POSTER
SAT-236

Pharmacokinetics and Pharmacodynamics of the Parathyroid Hormone Analog PTH 1-34 (Teriparatide) Delivered via an Orally Administered Robotic Pill (RT-102)

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Rani Therapeutics LLC, San Jose, CA and San Antonio, TX; Potential conflict of interest may exist for all authors. Refer to Meeting App.

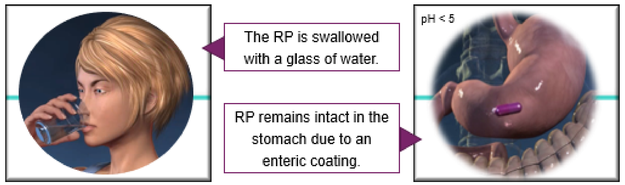
Rani THERAPEUTICS

INTRODUCTION AND STUDY RATIONALE

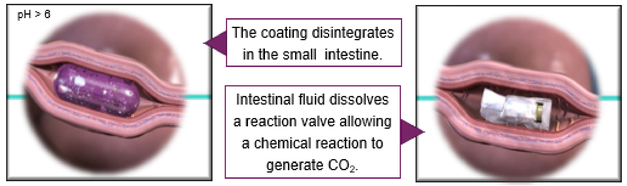
Rani Therapeutics is developing RT-102 as an oral, anabolic therapy for osteoporosis. Teriparatide is formulated for delivery as a rapidly dissolvable microtablet (sealed inside a dissolvable needle) and delivered by a robotic pill (RP) – a novel, orally ingestible delivery platform. As such, this represents a route of drug delivery which could potentially affect the kinetics of drug uptake, distribution, and elimination as well as efficacy of the drug. These nonclinical studies assessed the pharmacokinetic (PK) and pharmacodynamic (PD) profiles of teriparatide delivered via the RP.

HOW THE ROBOTIC PILL WORKS

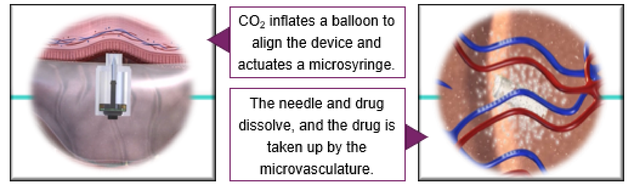
1. Enteric-Coated Robotic Pill is Ingested



2. Enteric Coating Disintegrates in Small Intestine



3. Drug is Delivered



MATERIALS AND METHODS

Pharmacodynamics



Female Sprague-Dawley rats each underwent an ovariectomy or sham surgery to initiate an 8-week bone depletion period. Beginning on Day 0, RT-102 drug substance was administered intraperitoneal (IP) at 2-, 5-, or 15 µg/kg to mimic RP delivery. Alternatively, Reference Article (Forteo® or Abaloparatide at 5 µg/kg) was administered SC. Dual Energy X-Ray Absorptiometry (DXA) imaging was performed to assess bone mineral density (BMD) after 6 weeks.

Pharmacokinetics



The PK profile of teriparatide delivered orally via the RP (RT-102) was determined in awake Beagle dogs over a range of doses. Reference PK curves were also generated with Forteo® administered by SC or IV injection. Serial blood samples were collected and serum concentrations of teriparatide were measured using a qualified ELISA.

PK data presented as mean ± SE;
PD data presented as mean ± 95% CI;
Horizontal dashed line represents normal (non-OVX) control;
** = p<0.05 vs. Model Control; Anova followed by Dunnett's.*

RESULTS

Fig 1. Mixed Bone Density

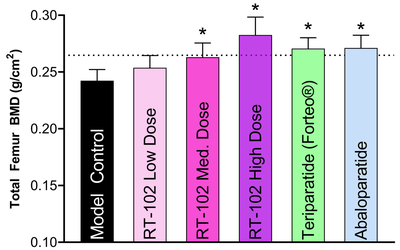


Fig 2. Cortical Bone Density

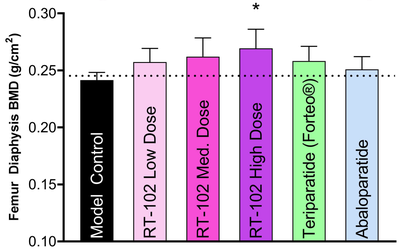


Fig 3. Trabecular Bone Density

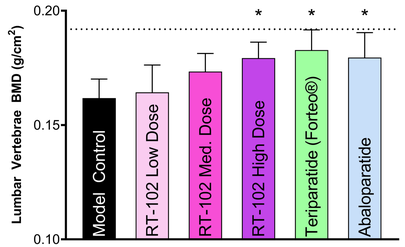


Table 1. Comparison of BMD for RT-102 and Forteo® at Equivalent Doses

	BMD (g/cm²)		Sig
	RT-102 (IP)	Forteo® SC	p-value
Total Femur	0.263 ± 0.011	0.271 ± 0.009	0.990
Diaphysis	0.262 ± 0.014	0.258 ± 0.011	1.000
Lumbar Vertebrae	0.173 ± 0.006	0.183 ± 0.008	0.855

Fig. 4. Mean Serum Teriparatide Concertation Following Various Routes of Administration

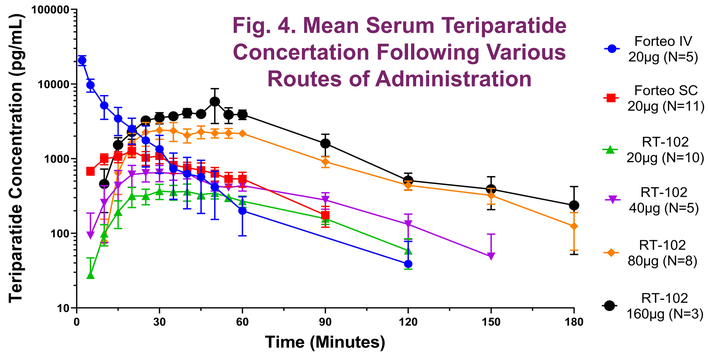


Table 2. Summary PK Parameters in Beagle Dogs

Study Group	C_{max} (pg/mL)	T_{max} (min)	AUC (pg*h/mL)	Bioavailability (%F)
IV 20µg	20,762 ± 3,103	2 ± 0	3,064 ± 891	100
SC 20µg	1,343 ± 227	21 ± 3	1,038 ±196	34 ± 6
RT-102 20µg	492 ± 77	37 ± 4	454 ± 61	15 ± 2
RT-102 40µg	979 ± 159	42 ± 13	798 ± 72	13 ±1
RT-102 80µg	3,511 ± 623	40 ± 6	3,009 ± 352	25 ± 3
RT-102 160µg	6282 ± 2616	48 ± 4	5353 ± 1244	22 ± 5

CONCLUSIONS

- **RT-102 capsules administered orally to canines yielded steep rises in serum teriparatide concentrations followed by rapid elimination within three hours.**
- **RT-102 drug substance delivered IP to mimic Robotic Pill delivery in a rodent model of osteoporosis was osteoanabolic and was similar to equivalent Forteo® doses injected SC.**
- **These data provide PK and PD proof-of-concept for potential to replace current injection therapy with oral RT-102 for treatment of osteoporosis.**

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

Check out RT-102 Phase I Clinical Data here at ENDO – Poster SAT-235
See the Robotic Pill with Follicle Stimulating Hormone – Poster FRI-415