Entera Bio

Corporate Presentation

September 2023

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Important factors that could cause actual results to differ materially from those reflected in Entera’s forward-looking statements include, among others: changes in the interpretation of clinical data; results of our clinical trials; the FDA’s interpretation and review of our results from and analysis of our clinical trials; unexpected changes in our ongoing and planned preclinical development and clinical trials, the timing of and our ability to make regulatory filings and obtain and maintain regulatory approvals for our product candidates; the potential disruption and delay of manufacturing supply chains; loss of available workforce resources, either by Entera or its collaboration and laboratory partners; impacts to research and development or clinical activities that Entera may be contractually obligated to provide; overall regulatory timelines; the size and growth of the potential markets for our product candidates; the scope, progress and costs of developing Entera’s product candidates; Entera’s reliance on third parties to conduct its clinical trials; Entera’s expectations regarding licensing, business transactions and strategic collaborations; Entera’s operation as a development stage company with limited operating history; Entera’s ability to continue as a going concern absent access to sources of liquidity; Entera’s ability to obtain and maintain regulatory approval for any of its product candidates; Entera’s ability to comply with Nasdaq’s minimum listing standards and other matters related to compliance with the requirements of being a public company in the United States; Entera’s intellectual property position and its ability to protect its intellectual property; and other factors that are described in the “Cautionary Statements Regarding Forward-Looking Statements,” “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” sections of Entera’s most recent Annual Report on Form 10-K filed with the SEC, as well as the company’s subsequently filed Quarterly Reports on Form 10-Q and Current Reports on Form 8-K. There can be no assurance that the actual results or developments anticipated by Entera will be realized or, even if substantially realized, that they will have the expected consequences to, or effects on, Entera. Therefore, no assurance can be given that the outcomes stated or implied in such forward-looking statements and estimates will be achieved. Entera cautions investors not to rely on the forward-looking statements Entera makes in this presentation. The information in this presentation is provided only as of the date of this presentation, and Entera undertakes no obligation to update or revise publicly any forward-looking statements, whether as a result of new information, future events or otherwise, except to the extent required by law.

Entera Bio: Leader in Orally Administered Protein Therapies

- **Proprietary oral delivery technology enables first-in-class, mini tablet formats of protein and peptide replacement therapies**
- Underserved conditions where **oral administration can significantly shift treatment outcomes**, versus standard of care injectable proteins
- **Our oral hPTH*(1-34) teriparatide mini tablets** have been administered to a total of 240 subjects (153 patients) across Phase 1 and Phase 2 studies, with **demonstrated PK/bioavailability and clinical benefit across two distinct diseases**
- **High-risk, no prior fracture osteoporosis (EB613, Phase 3) and hypoparathyroidism (EB612, Phase 1B) are serious – both underserved diseases which disproportionately afflict women, globally**
- **Pre-clinical research on GLP-2, kappa agonist, other peptides through feasibility, seeking strategic partnerships**
- **Nasdaq: ENTX**

*Parathyroid hormone (PTH) is an 84-amino acid hormone and the primary regulator of calcium and phosphate metabolism in bone and kidney. The synthetic analog of PTH, hPTH (1-34) peptide, Forteo® (teriparatide injection) has been approved in the US and EU (Forsteo®) for the treatment of osteoporosis since 2002/2003.

Experienced Leadership Team

Miranda Toledano, MBA Chief Executive Officer	20+ years of biotech C-level leadership and wall street experience; Previously co-founder/COO/CFO TRIGR (Acquired by Compass Therapeutics, Nasdaq: CMPX); Head of HC Investment Banking at MLV/FBR (Acquired B Riley); VP Investments, Royalty Pharma (Nasdaq: RPRX)
Art Santora, MD, PhD Chief Medical Officer	35 years of endocrinology/ special care and pharmaceutical experience; 28 years at Merck (lead clinical physician for Fosamax®); Medical Officer at the US FDA in the Division responsible for osteoporosis and other diseases of bone and calcium metabolism
Hillel Galitzer, PhD, MBA Chief Operating Officer	20+ years of biotech , early R&D, supply chain and operating experience. Previously, served as analyst/COO at Hadasit Bio Holdings Ltd., (TASE: HDST); co-founder and former COO of Optivasive Inc.
Gregory Burshtein, PhD VP of R&D	20+ years experience in academic and biopharmaceutical research focusing on advanced oral drug delivery, protein based oral drug delivery and oral delivery of biologic molecules
Anke Hoppe, BSc VP of Clinical Operations	30 years of clinical operations experience in global pharma and various clinical research organizations (Sanofi, Syneos, Covance, Vertex Pharmaceuticals)
Dana Yaacov, CPA, MBA Chief Financial Officer	15 years of finance management and accounting experience; Previously served as Senior Manager at PwC Israel overseeing audits of public and private companies.

Clinical & Scientific Advisory Board

Professor John P. Bilezikian	Vice-Chair, Department of Medicine for International Research and Education; Chief, Emeritus, of the Division of Endocrinology; Director, Emeritus, of the Metabolic Bone Diseases Program at Columbia University Medical Center
Professor Maria Luisa Brandi	Professor of Endocrinology, FIRMO Foundation, Italy
Professor Bart Clarke	Professor of Medicine and Consultant, Division of Endocrinology, Diabetes, Metabolism, and Nutrition, Mayo Clinic
Professor Felicia Cosman	Professor of Medicine, Emerita, Columbia University College of Physicians and Surgeons, Division of Endocrinology; Co-Editor in Chief of the journal Osteoporosis International
Professor William Fraser	Professor of Medicine at Norwich Medical School at the University of East Anglia and Consultant in Metabolic Medicine at the Norfolk and Norwich University Hospital, UK
Dr. Roger Garceau	Former Chief Medical Officer and EVP at NPS Pharmaceuticals and Shire plc (Natpara®); Sanofi/Pharmacia
Professor Steven R. Goldstein	Professor of Obstetrics and Gynecology at New York University School of Medicine and former President of The International Menopause Society, the North American Menopause Society
Professor Sophia Ish-Shalom	Vice President of the Israeli Foundation for Osteoporosis and Bone Diseases (IFOB) , Endocrine Clinic Elisha Hospital prior Head of Bone and Mineral Metabolism Unit, Rambam Health Care Campus , Israel
Professor Socrates Papapoulos	Emeritus Professor in Diseases of Bone & Mineral Metabolism, Advisor Center for Bone Quality, Leiden University Medical Center, The Netherlands

Oral Bioavailability Challenges:

Most therapeutic peptides/proteins are Administered via IV, SC or IM Injections due to proteolytic degradation, variability and lack of absorption from GI Tract

International Journal of Pharmaceutics: X

The combined effect of permeation enhancement and proteolysis inhibition on the systemic exposure of orally administrated peptides: Salcaprozate sodium, soybean trypsin inhibitor, and teriparatide study in pigs

Gregory Burshtein, Constantin Itin, Jonathan C.Y. Tang, Hillel Galitzer, William D. Fraser, Phillip Schwartz

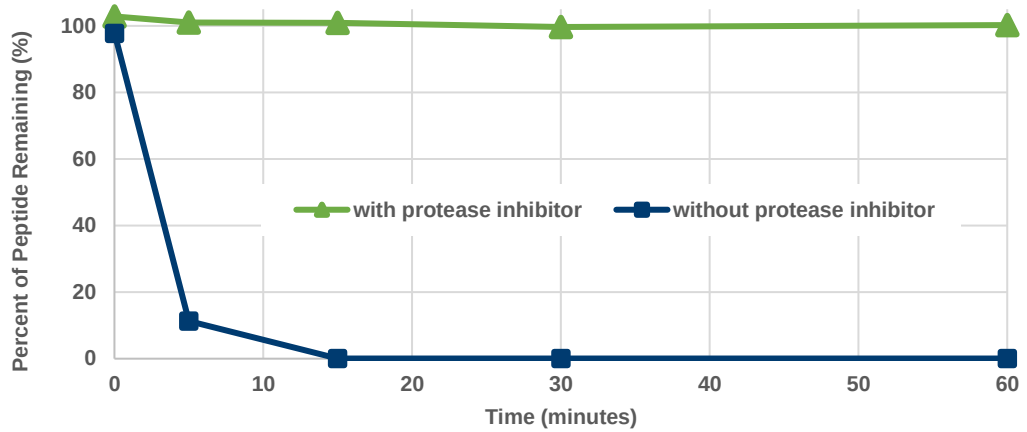
Proteolysis Inhibition to Maintain the Stability of the Peptide: Buffering agents elevate gastric pH, deactivating pepsin; SBTI reduces enzymatic degradation of peptide drug **(Stability)**

Transcellular Permeation Enhancer (SNAC): Enables absorption of the peptide via enterocyte membrane into the plasma **(Bioavailability)**

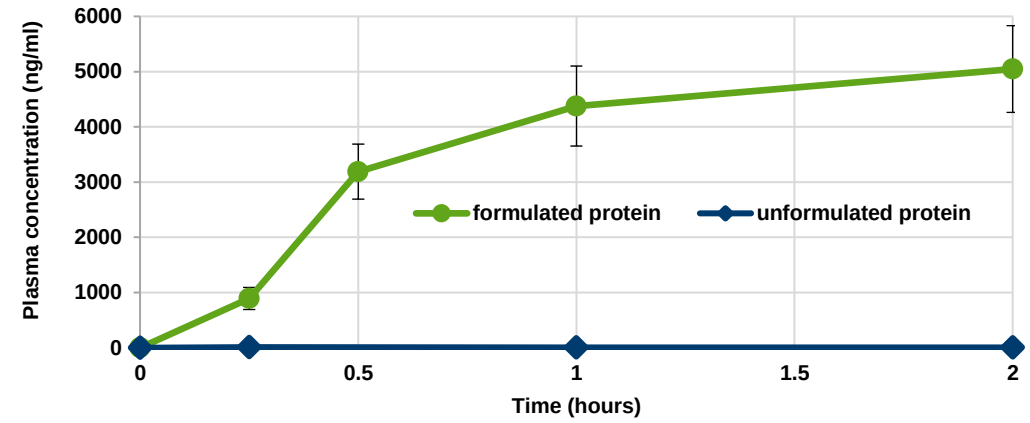
The result is a convenient, daily mini tablet form

Entera Proprietary Oral Delivery Platform

SBTI Stabilizes the Protein



SNAC Dramatically Increases Systemic Plasma Levels of the Protein

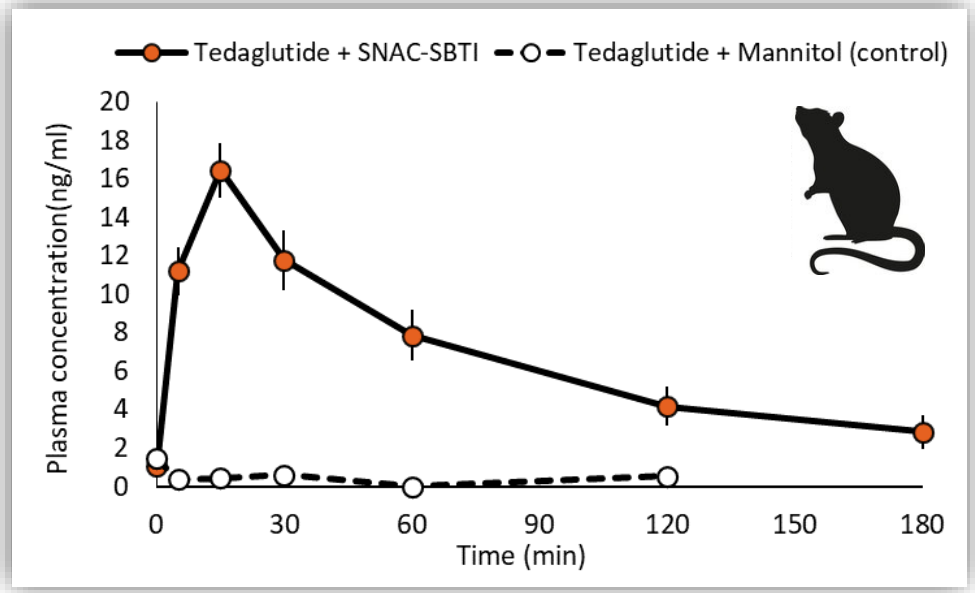


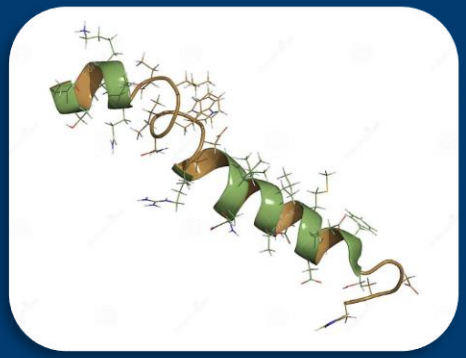
Note: SNAC (Salcaprozate sodium) increases gastric epithelial membrane fluidity without affecting tight junctions, thereby allowing transcellular passage into systemic circulation of the protein API. SNAC is a component of Novo Nordisk's Rybelsus® which has been approved by the FDA and EMA.

Entera Oral Delivery of GLP-2 Analog (Teduglutide) Tablets Published May 2023

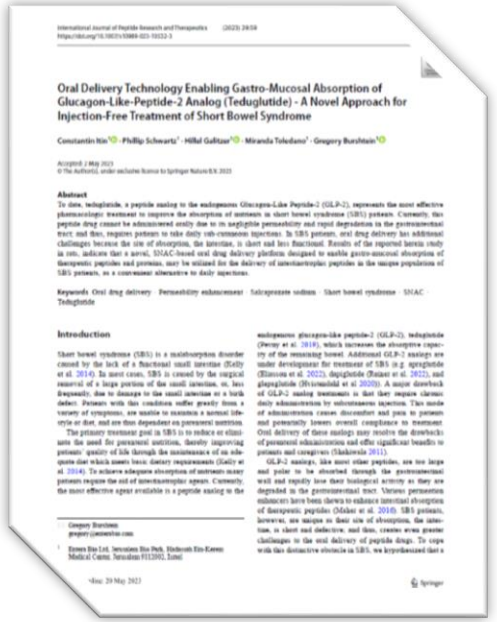
	Oral Tedaglutide	Control formulation
Teduglutide dose	**0.7mg**	0.7mg
Formulation excipients	**SNAC+SBTI**	Mannitol
Dosage form	**Minitablets**	Minitablets
Number of animals (n)	**7**	5

	Oral Tedaglutide	Control formulation
Cmax	**17.1 ng/ml**	0.6 ng/ml
CV% Cmax	**19.6%**	200%
AUClast	**1248**	68
CV% AUC	**40.4%**	196.7%





Teduglutide is a 33 amino acid linear glucagon-like peptide-2 (GLP2) analog with molecular weight of 3.8kDa.


Oral Delivery Technology Enabling Gastro-Mucosal Absorption of Glucagon-Like-Peptide-2 Analog (Teduglutide) - A Novel Approach for Injection-Free Treatment of Short Bowel Syndrome

Entera's oral delivery platform enabled gastro-mucosal absorption of GLP-2 pre-clinically. This unique benefit overcomes a major barrier to oral GLP-2 delivery; could be utilized to treat patients with Short Bowel Syndrome and other severe intestinal and malabsorption metabolic conditions

EB613 (oral PTH (1-34), teriparatide)
First Daily Oral Osteoanabolic Mini Tabs for High-Risk, No Prior Fracture Post-Menopausal Women

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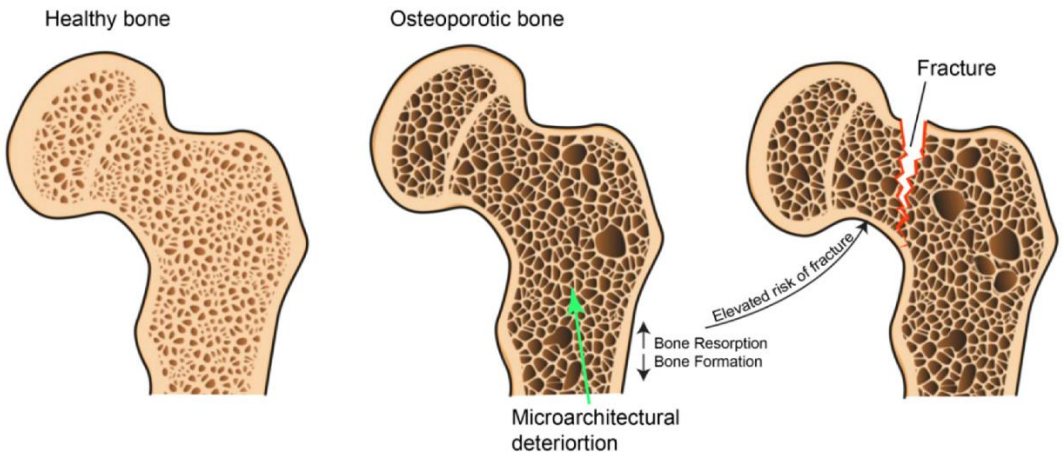
Osteoporosis Results From An Imbalance In The Bone Remodeling Cycle That Occurs When Bone Resorption Outpaces Bone Formation

Bone Density Healthy vs. Osteoporotic

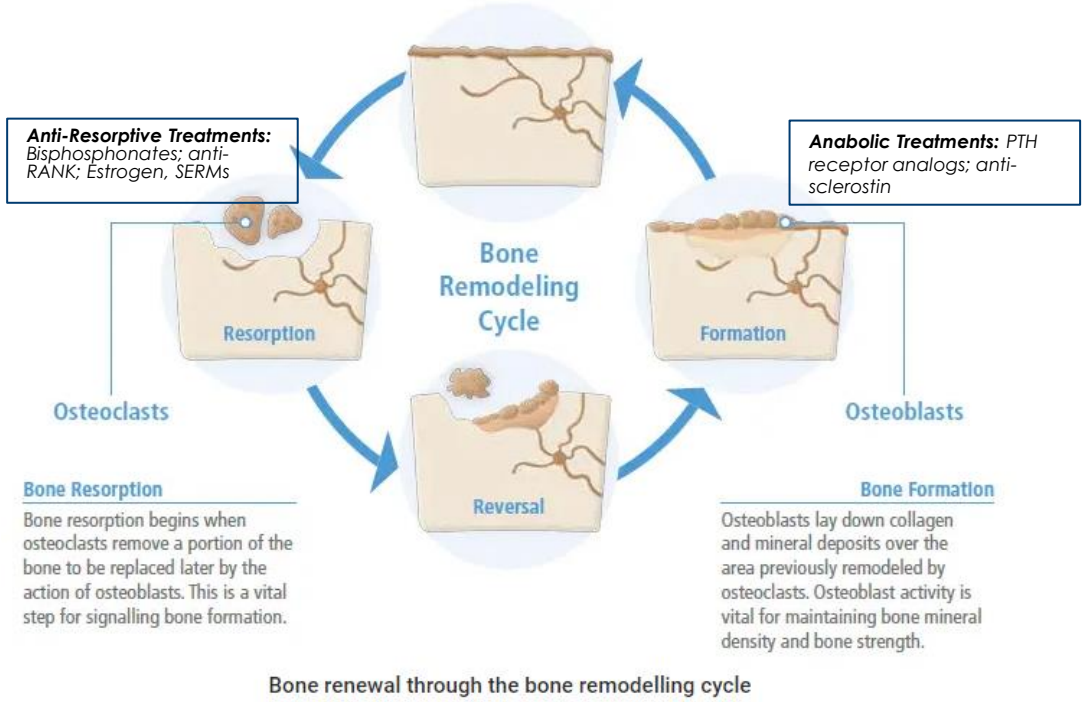


Osteoporosis is a disease associated with low bone mass and enhanced skeletal fragility and is most commonly caused by:

1. Menopause in women
2. Aging in both women and men
3. Glucocorticoid steroid use (greater than 3 months)

Osteoporosis and the Bone Remodeling Cycle

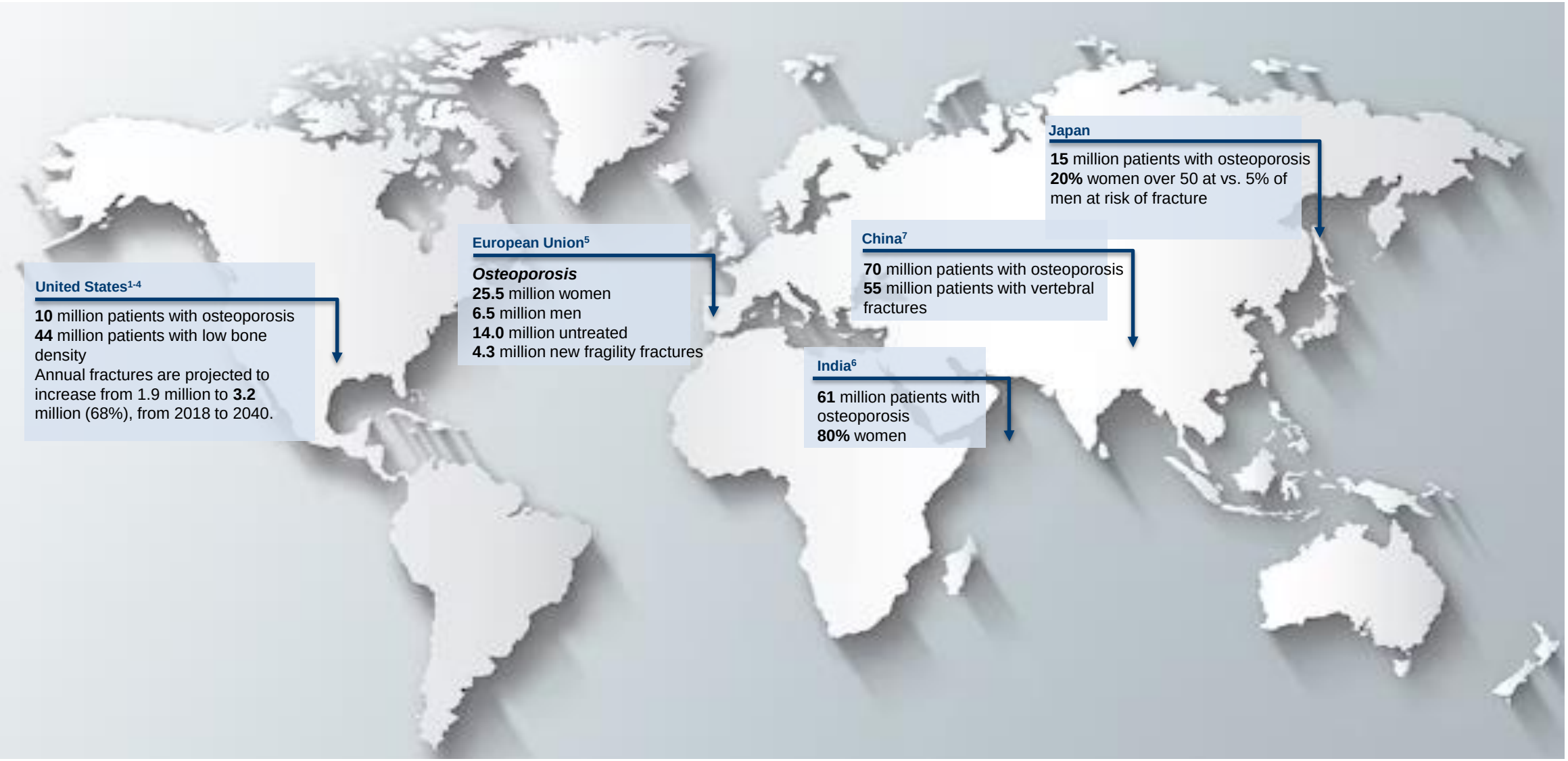
The Bone Remodeling Cycle can be separated into two distinct processes: **Resorption (osteoclasts) and Formation (osteoblasts)**



Bone renewal through the bone remodelling cycle

Sources: International Osteoporosis foundation accessed March 2022; Salamanna, F. et al.

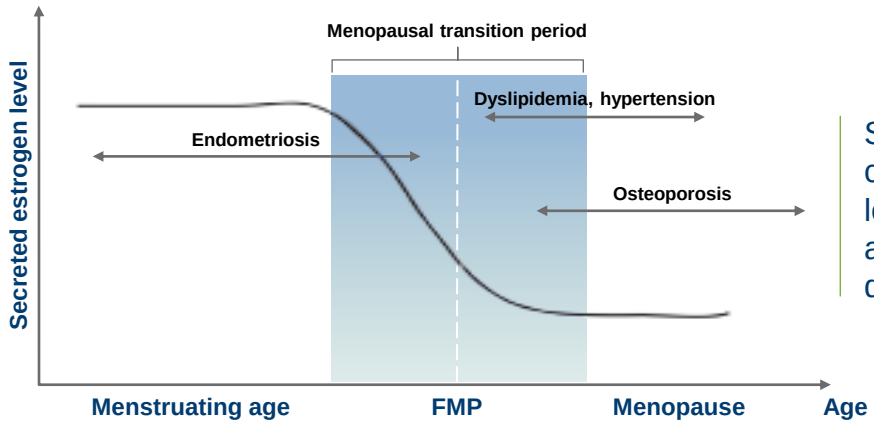
Globally, Osteoporosis Afflicts More Women than Heart Attack, Stroke, and Breast Cancer Combined



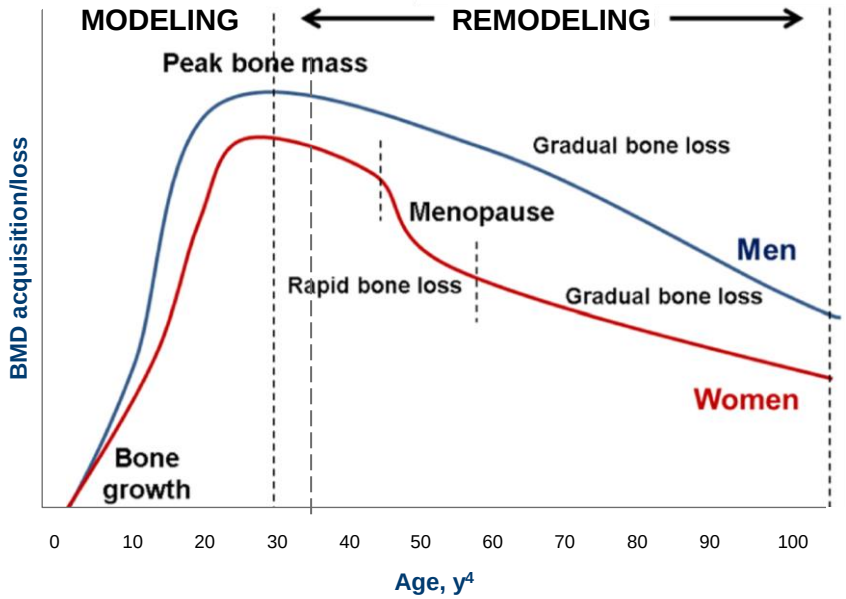
1. Office of the Surgeon General. *Bone Health and Osteoporosis: A Report of the Surgeon General*. 2004. **2.** Bone Health and Osteoporosis Foundation. Published October 2021. Accessed May 2023. https://www.bonehealthandosteoporosis.org/news/national-osteoporosis-foundation-is-now-bone-health-and-osteoporosis-foundation/ **3.** National Osteoporosis Foundation. Accessed May 2023. https://www.bonehealthandosteoporosis.org/wp-content/uploads/2015/12/Osteoporosis-Fast-Facts.pdf **4.** Lewiecki EM et al. *JBMR Plus*. 2019;3(9):e10192. doi:10.1002/jbm4.10192 **5.** Willers C et al. *Arch Osteoporos*. 2022;17(1):23. doi:10.1007/s11657-021-00969-8 **6.** Khinda R et al. *Int J Environ Res Public Health*. 2022;19(5):2999. doi:10.3390/ijerph19052999 **7.** Wang L et al. *JAMA Netw Open*. 2021;4(8):e2121106. doi:10.1001/jamanetworkopen.2021.21106

Osteoporosis and Menopause

- As hormones change to accommodate normal menopausal changes, **estrogen levels start to fluctuate and then drop**[1]
- Since **estrogen helps prevent bones from getting weaker** by slowing the natural breakdown of bone, its reduction during menopause significantly speeds up bone loss[2]
- One in 2 postmenopausal women will have osteoporosis, and **most will suffer a fracture during their lifetime**[2]



Schematic showing changes in estrogen level with age, and subsequent disease patterns.[3]



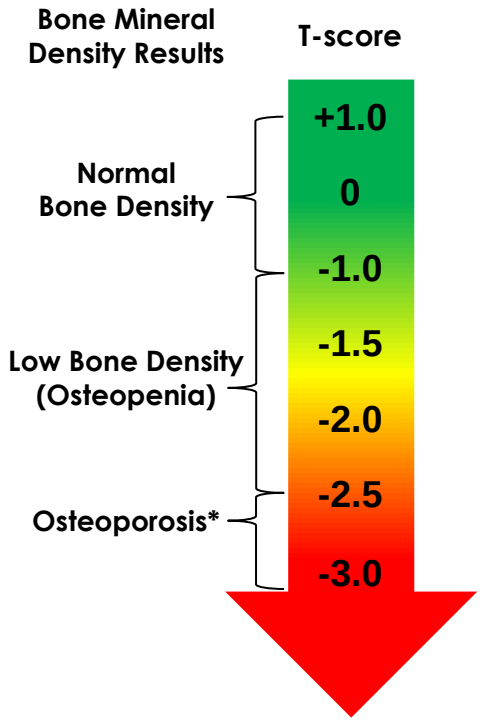
BMD, bone mineral density; FMP, final menstrual period.

1. North American Menopause Society. Published January 2023. Accessed May 2023. https://www.menopause.org/docs/default-source/press-release/late-reproductive-stage-symptoms-vs-menopause.pdf **2.** Endocrine Society. Published January 24, 2022. Accessed May 2023. https://www.endocrine.org/patient-engagement/endocrine-library/menopause-and-bone-loss **3.** Wada-Hiraike O. *Endocrines*. 2021;2:457-471. doi:10.3390/endocrines2040041 **4.** Kruger MJ, Nell TA. *AIDS Res Ther.* 2017;14(1):35. doi:10.1186/s12981-017-0162-y

Healthcare Providers (Endo, PCP, GYN) Typically Use T-score BMD Classifications, Patient Fracture History and Preference To Drive Therapy Selection

- ***Injections deter many patients from using extremely effective PTH therapy, contributing to a treatment gap in high-risk patients***
- ***An oral PTH analogue tablet formulation with adequate bioavailability, similar safety and effects on BMD may serve to significantly increase care to high-risk osteoporosis patients (est. 40% of pop, currently estimated at 1.6 million women in the US only)***

T-Score Scale

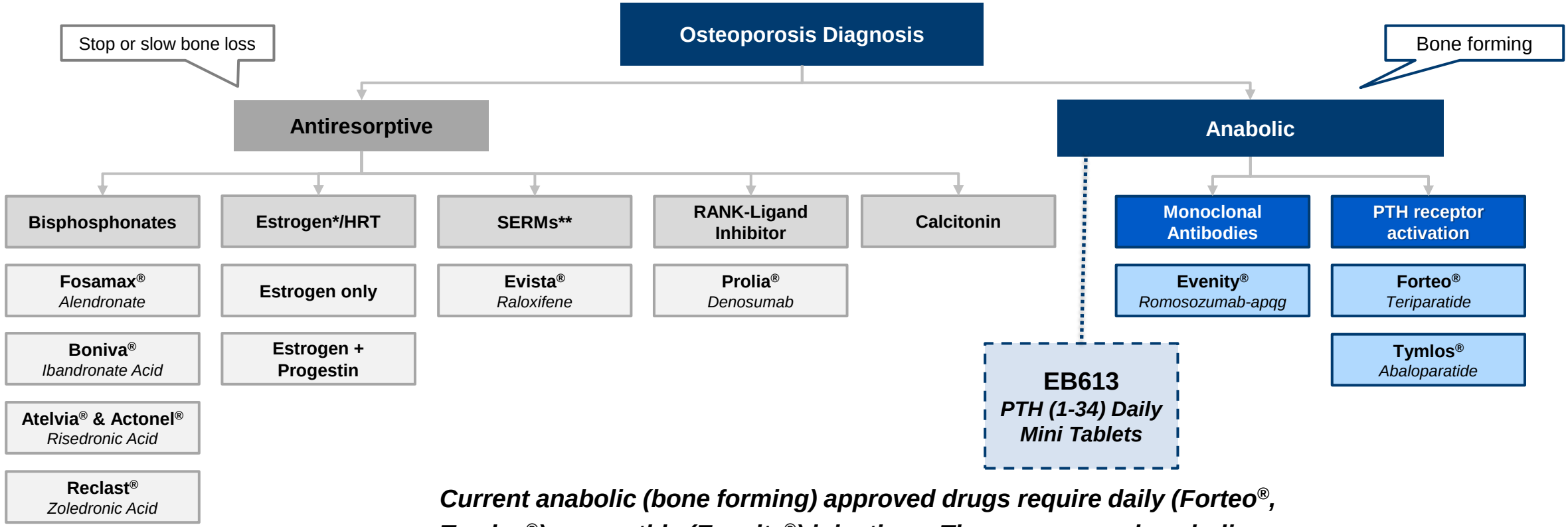


Low BMD Category	Percent of Patients with low BMD		Treatment Recommendation
	Internists	Endocrinologists	
Osteopenia	55%	27%	Vitamin D and Calcium Supplements
High Risk Osteoporosis *(T-scores between -2.5 and -3.0 **without a history of fractures**)*	35%	43%	**Bisphosphonates/Prolia Despite guidelines, LIMITED injectable anabolic penetration**
Very High Risk Osteoporosis *(T-scores ≤ -3.0 or ≤ -2.5 with prior fragility fractures)*	10%	23%	Injectable Anabolics: Forteo, Tymlos, PTH generic injectables, Evenity

EB613 ***PTH (1-34) Daily Mini Tablets Position***

Source: Triangle Insights Primary Research Apr. 2022;, Low BMD Category based on AACE guidelines (Camacho 2020, Endo Practice)

Current Osteoporosis Pharmacologic Treatment Is Segmented Into: Anti-Resorptive & Anabolic Options



Current anabolic (bone forming) approved drugs require daily (Forteo®, Tymlos®) or monthly (Evenity®) injections. There are no oral anabolic agents currently available to patients

Notes: * Estrogen products are indicated for prevention of osteoporosis as a secondary benefit when used to control menopausal symptoms. Not a 1st line treatment due to adverse reactions, **SERMs – Selective estrogen receptor modulators

Sources: Osteoporosis, accessed March 2022, retrieved from: hopkinsmedicine.org; DerSarkissian, C. Osteoporosis: Diagnosis and Treatment. 2021, Retrieved from: webmd.com; Frost & Sullivan, EnteraBio Initiation of Coverage, 2019;.

EB613 Phase 2 Results

A Six-Month Study of Oral PTH in Postmenopausal Women with Low Bone Mass – 6 Month Bone Mineral Density (BMD) Results

EnteraBio

EB613 Phase 2 Clinical Trial Design in High Risk, No Prior Fracture Post-Menopausal Women with Osteoporosis

- **6-Month, Randomized Dose-Ranging Placebo-Controlled Study in Post-Menopausal Women with Osteoporosis**
- **Conducted at 4 sites in Israel between June 2019 and May 2021; Final enrollment = 161 patients**

Screening

Key inclusion criteria

- 50+ years old and 3+ years post menopause
- **Low bone mass; HIGH RISK NO PRIOR FRACTURE**

Key exclusion criteria

- Osteoporosis treatment within last 2 years
- Severe osteoporosis that precludes placebo

Randomization N=160 (target)

Treatment*

Arm 1: Placebo tablets QD

Arm 2: 0.5 mg *

Arm 3: 1.0 mg *

Arm 4: 1.5 mg QD

Arm 5: 2.5 mg QD * **

Arm 6: 2.5mg titrated QD **

Endpoints

Primary – at 3 months

- Serum P1NP placebo adjusted change from baseline at 3 months

Secondary – at 6 months

- BMD change from baseline at 6 months
- P1NP, Osteocalcin, Bone Alkaline Phosphatase
- Serum CTX, Urine NTX/Creatinine
- Plasma hPTH (1-34) at $T_{15\ min}$

Data

3 M **Partial** & Final interim analysis of primary endpoint**

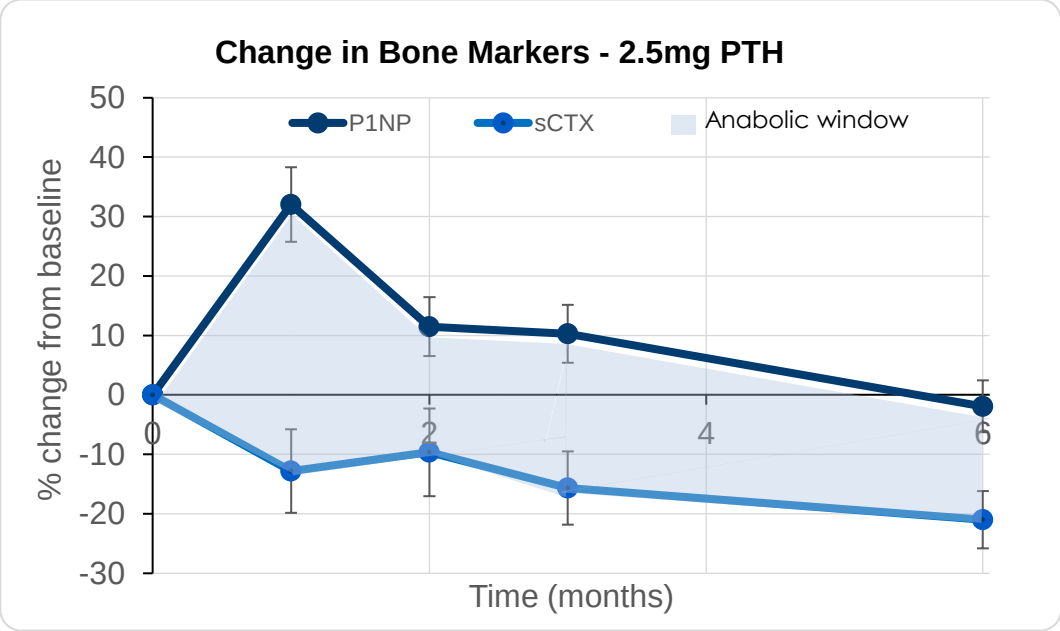
6 M **Final analysis / Topline data – All endpoints**

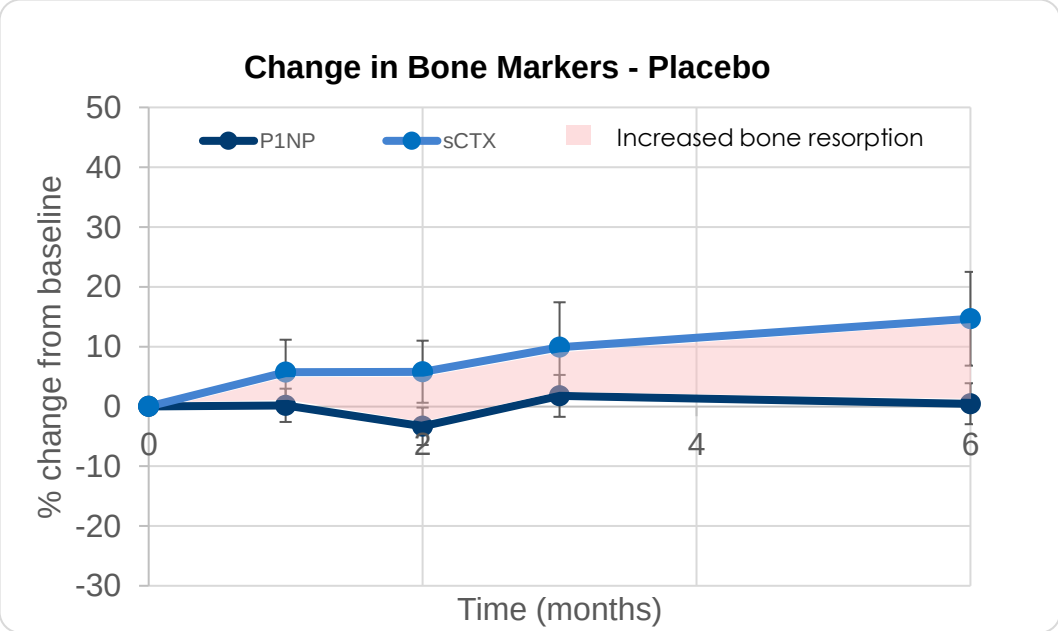
* Following an interim analysis, a 2.5mg arm was added and recruitment to the 0.5mg & 1.0 mg arms was stopped

** Following AEs typical of orthostasis additional subjects in the 2.5mg group received 1.5mg for 1 month, 2.0mg for the next month and 2.5mg during months 3 to 6 (Titrated).

EB613: Met Pharmacodynamic Endpoint, Bone Turnover Biomarkers

- **Primary Endpoint:** Statistically significant increases in P1NP (key anabolic marker) at Month 1 (p<0.001), Month 2 (p<0.005) and Month 3 (p<0.05), respectively for the 2.5 mg EB613 dose group
- Statistically significant decrease in Serum CTX (marker of resorption) of 21% from baseline to Month 6 (p<0.01)
- **EB613 demonstrated a sustained "Anabolic Window" (P1NP increases while CTX decreases) indicating a potential dual MOA of bone building with mild anti-resorptive properties**



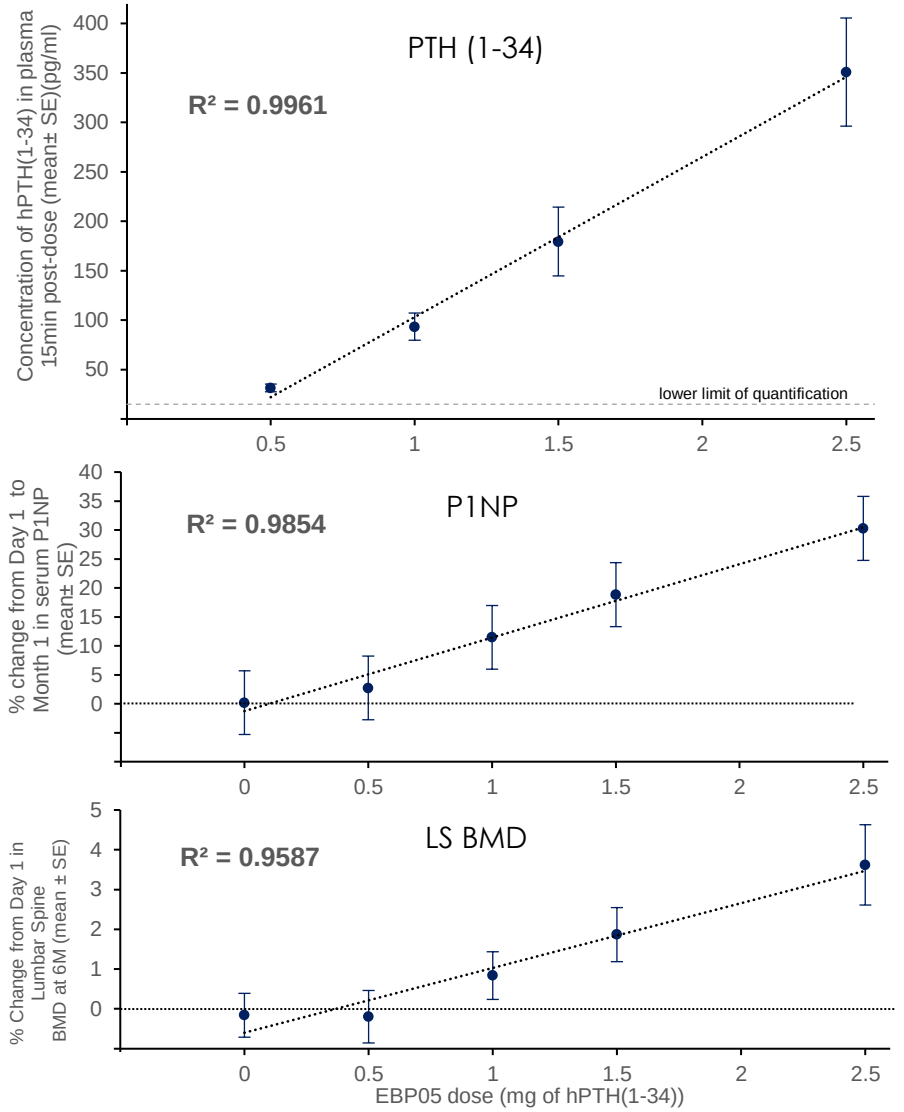


EB613 Mini Tablets Had Significant Dose Response Across BMD, PK and PD

EB613 (a.k.a. EBP05, hPTH(1-34) min-tablets) showed a linear dose response across PTH exposure, P1NP biomarker and BMD Measurements

- Dose proportional effect (R^2 = 0.959) on Lumbar Spine BMD in postmenopausal women with osteoporosis or low BMD following 6 months of treatment
- At the 1-month time point, where the maximal increase in P1NP was observed, a correlation (R^2 = 0.985) was shown between EB613 dose and mean change in serum P1NP
- A correlation (R^2 = 0.996) was also found between the dose of EB613 and mean hPTH(1-34) plasma levels 15 minutes following drug administration

EB613 produced a statistically significant BMD dose response* in lumbar spine BMD (p<0.0001), femoral neck BMD (p<0.002) and total hip BMD (p<0.008)

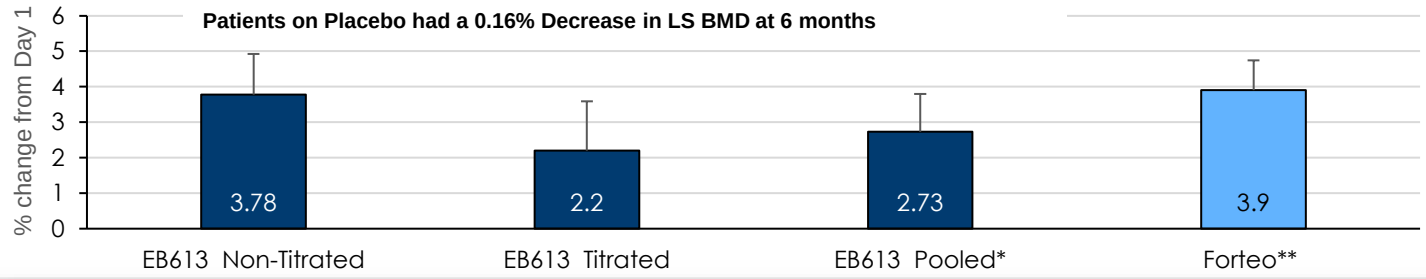


Phase 2 Study Presented at Late Breaker LB-1116 and Poster FRI-237– ASBMR 2021; A Six-month Phase 2 Study of Oral PTH (EBP05) in Postmenopausal Women with Low Bone Mass – Dose Proportional Absorption and Effect on Lumbar Spine BMD Presented as Poster at ASBMR 2022

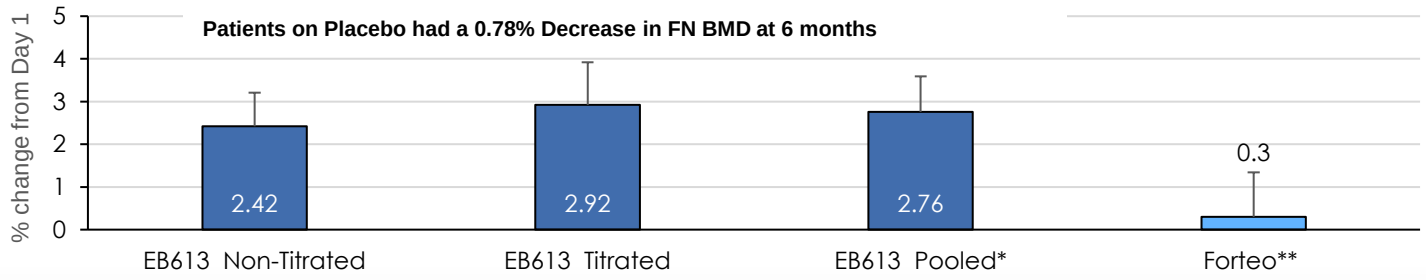
*Dose response p values are based on A linear regression analysis of changes in BMD in all study arms

EB613 Increased BMD at All Major Skeletal Sites at 6 Months (TH, LS, FN)

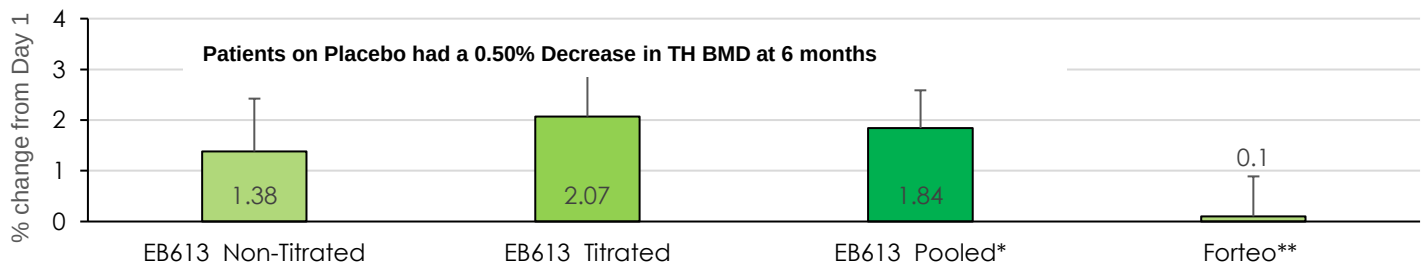
Placebo adjusted Lumbar Spine BMD



Placebo adjusted Femoral Neck BMD



Placebo Adjusted Total Hip BMD



EB613 data first presented at Late Breaker LB-1116 and Poster FRI-237– ASBMR 2021 ; Mean values ±SE of difference between active and placebo presented
*Pooled data includes Titrated & Non-Titrated subjects
** Forteo data based on Leder BZ et.al. JCEM (2015) Placebo and Teriparatide 20ug results for mean and ±SD

- Patients on placebo had decreases in BMD score across all skeletal sites at 6 months
- **EB613 Lumbar spine BMD increases similar to Forteo® while total hip and femoral neck BMD increases were greater than Forteo® at 6 months in a similar population (osteoporosis, no prior fracture)****
- **Total Hip BMD is expected to replace fracture as a clinical endpoint (ASBMR-FNIH BQP)**
- **EB613 tabs showed a 2.07% increase in total Hip BMD at 6 months**

Titration Schedule:

- **EB613 Non-Titrated: 6 months @2.5mg**
- **EB613 Titrated: 4 months @2.5mg**

ENTERA BIO

EB613 Phase 2 Safety Profile Consistent with PTH Targeted Injectables

- **Adverse event profile - similar to AE profile reported with Forteo® and typical of orthostatic hypotension**
- **EB613 not associated with serum calcium increases or hypercalcemia adverse events**
- **2.5 mg dose with titration** (1.5mg for 1 month, 2.0mg for the next month and 2.5mg during months 3 to 6) well tolerated
- AEs commonly attributed to vasodilatation with subcutaneous injectable PTH were observed - headache, nausea, presyncope and dizziness - **There were no serious drug-related AEs**

Most Common Treatment Emergent AE (AEs in over 5% of patients, N=118)

	N	%
Headache	21	18%
Nausea	18	15%
Dizziness	13	11%
Nasopharyngitis	7	6%
Back pain	7	6%
Palpitations	6	5%
Dyspepsia	6	5%
Presyncope	6	5%

Osteoporosis Market Overview
Sales and Current Prescription Trends

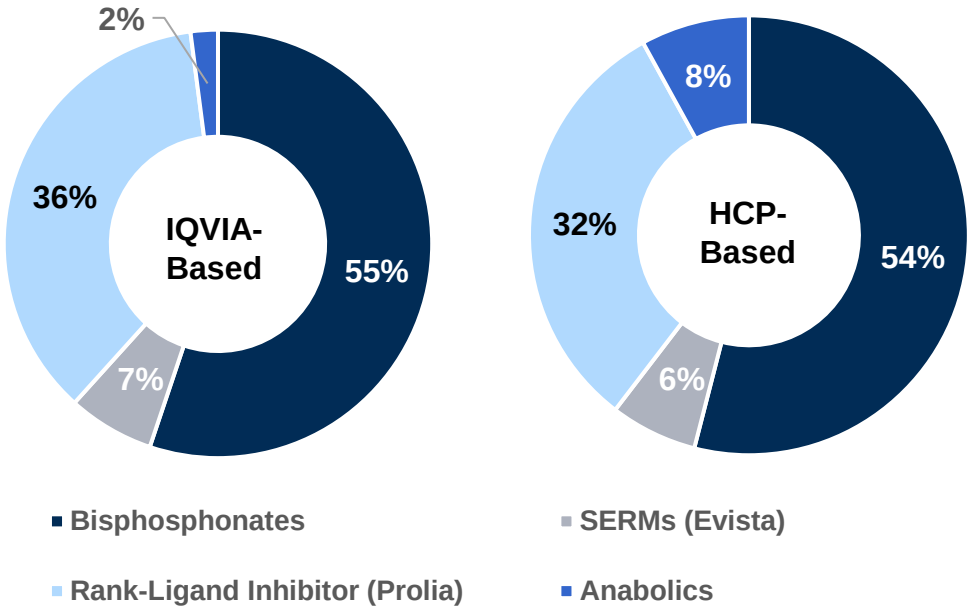
EnteraBio

Anabolic Treated Patients Comprise Less Than 10% of Currently Treated Osteoporosis Patients, Mostly Very High Risk Patients with Prior Fracture (Endocrinologists and PCPs form majority of the current prescribing base)

Population Treated by Class of Osteoporosis Medication (2022)

	IQVIA-Based	HCP Primary-Based
Total Osteoporosis Treated Population	**~3.16M**	**~3.23M**
Bisphosphonate Patients	~1.74M *(~55%)*	~1.74M *(~54%)*
SERMs Patients	~206K *(~7%)*	~206K *(~6%)*
Rank-Ligand Inhibitor Patients	~1.14M *(~36%)*	~1.02M *(~32%)*
Anabolic Patients	~65K *(~2%)*	~260K *(~8%)*

Share of Osteoporosis Treated Population by Medication Class



Bisphosphonates include Fosamax®, Boniva®, Atelvia®, Reclast®, and generic versions of listed products;
SERMs include Evista® and generic raloxifene;
Rank-Ligand Inhibitors include Prolia®;
Anabolics include Evenity®, Forteo®, generic teriparatide, and Tymlos®

Source: IQVIA prescription data (note the capture rate of IQVIA may be low due to injectable administration of anabolic drugs on the market); HCP = Prescriber survey conducted by TIG Primary Research Apr. 2022

EB613 Poised To Create A Paradigm Shift In The Treatment of Osteoporosis To Be The First Daily Tablet Anabolic Therapy

Key Product Needs	Forteo® (Lilly)	Tymlos® (Radius)	Evenity® (Amgen)	Prolia® (Amgen)	Bisphosphonates (generics)	Entera EB613
Treats Osteoporosis	✓	✓	✓	✓	✓	✓
Rebuilds Bone	✓	✓	✓			✓
Oral Dosing					✓	✓
No Refrigeration		✓			✓	✓
Self-Administered	✓	✓			✓*	✓

Current Anabolic drugs, including PTH (1-34) (teriparatide) injections - Forteo® or PTH Injectable Generics, Tymlos® and Evenity® **effectively increase the rate of bone formation** but require **daily or monthly injections**

EB613 is positioned to be the first potential oral daily tablet osteoanabolic treatment for osteoporosis

Source: Triangle Insights Primary Research Apr. 2022

*Zoledronic acid is administered by intravenous administration

EB613

Phase 3 Plan and Overview of FDA Process

EnteraBio

EB613 Phase 3 Clinical Trial Design

- Designed with FDA Concurrence (Pursuant to Type C and Type D Meeting)
- **A Single Global Phase 3, 24-Month Double-Blind, Placebo-Controlled Registrational Study**
- **Total Hip (TH) BMD as Primary Endpoint**

Screening

Key inclusion criteria

- 50-80 yrs old
- At least 5 yrs post menopause
- BMD: T-score ≤ -2.5 , **no prior fracture**

Key exclusion criteria

- Subjects with very low BMD: if < 75 years old BMD T-score ≤-3.5; if ≥75 years old BMD T-score ≤-3.0
- Osteoporosis treatment within last 2 yrs

2:1 Randomization N=1,000 (target)

24 M Treatment

Titration to 2.5mg Mini Tablets

Arm 1:

EB613 2.5mg, N~667*

Arm 2:

Placebo tablets, N~333*

Endpoints

Primary –

- Mean Change in TH BMD of EB613 daily PTH mini tablets vs. placebo at 24 months

Secondary –

- **Change in TH BMD vs. STEs associated with fracture reduction at 24 months****
- TH, LS, FN, BMD changes from baseline at 6,12,18 and 24 months
- LS, FN BMD changes from baseline at 24 months

Exploratory -

- Bone Turnover Biomarkers

Data

- **12 M** Interim analysis – First 300 to complete the 12 month visit
- **24 M** Final analysis / Topline data – Primary & Secondary endpoints

*N=600 with 2:1 randomization agreed to be sufficient to support safety and efficacy for an NDA under 505(b)2 (per FDA guidance at Type C meeting).

**Note: 24-month STEs are those reported by FNIH-ASBMR-SABRE (Eastell 2022).

EB613 Phase 3 Clinical Trial Design Uses ASBMR-FNIH STEs

- **The primary endpoint agreed upon is Mean Change from Baseline in Total Hip BMD of EB613 vs. placebo at 24 months. As a key secondary endpoint, Entera intends to assess this using the pre-defined, published ASBMR- FNIH Surrogate Threshold Effects (STEs, see right panel)**

- STEs are quantitative thresholds depicting the difference in total hip BMD vs. placebo at 24 months that predict a reduction in fracture risk with 95% certainty

- Placebo adjusted Total Hip BMD STEs:
  - 1.42% - vertebral fractures
  - 1.83% - all fractures
  - 2.13% - nonvertebral fractures
  - 3.18% - hip fractures

- Entera's proposed Phase 3 study will evaluate the % change in BMD of EB613 measured at the hip vs. placebo. This change will be tested to see which STEs are surpassed. Beginning with vertebral followed by all fractures and nonvertebral fractures

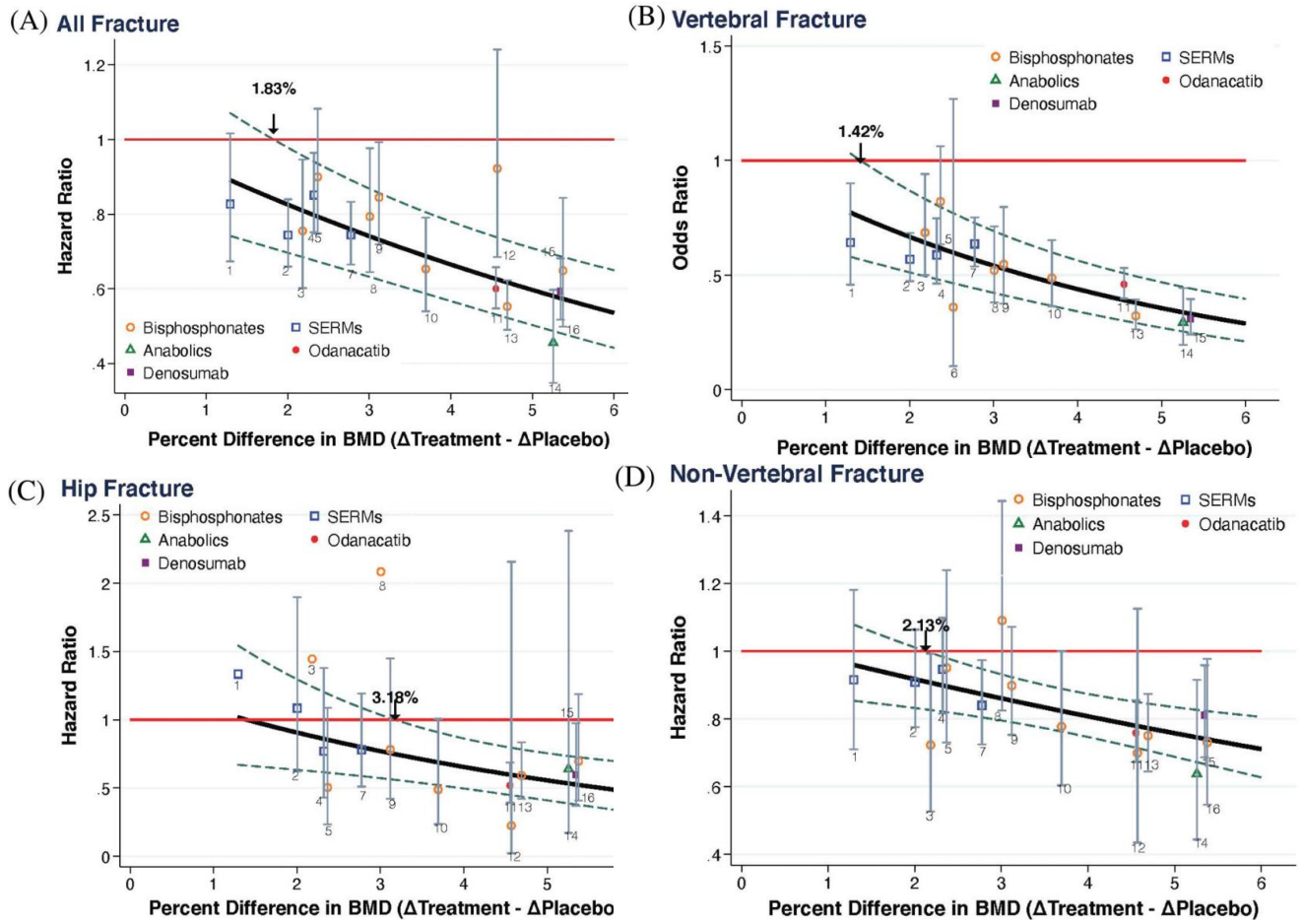


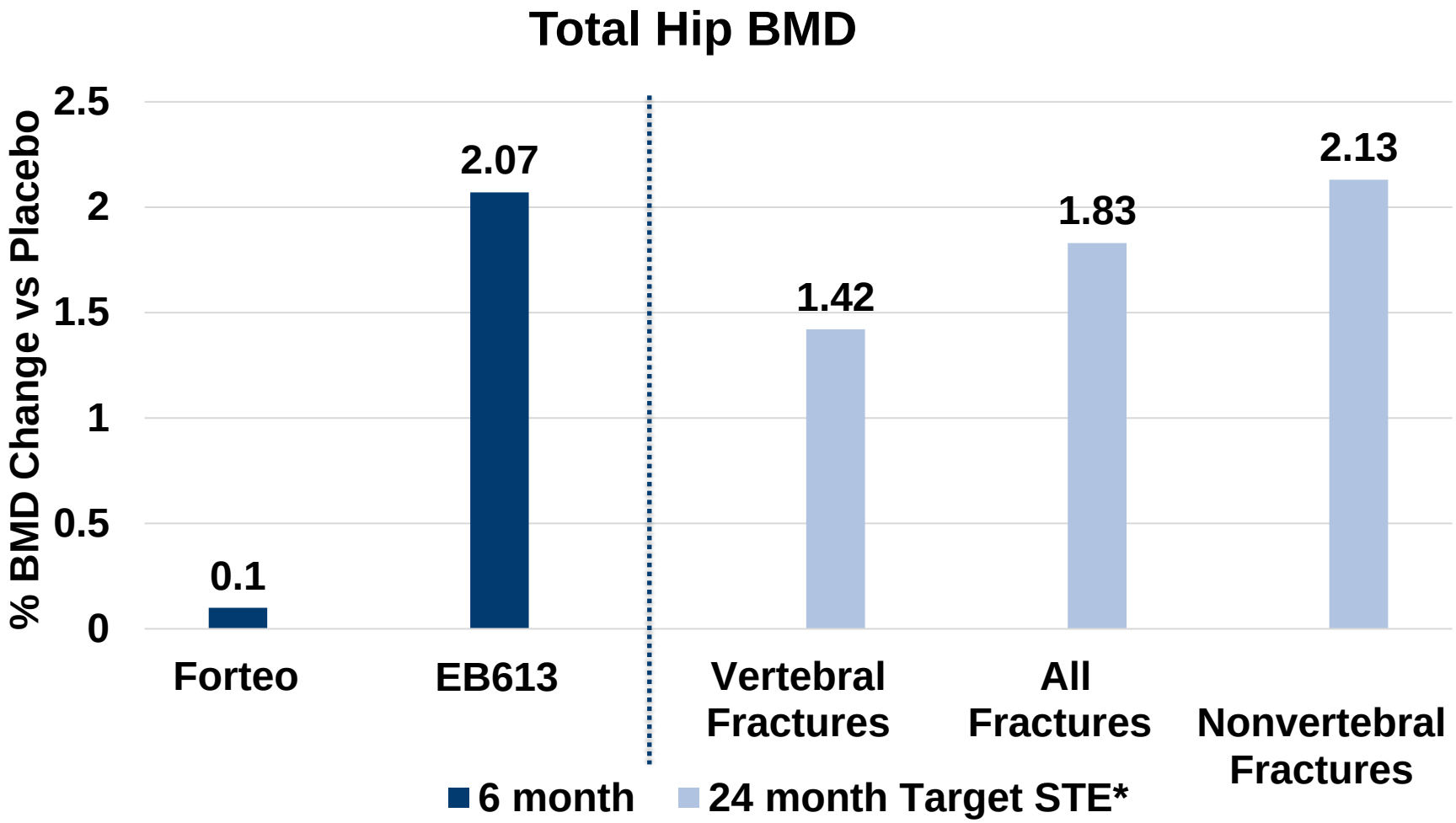
Fig 1. Relationship between difference in the change in total hip BMD between active and placebo groups at 24 months and the hazard or odds ratio of all, vertebral, hip and nonvertebral fractures. The red horizontal line is the ratio of 1 (no treatment effect) and the STE is the point where the upper 95% prediction limits intersects this line; eg, 1.83% for the all fracture outcome. The class of drugs is indicated in the legend. For each trial, the point estimates and 95% confidence intervals for relative risks are given and the numbers 1–16 relate to the studies listed in Table 1.

Eastell et al. J Bone Miner Res. 2022; 37 (1): 29-35

Change in Total Hip BMD - Primary End Point Analysis for Phase 3

EB613 (Titrated 2.5mg dose, Phase 2) vs. Forteo® (Leder Study) at 6 Months

FNIH Surrogate Threshold Effects (STEs*) at 24 Months to be Used in EB613 Phase 3



Notes:. Leder BZ et.al. JCEM (2015) (historical data from Abaloparatide vs. Forteo)

*STE – (Surrogate Threshold Effect), Eastell et. al. Journal of Bone and Mineral Research, 2021, pp 1–7

ENTERA BIO

Brief Historical Overview of EB613 Regulatory Trajectory From End of Phase 2 Mtg 2022 to Date

EB613*: Potentially the First Daily Oral PTH Mini Tablets, OsteoAnabolic Treatment for Osteoporosis

- **June 2021: Phase 2 study met biomarker/PD (P1NP, CTX) and 6-month BMD** endpoints** in post-menopausal women with osteoporosis (ASBMR 2021)
- **January 2022: End of Ph2 Minutes** – FDA suggests placebo-controlled rather than the NI H2H vs. Forteo®
- **June 2022 - October 2022: Type C Meeting** - FDA concurrence that a *placebo-controlled Ph3* study with TH BMD as primary endpoint could support an NDA
- **March 2023 Type D Meeting –** Evaluation of primary endpoint TH BMD expected with qualification of ASBMR-FNIH program – discussions ongoing
- **June 23rd 2022: The FDA Biomarkers Qualification Program accepted the ASBMR-Foundation for the National Institutes of Health (FNIH) Strategy to Advance BMD as a Regulatory Endpoint (SABRE)** project team's Qualification Plan to use the treatment-related change in bone mineral density (BMD) as a surrogate endpoint for fractures in future trials of new anti-osteoporosis drugs
- **Expect updates from ASBMR-FNIH SABRE qualification later in 2023 – Critical Path for Entera Ph3**

*EB612 and EB613 are **hPTH(1-34) teriparatide Tablets** BMD = Bone Mineral Density; ** TH = Total Hip

EB613 Positioning

- *PTH receptor activation is a validated mechanism of action for treating osteoporosis, as evidenced by FDA/EMA approvals of efficacious agents such as the injectable Forteo® (2002) and Tymlos® (2017)*
- In this silent disease, patients remain reluctant to take daily injections even as their BMD scores decline and only turn to anabolic (bone forming) drugs, **currently available only as injections, when their disease becomes very severe (with multiple fractures) reaching only ~8% of the treated patients**
- Based on recent third-party market research and published Guidelines (AACE 2020, NAMS) healthcare providers would support the use of anabolics earlier in the treatment paradigm (high risk patients with no prior fracture) - yet hampered to date due to difficulty of administration (injectables) and very high price
- **EB613, as a first in class oral PTH treatment with daily 'mini' tablets** - offering a viable anabolic therapeutic option to lower the risk of fracture in high-risk osteoporotic patients, accounting for ~40% of the estimated 3.2 million *treated* patients in the U.S.
- Successful Conclusion of FDA Type C Meeting; 24 month Total Hip BMD established as primary endpoint in placebo-controlled design
- **No requirement for fracture endpoint or an active control in the proposed pivotal study**

EB612 Oral PTH (1-34) First Daily Oral PTH Mini Tablet Peptide Replacement Therapy for the Treatment of Hypoparathyroidism

EnteraBio

Hypoparathyroidism: PTH Orphan Indication with Sub-Par Clinical Care

Hypoparathyroidism Overview

Hypoparathyroidism (HypoPT) is a rare condition in which the parathyroid glands fail to produce sufficient levels of **Parathyroid hormone (PTH)**

- PTH (along with vitamin D and calcitonin) plays a role in regulating the levels of calcium and phosphorus in the blood and in determining bone growth and bone cell activity
- HypoPT is characterized by hypocalcemia and hyperphosphatemia
- Clinical management includes frequent high doses of calcium and activated Vitamin D which are associated with severe long-term morbidities:

Cardiovascular Heart failure, blood vessel calcification

Renal Kidney stones, renal failure

Neurologic Cognitive impairment, basal ganglia calcification

Skeletal Reduced bone turnover

Unmet Need and Market Opportunity

How many people are affected by HypoPT?

- Approximately 200K afflicted with hypoparathyroidism in the US, EU and Japan

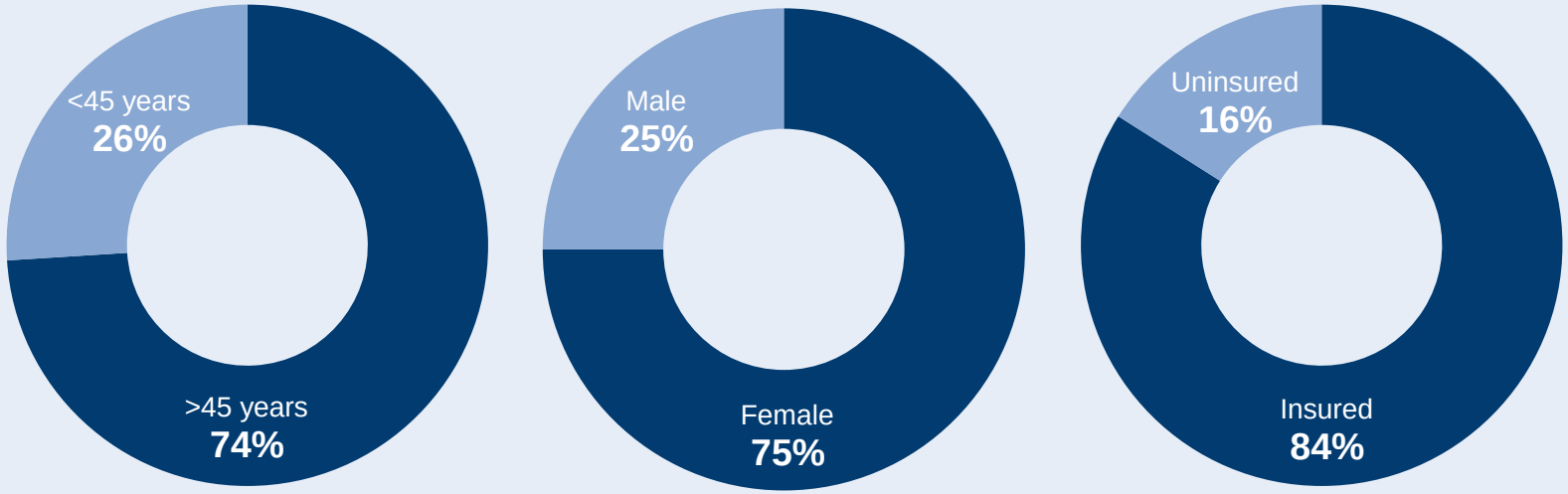
What is the market opportunity in HypoPT?

- Current standard of care (calcium and vitamin D supplements) creates long term co-morbidities
- Natpara® (parathyroid hormone) injection will be permanently phased out globally by end of 2024 due to supply issues (Takeda)
- TransCon PTH, once-daily Injectable, long-acting prodrug of parathyroid hormone (PTH(1-34)) developed by Ascendis Pharma received FDA CRL (May 2023, CMC) and EU MAA submitted (November 14, 2022)
- Eneboparatide, once-daily injectable long-acting parathyroid hormone 1 (PTH1) receptor agonist, developed by Amolyt Pharma initiated Phase 3 (May 2023)

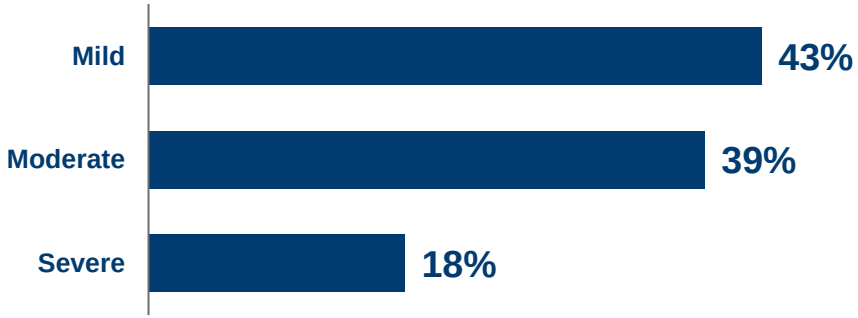
References:
https://rarediseases.org/rare-diseases/hypoparathyroidism
https://www.takeda.com/en-us/newsroom/news-releases/2019/takeda-issues-us-recall-of-natpara-parathyroid-hormone-for-injection-due-to-the-potential-for-rubber-particulate/
TransCon™ PTH Top-Line Phase 3 Data from PaTHway (ascendispharma.com)

Hypoparathyroidism

Hypoparathyroidism in the United States[1,2]



Symptom severity despite use of calcium and vitamin D[2]



- Published studies have reported the prevalence of chronic hypoparathyroidism to range from 6.4 to 37.0 per 100,000 population in different countries[3]
- There are approximately 70,000 people with hypoparathyroidism in the United States[1]
- The overall prevalence of hypoparathyroidism in the European Union was estimated at 3.2 per 10,000 population in 2020 (over 140,000 people)[4]
- Globally, hypoparathyroidism affects approximately 200,000 people[5]

1. National Organization for Rare Disorders. Published January 24, 2017. Accessed May 2023. https://rarediseases.org/rare-diseases/hypoparathyroidism/ **2.** Powers J et al. *J Bone Miner Res*. 2013;28(12):2570-2576. doi:10.1002/jbmr.2004 **3.** Bjornsdottir S et al. *J Bone Miner Res*. 2022;37(12):2602-2614. doi:10.1002/jbmr.4675 **4.** Karpf D. *Endocrine Abstracts*. 2020;70AEP140. doi:10.1530/endoabs.70.AEP140 **5.** Future Market Insight. Accessed May 2023. https://www.futuremarketinsights.com/reports/hypoparathyroidism-treatment-market

EB612: Potentially First Oral PTH (1-34) Daily Tablets for Hypoparathyroidism, Summary of PK and Pilot Phase 2 Data

Study Design

Phase 2a, open-label, multicenter pilot study to evaluate the safety, tolerability and PK (NCT02152228)

Population: N=19 with hypoPT≥1 year, taking ≥1gr/day Ca and 25(OH)D 20ng/ml

Treatment: first 3 doses of PTH (1-34) 0.75 mg/dose administered at research center; subjects then self administered 4 times/day

Results

Efficacy:

42% reduction (p=0.001) from baseline in median calcium supplement use

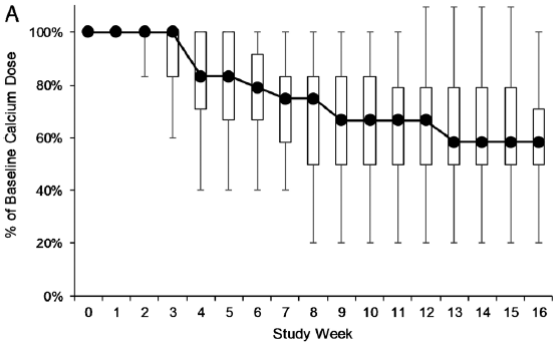
Maintenance of median Ca levels above the lower target level for Hypoparathyroidism patients (>7.5 mg/dL) throughout the study

Rapid decline of 23% (p=0.0003) in median serum phosphate levels 2 hours following the first dose that was maintained for the duration of the study

Safety: One subject experienced 4 AEs and left the study after the first day (withdrew consent), another subject experienced an SAE prior to the administration of the first dose and, hence, unrelated to the drug

Oral Calcium Intake

Per Protocol Analysis (N=15)



Phase 2, open-label, 2-period partial crossover study to evaluate the PK and PD (NCT03516773)

Population: N=16 with hypoPT ≥1 year, taking supplemental Ca and either alfacalcidol or calcitriol

Treatment: two doses (0.75 and 2.25) and three regimens of Oral hPTH (1-34) and Natpara® [hPTH(1-84)] 100 µg SC injection QD

Efficacy: Oral hPTH (1-34) 2.25 mg QID for one day is associated with an increase in serum albumin-corrected calcium and 1,25(OH)2D and a decrease in serum phosphate

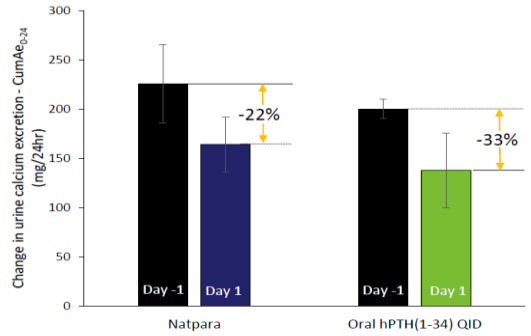
The magnitude of these changes are comparable to Natpara® 100 µg QD

Two, thee and four doses/day regimens showed a dose-dependent increase in 1,25(OH)2D, indicating that the long-term treatment even with the less frequent regimens may be an effective treatment option

Safety: There were no treatment emergent adverse events of hypercalcemia reported and no treatment-emergent Serious Adverse Events

Improved/ Decreased Urinary Ca

Excretion Over a 24-Hour Period



Entera Next Generation Platform – Current Phase 1 PK/PD Clinical Trial

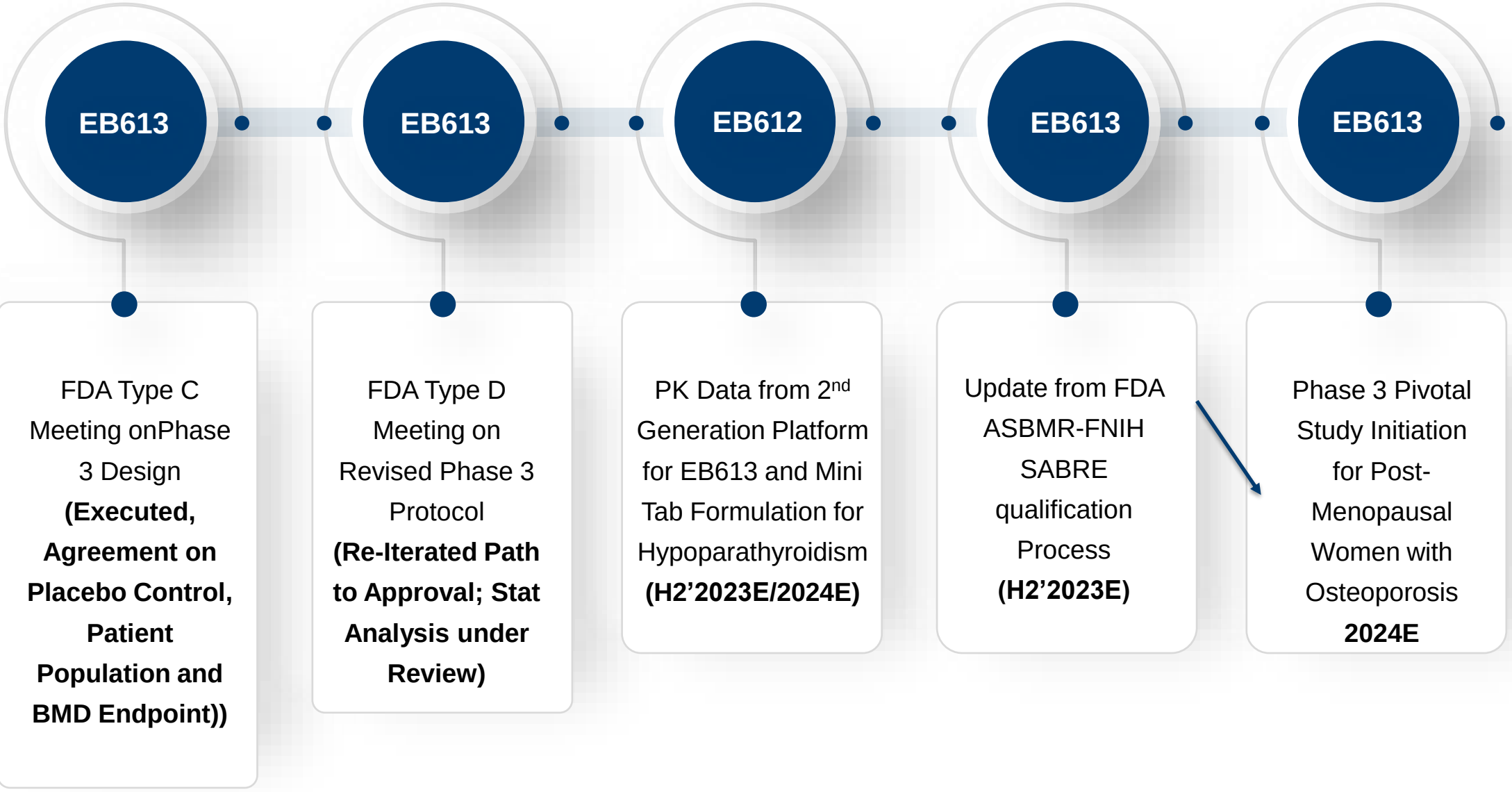
- *During 2022, we completed pre-clinical work on proprietary new generations of our oral peptide delivery platform*
- **Potential for curbed dosing of mini tablets across more complex therapeutic proteins and follow-on candidates for EB612/613**
- **A Phase 1b, Open-label, Partially Randomized Study was initiated in May 2023 to Assess Safety and Compare Pharmacokinetics of New Oral hPTH(1-34) Tablet Formulations vs. Current Formulation (EBP05) and SC Forteo®**

Design	Treatments	Data Expected	Objectives
• 45 healthy subjects divided into 3 cohorts • Adult males aged 18-35 divided into 3 cohorts • NCT05965167	**Cohort 1:** Randomized EB613 1.5mg, 2.5mg, Forteo®. First New Formulation Q.D., B.I.D.		**Primary –** • To assess the pharmacokinetic profile of the various formulations • To assess the safety profile of the new formulations
	Cohort 2: 4 Variations of the New Formulation 1.5mg, 2.5mg Q.D., B.I.D.	H2'2023E	**Exploratory -** • To assess and compare the effects of the various treatments on serum calcium (albumin-corrected total calcium), phosphate, intact hPTH(1-84), and serum 1,25-(OH)2D
	Cohort 3: Selection of Optimal Formulation(s) Based on Desired PK/PD Repeat Comparison with Earlier Formulations	H1'2024E	

EB612 Positioning

- EB612 is potentially the first oral PTH (1-34) daily tablet peptide replacement therapy for the treatment of hypoparathyroidism
- Hypoparathyroidism (HypoPT) is a rare condition in which the parathyroid glands fail to produce sufficient levels of Parathyroid hormone (PTH)
- **Pilot Phase 2 oral presentation (ASBMR 2015) and peer-reviewed publication in JBMR (March 2021)**
  - 42% reduction (p=0.001) from baseline in median calcium supplement use
  - Maintenance of median Ca levels above the lower target level for Hypoparathyroidism patients (>7.5 mg/dL) throughout the study
  - Rapid decline of 23% (p=0.0003) in median serum phosphate levels 2 hours following the first dose that was maintained for the duration of the study
  - 80% of the subjects had a decrease in urinary calcium levels by the end of the study
- **Phase 2 PK-PD study versus Natpara® presented (ASBMR 2019)**
- **Novel formulation leveraging our 2nd generation peptide delivery platform PK data is expected as of H2'2023**

Key Recent and Near-Term Milestones



Thank You

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