hyo-Jin Kim[2], Jiseon Kim[2], Jong-Gyun Kim[2], Sae-Won Kim[2], Suyeon Lee[2], Deepa Mohan[1], Nidhi Patel[1], Kyoungmin Song[2], April Toledo Vo[1], Alyson Yamaguchi[1], Sang-In Yang[2]

[1]Rani Therapeutics LLC, San Jose, CA; [2]ProGen, Seoul, Republic of Korea. Potential conflict of interest may exist for all authors. Refer to Meeting App.

INTRODUCTION AND STUDY RATIONALE

PG-102 is a novel, long-acting bispecific agonist composed of GLP-1 and GLP-2 peptides fused to a central Fc domain currently in Phase 2 trials for obesity and type 2 diabetes.

However, as with most incretin mimetics, PG-102 requires injections which can lead to patient discomfort, reduced acceptance, and suboptimal adherence to therapy. To address this challenge, we have developed RT-114, an orally ingestible robotic pill which delivers PG-102 transenterically upon reaching the small intestine.

This nonclinical study was designed to compare the oral delivery of PG-102 via RT-114 with a subcutaneous (SC) injection of PG-102.

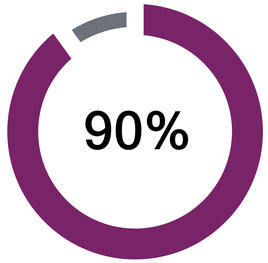
MATERIALS AND METHODS

Sixteen healthy canines were randomized to receive a single 12 mg dose of PG-102 either by SC injection (N=6) or orally via RT-114 (N=10). Over a 14-day period, PK (measured as serum drug concentrations by ELISA), PD outcomes (food intake and body weight), as well as safety, tolerability, and delivery reliability were evaluated. Data presented as mean ± SE. PK data are weight normalized.

RESULTS

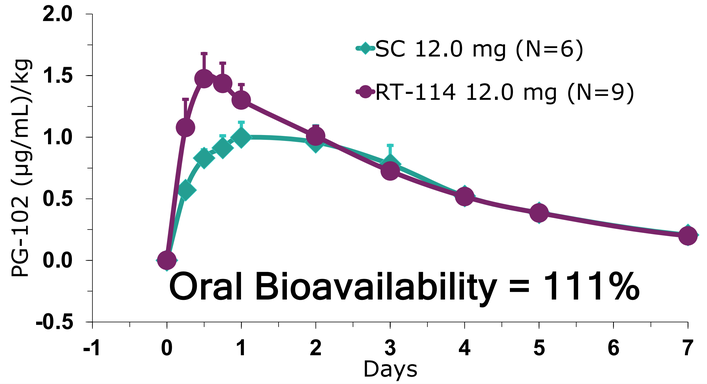
Fig 1. RP Success Rate





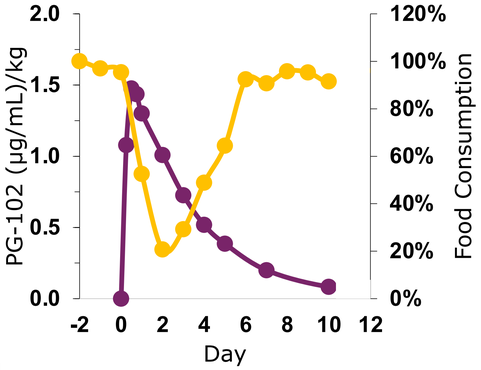
The RP successfully delivered drug in 9 of 10 subjects

Fig 2. PK of Oral vs SC PG-102 in Dogs



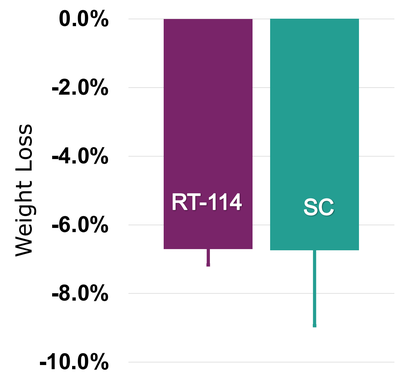
Route	C_{max} (µg/mL)/kg	T_{max} (days)	AUC_{last} (µg/mL*day)/kg
RT-114	1.51 ± 0.19	0.7 ± 0.2	5.48 ± 0.33
SC	1.06 ± 0.13	1.3 ± 0.3	4.92 ± 0.52

Fig 3. PK/PD Relationship for RT-114



Daily food intake moved inversely to serum drug concentrations

Fig. 4. Average Peak Weight Loss



Average peak weight loss was 6.7 ± 0.5% for RT-114 and 6.7 ± 2.2% for SC

HOW THE ROBOTIC PILL WORKS

Patients swallow the RP with a glass of water



In the stomach, the RP is protected by an enteric coating



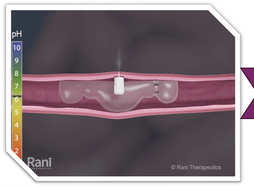
In the small intestine the RP shell dissolves and a chemical reaction to generate CO_2 is started



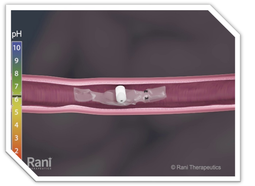
CO_2 gas inflates a ballon to align the device and actuates a microsyringe



Drug is delivered



The needle dissolves, balloon deflates, and remnants pass through the GI tract



Visit www.ranitherapeutics.com to learn more or scan the QR code to see a video of the Robotic Pill in action