

# RT-102 Phase I Study Part 2: Repeat-Dose Update



December 2022

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# Forward-Looking Statements

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# Presentation Overview

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- Topline results from Part 2 of our RT-102 Phase 1 study
  - Seven-day repeat-dose study in healthy volunteers
- First repeat-dose study of RaniPill capsule in humans collecting data on:
  - Safety
  - Tolerability
  - Device Reliability
- Important data
  - For the RT-102 program and Phase 2 plan for 2023
  - For RaniPill platform in general

# RT-102 Phase 1 Study Design

**Objective: To Evaluate the Safety, Tolerability and Pharmacokinetics of Parathyroid Hormone (1-34) (PTH) Administered Orally via RaniPill™ Capsule**

## Part 1 : Single ascending doses of RT-102

- RT-102 Group 1: 20µg (N=15)
- RT-102 Group 2: 80µg (N=15)
- Control Group: Forteo® SC 20µg (N=10)

## Part 2: Repeat-doses of RT-102

- Once daily dose of RT-102 20µg for 7 days in healthy and post-menopausal women (N=10)

# Part 1 Summary

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- Safety & Tolerability
  - Both doses of RT-102 were well tolerated
  - No serious adverse events (SAEs) reported in the study
  - No adverse events (AEs) related to RaniPill reported
- Device Performance
  - Drug delivery success rate of 95%
- Pharmacokinetics
  - Bioavailability of PTH delivered via RT-102 was >300% higher than subcutaneous (SC) injection

Part 2:  
Arvinder Dhalla, PhD  
Vice President, Clinical Development



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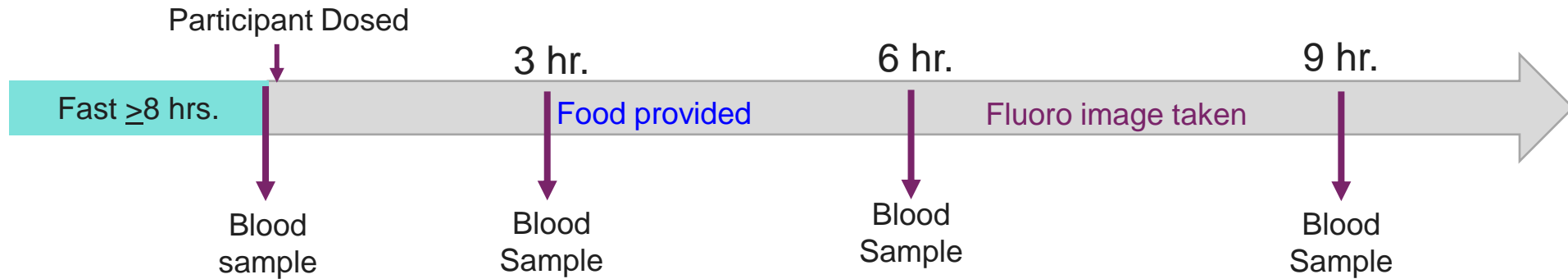
## Part 2 Study Overview

### A Phase I Study to Evaluate the Pharmacokinetics of Parathyroid Hormone (1-34) (PTH) Administered Orally via RaniPill™ Capsule

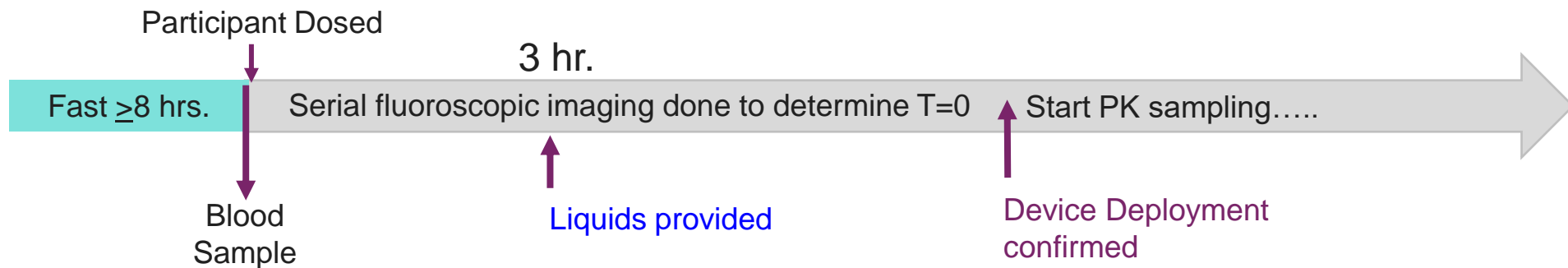
Objective	To evaluate the safety and tolerability of repeat-doses of RT-102
Study Population	Healthy women and Post-menopausal women (N=10)
Study Site	Single Site in Australia
Study Group	A single group receiving RT-102 20µg dose for 7 days
End Points	<ul style="list-style-type: none"><li>• Safety and tolerability of repeat-doses of RT-102</li><li>• Reliability of drug delivery</li></ul>
Start Date	August 1, 2022

# Repeat-Dose: Study Procedures

## Days 1-6



## Day 7



Participation in the study was considered complete if a participant was able to complete all doses for 7 days and go through pharmacokinetic sampling on Day 7





# Topline Results

# Study Demographics

	Healthy Women	Post-Menopausal
	N=5	N=5
<b>Age</b>	25.6 years (22 - 35)	60 years (54 - 65)
<b>Race</b>	<b>% (n/N)</b>	<b>% (n/N)</b>
Hispanic	20 (1/5)	0 (0/5)
White-non-hispanic	20 (1/5)	100 (5/5)
Asian	40 (2/5)	0 (0/5)
Asian-Pacific Islander	20 (1/5)	0 (0/5)
	Mean ± SD (Min - Max)	Mean ± SD (Min - Max)
Weight (kg)	60.6 ± 9.8 (50.2 - 76)	64.3 ± 10.1 (55.6 - 75.4)
Body Mass Index (kg/m <sup>2</sup> )	23.7 ± 2.5 (20.4 - 26.9)	25.3 ± 5 (20.9 - 31.7)

# Exclusions after Enrollment

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- Enrollment was done on a rolling basis to complete ten subjects, total number of participants enrolled were 17
- Seven participants did not complete 7 days of dosing due to exclusions per protocol
  - Two participants started menstruation on Day 4
  - One participant had cannulation issues on Day 7
  - One participant had elevated eosinophils on Day 4 due to an earring infection
  - One participant had >7 hr. gastric residence time (GRT) on Day 7
  - Two participants had pill remnants exceeding the number ( $\geq 3$ ) allowed by protocol

**None of the participants stopped the dosing due to any adverse events related to the RaniPill**

# Adverse Events

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	<b>Adverse Event</b>	<b>Incidence</b>
<b>PTH-related</b>	Constipation*	1 (10%)
	Diarrhea*	1 (10%)
<b>RaniPill-related</b>	Abdominal Pain	1 (10%)

\* Same subject reported both AEs on different days

# Daily Drug Delivery by RaniPill with Repeat-Dosing

Drug signal detected in 63 out of 69 deployments\* = **at least 91% Success Rate**

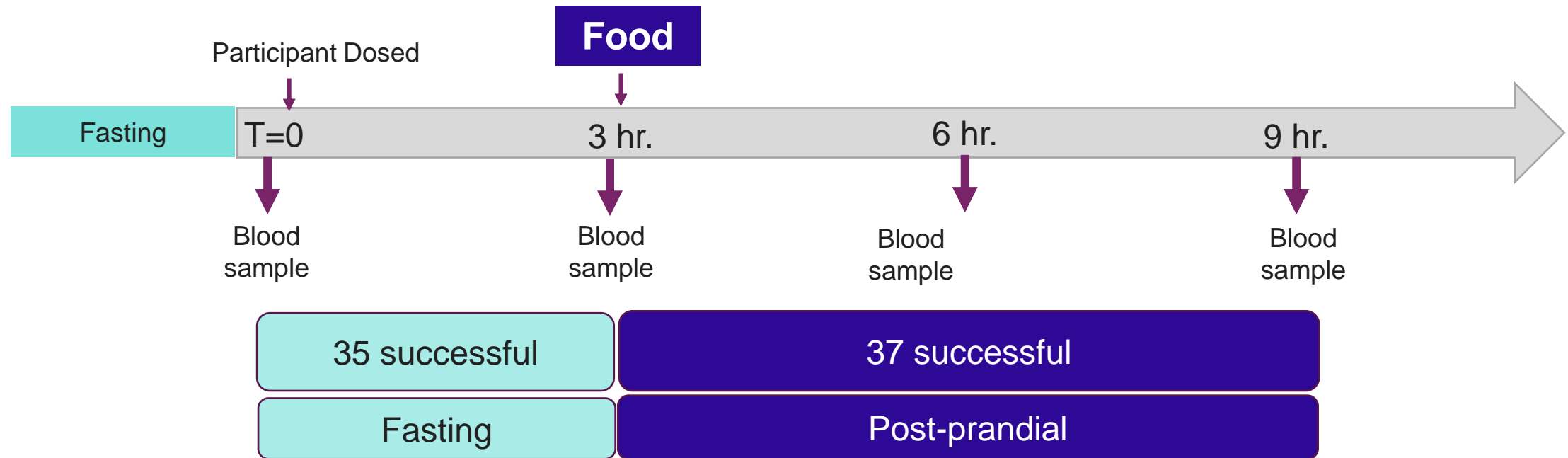
#	Subject Type	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
1	HW	✓	✓	✓	✓	✓	✓	✓
2	HW	✓	✓	✓	✓	✓	✓	✓
3	HW	✓	✗	✓	✓	✓	✓	✓
4	HW	✗	✓	✓	✓	✓	✓	✓
5	HW	✓	✗	✓	✓	✓	✓	✓
6	PM	✓	✓	✓	✓	✓	✓	✓
7	PM	✗	✓	✓	✓	✓	✓	✓
8	PM	NA	✓	✓	✗	✓	✗	✓
9	PM	✓	✓	✓	✓	✓	✓	✓
10	PM	✓	✓	✓	✓	✓	✓	✓

\*Deployment confirmed by imaging but not tracked; samples taken at 3 hr. intervals post-dose. Some misses could be due to mismatch of sampling and deployment time

# Presence of Food Did Not Impact Device Performance

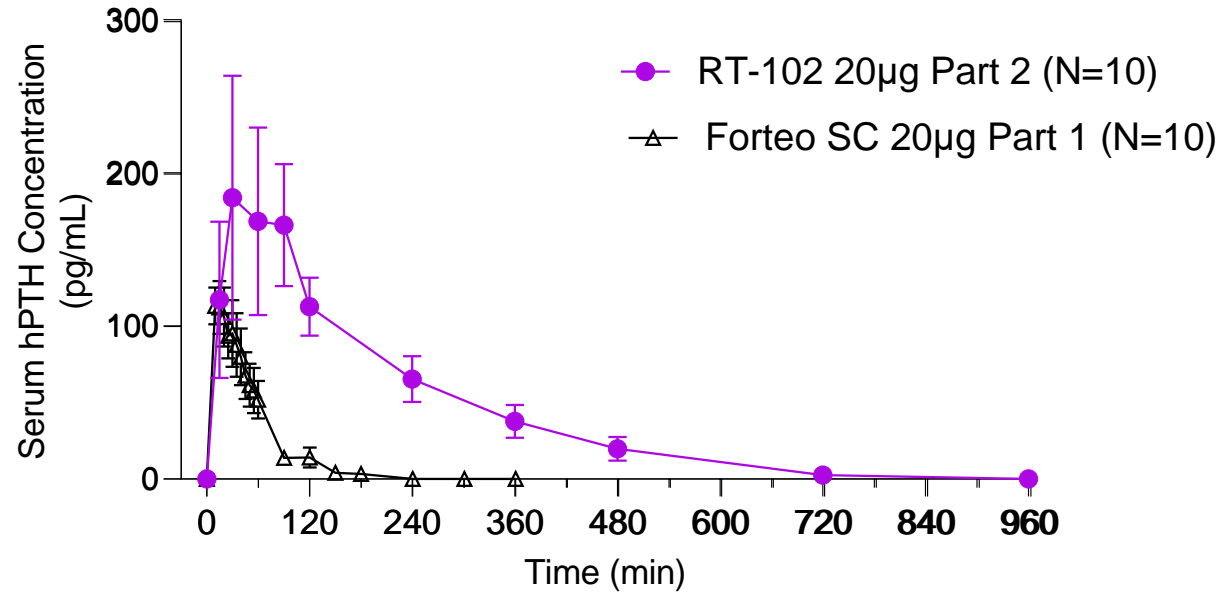
- On Days 1-6, food was consumed at 3 hrs. after capsule administration to all enrolled subjects
- During this period, there were a total of 72 successful deployments
- 35 were recorded before food was consumed (fasted)
- 37 were recorded after food was consumed (post-prandial)

***These data suggest that drug delivery by the RaniPill was unaffected by presence of food***



# PK Profile of PTH Delivered via RaniPill

Drug levels were observed in all 10 subjects on Day 7 = 100% success rate



- These data corroborate the high bioavailability observed in Part 1 and suggest that RT-102 may be efficacious at doses lower than 20µg

# Repeat Doses of RT-102 Key Takeaways

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- RT-102 was well tolerated with repeat dosing
- No SAEs were reported in the study
- Device remnants were eliminated without sequelae in all subjects



- RT-102 RaniPill delivered PTH with reliability of >90%
- Device performance was unaffected by presence of food



- Cmax comparable to SC Forteo
- No accumulation of PTH observed



Next Steps  
Talat Imran, CEO



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# Next Steps and Upcoming Potential Milestones

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- Pre-IND meeting request
- Conduct 28-day GLP study
  - Early 2023
- Initiate Phase 2 Study
  - 2H 2023
- Plan to publish RT-102 Phase 1 Study results
- Additional 2023 prospective milestones:
  - Initiation of a Phase 1 study of RT-111 containing an ustekinumab biosimilar
  - Initiation of a Phase 1 study of RT-105 containing an adalimumab biosimilar
  - Initiation of a Phase 1 study of RT-110 containing PTH for hypo-parathyroidism

# Appendix

# Study Demographics

	Total Cohort (N=17)		Completed Dosing (N=10)	
	Healthy Women	Post-menopausal	Healthy Women	Post-menopausal
	N=11	N=6	N=5	N=5
Age	28 years (22 - 49)	58.8 years (53 - 65)	25.6 years (22 - 35)	60 years (54 - 65)
<b>Race</b>	<b>% (n/N)</b>	<b>% (n/N)</b>	<b>% (n/N)</b>	<b>% (n/N)</b>
Hispanic	18.2 (2/11)	0 (0/6)	20 (1/5)	0 (0/5)
White-non-hispanic	45.4 (5/11)	100 (6/6)	20 (1/5)	100 (5/5)
Asian	11.8 (2/11)	0 (0/6)	40 (2/5)	0 (0/5)
Asian-Pacific Islander	11.8 (2/11)	0 (0/6)	20 (1/5)	0 (0/5)
	Mean ± SD (Min - Max)	Mean ± SD (Min - Max)	Mean ± SD (Min - Max)	Mean ± SD (Min - Max)
Weight (kg)	62.2 ± 8.7 (50.2 - 77.6)	63.7 ± 9.2 (55.6 - 75.4)	60.6 ± 9.8 (50.2 - 76)	64.3 ± 10.1 (55.6 - 75.4)
Body Mass Index (kg/m <sup>2</sup> )	24.2 ± 2.6 (20.4 - 29.9)	24.8 ± 4.7 (20.9 - 31.7)	23.7 ± 2.5 (20.4 - 26.9)	25.3 ± 5 (20.9 - 31.7)

# Adverse Events

	Adverse Event	All Enrolled Participants (N=17)	Participants Completed 7 days (N=10)
<b>PTH-related</b>	Constipation*	1 (5.9%)	1 (10%)
	Diarrhea*	1 (5.9%)	1 (10%)
	Headache	1 (5.9%)	0
<b>RaniPill-related</b>	Abdominal Pain	2 (11.8%)	1 (10%)
	Burping	1 (5.9%)	0

Data from Part 2 of the Phase 1 study of RT-102.

\* Same subject reported both AEs on different days

# Device Performance with Repeat Doses

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Data from 10 participants who completed the 7-day repeat-dosing

Drug signal detected in 63 out of 69 deployments\*

**At least 91% Success Rate**

Data from all 17 participants

Drug signal detected in 82 out of 93 deployments\*

**At least 88% Success Rate**

\*Deployment confirmed by imaging but not tracked

Samples taken at 3 hr. intervals post-dose

Some misses could be due to mismatch of sampling and deployment time



RT-102 Phase 1: Oral Administration  
of PTH (1-34) Via the RaniPill and  
PD Studies for Osteoporosis

# RT-102 Phase 1 Study Overview

## Study Design

To evaluate the safety, tolerability and pharmacokinetics (PK) of Parathyroid Hormone (1-34) (PTH) administered orally via the RaniPill Capsule in single ascending doses\*

### Study Details

- Two RT-102 treatment groups in healthy women volunteers
  - RaniPill containing 20µg of PTH
  - RaniPill containing 80µg of PTH
- Control group of 20µg SC Forteo®\*\*
- Single site in Australia

### Methods

- Transit of RaniPill capsule in GI tract tracked via frequent fluoroscopic imaging\*\*\*
- Deployment confirmed before starting PK sampling
- PK sampling done for 360 minutes

### Endpoints

- PK parameters of RT-102
- Safety and Tolerability of RT-102

\* Part 1 of the Phase 1 study is single-ascending doses. Part 2, involving repeat doses, is ongoing.

\*\* Forteo® is a registered trademark of Eli Lilly and Company.

\*\*\* Per protocol, in instances where RaniPill capsule did not exit the stomach within 7 hours, participants were excluded from the study. Based on the exclusion criteria, 3 participants were excluded from the study. 1 additional subject was excluded due to vomiting the capsule intact.



# RT-102 Phase 1 (Part 1) Study Results

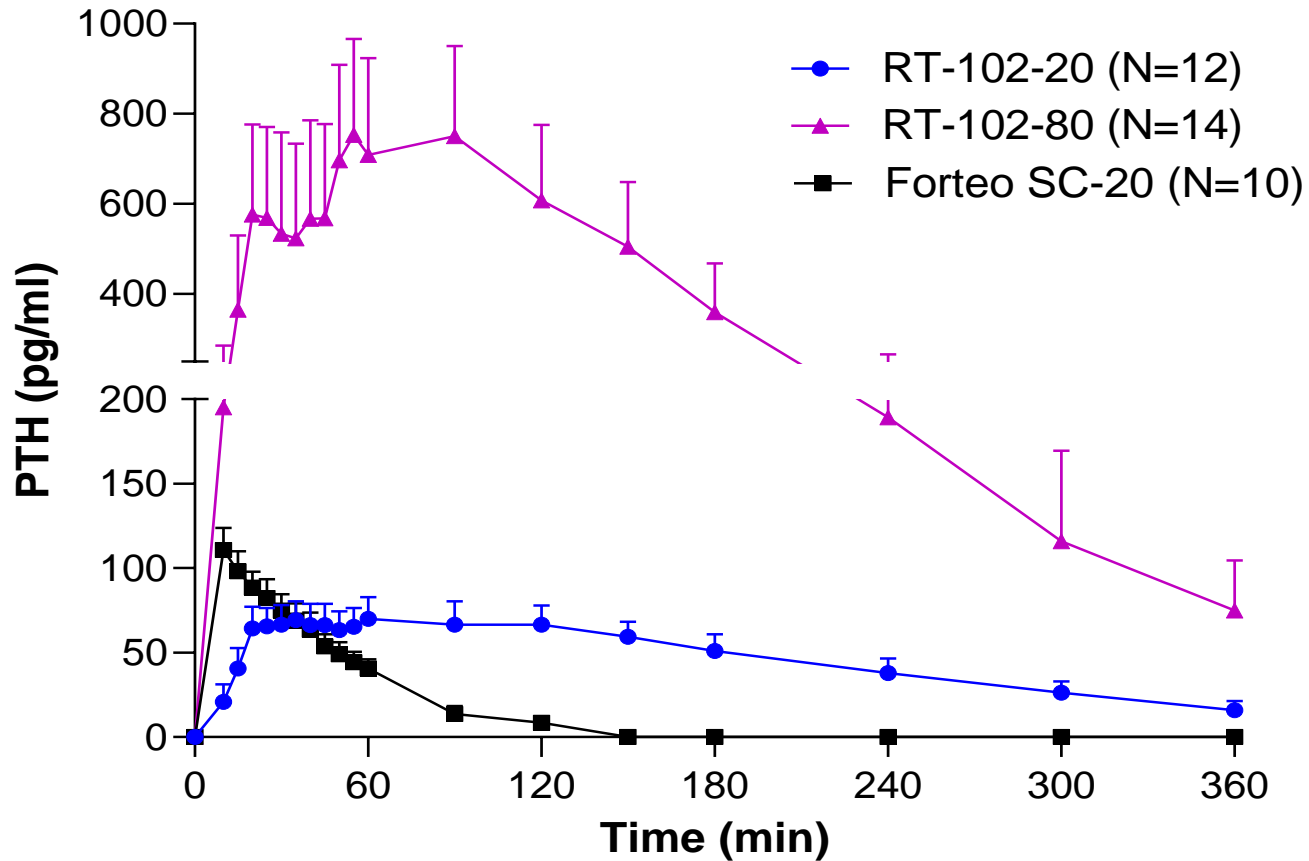
## Study Results

- RT-102 was generally well-tolerated by all subjects
- No serious adverse events noted in the study
- No subject excluded due to difficulty swallowing the capsule
- Capsule remnants passed out in all subjects

### Incidence of Adverse Events

	Adverse Events	RT-102 20µg (N=15)	RT-102 80µg (N=14)*	Forteo SC 20µg (N=10)
	<b>All</b>	<b>0</b>	<b>2 (14%)</b>	<b>5 (50%)</b>
<b>Drug-Related Adverse Events</b>	Light headedness	0	0	2 (20%)
	Nausea	0	1 (7%)	3 (30%)
	Vomiting	0	1 (7%)	0
<b>RaniPill-Related Adverse Events</b>	All	0	0	N/A

# RaniPill Delivered PTH with Higher Bioavailability than SC

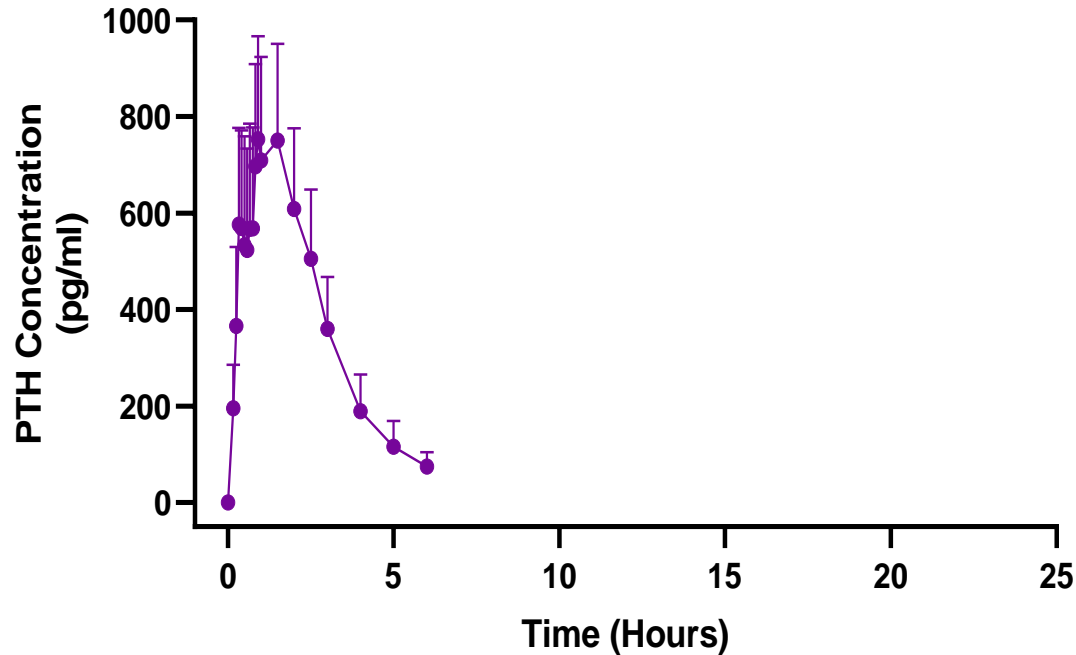


PK Parameters

	Forteo SC 20µg	RT-102 20µg	RT-102 80µg
Cmax (pg/mL)	128 ± 20	98 ± 10	971 ± 223
Tmax (minutes)	13	68	60
AUC (pg*h/mL)	126 ± 64	342 ± 36	2600 ± 649
Relative BA (%)		~300%	~400%

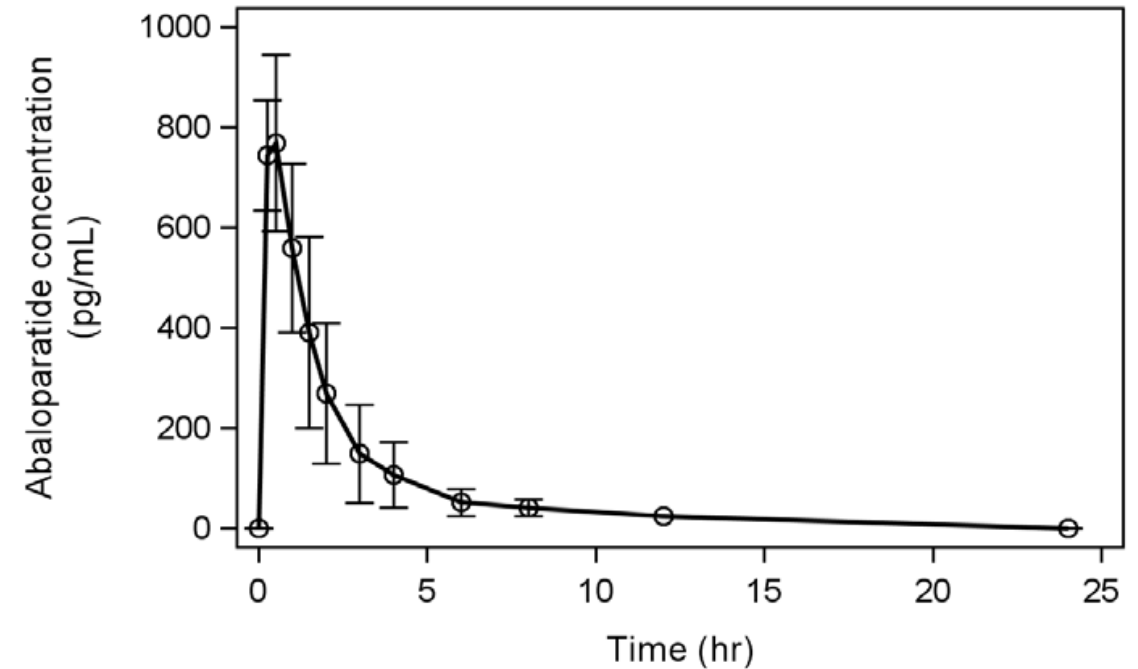
# RT-102 80µg PK Profile is Similar to Tymlos®\* at 80µg\*\*

RT-102 Phase I Data - Dose 80µg



- $C_{max}$  971 (223) pg/mL
- $AUC_{0-24}$  2600 (649) pg·hr/mL

Tymlos Package Insert - Dose 80µg



- $C_{max}$  812 (118) pg/mL
- $AUC_{0-24}$  1622 (641) pg·hr/mL

80µg abaloparatide (Tymlos) showed bone mineral density improvements significantly greater than 20µg teriparatide (Forteo) at several bone sites in a Phase 3 study\*\*\*

# RT-102 DS\* is Osteoanabolic in a Rat Model of Osteoporosis

## Study Objective

To evaluate the effect of daily dosing with RT-102 drug substance (\*DS; teriparatide in Rani formulation) on bone mineral density (BMD) in an ovariectomized (OVX) rat model of osteoporosis

## Model & Study Design

Model: Juvenile female rats with 8 weeks of bone depletion following ovariectomy

Design: Groups of 10 rats received daily doses for 6 weeks of saline or drugs (@5 µg/kg/day) as follows:

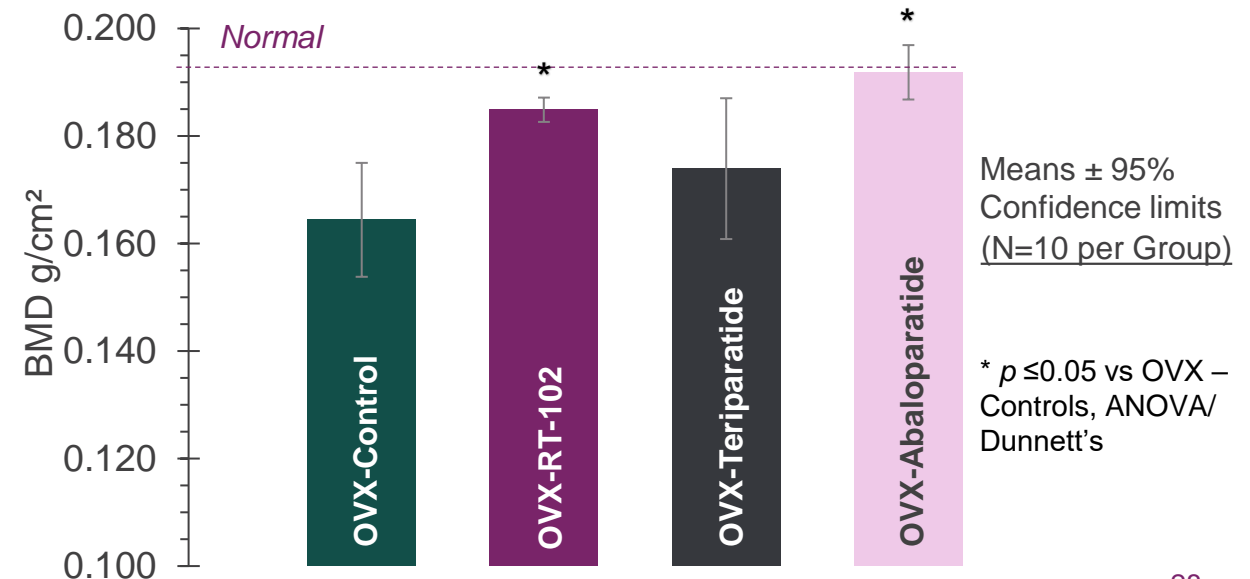
- OVX-Controls: Saline via IP route\*
- OVX-RT-102: RT-102 DS via IP route\*
- OVX-Teriparatide: Teriparatide via SC route
- OVX-Abaloparatide: Abaloparatide via SC route

\* IP or intraperitoneal route mimics RaniPill delivery

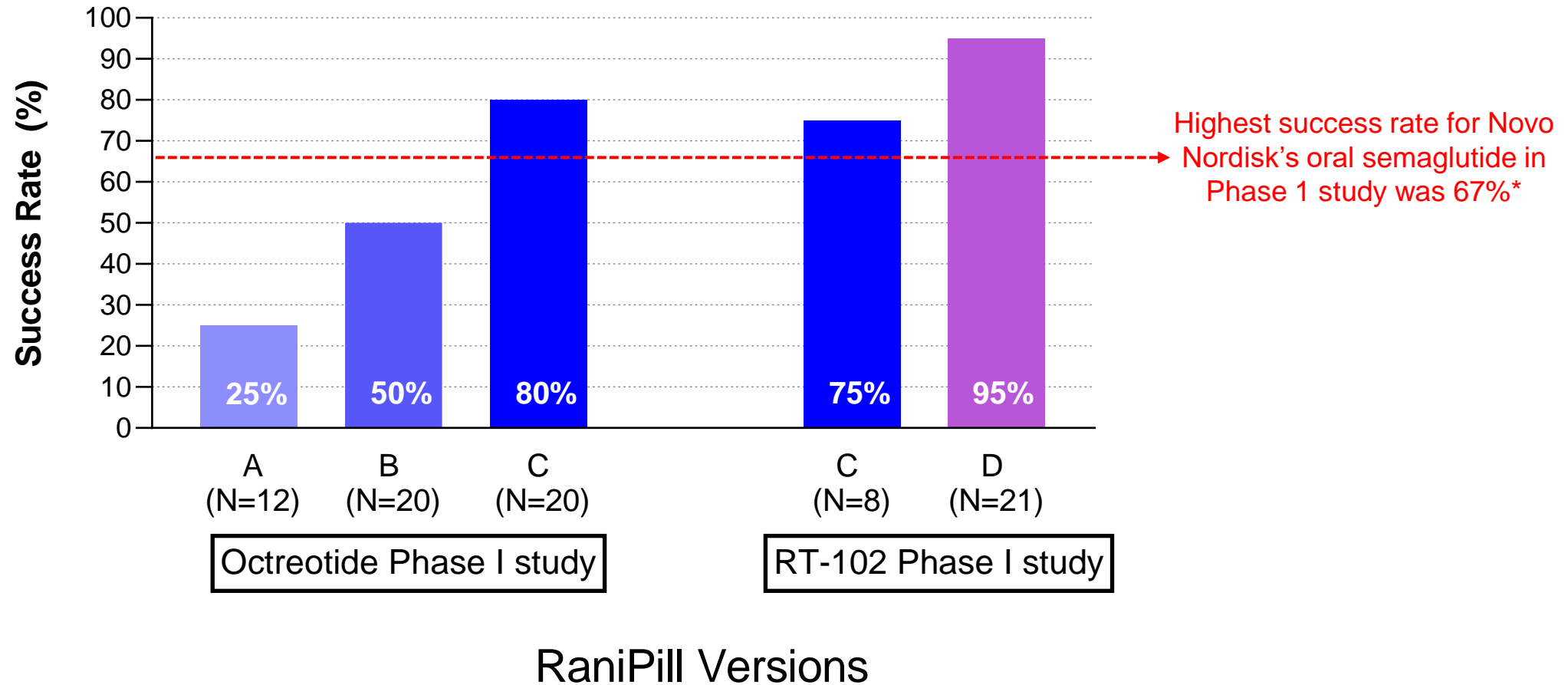
## Key Endpoint

- Change in BMD following 6 weeks of treatment

## Results: Osteoanabolic Effect of RT-102 DS on Whole Body BMD



# Device Performance: Progression of Drug Delivery Success Rate



# Phase I (Part 1) Study Summary

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Adverse events related to the RaniPill platform



95%

RaniPill platform drug delivery success rate\*



>300%

RT-102 bioavailability compared to SC injection

