UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): August 1, 2022

Entera Bio Ltd.

(Exact Name of Registrant as Specified in Its Charter)

Israel	001-38556	00-0000000
(State or other jurisdiction of incorporation)	(Commission File Number)	(I.R.S. Employer Identification)

KIRYAT HADASSAH, MINRAV BUILDING – FIFTH FLOOR, JERUSALEM, Israel 9112002

(Address of principal executive offices) (Zip Code)

+972-2-532-7151

(Registrant's Telephone Number, Including Area Code)

(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a -12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d -2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e -4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Ordinary Shares, par value of NIS 0.0000769	ENTX	Nasdaq Capital Market
Warrants, each Warrant exercisable for half of an Ordinary Share at an exercise price of $5.85 per Ordinary Share	ENTXW	Nasdaq Capital Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On August 1, 2022, Entera Bio Ltd., a company organized under the laws of the State of Israel (the "Company", "we", "us", or "our") made available an updated corporate presentation. A copy of the presentation is attached hereto as Exhibit 99.1 and incorporated by reference in this Item 7.01. A copy of the presentation is also available on our website at https://investors.enterabio.com.

Use of our Website and Social Media to Distribute Material Company Information

We use our website as a channel of distribution for important Company information. We routinely post on our website important information, including press releases, investor presentations and financial information, which may be accessed by clicking on the "Investors" section of www.enterabio.com. We also use our website to expedite public access to time-critical information regarding our Company in advance of or in lieu of distributing a press release or a filing with the SEC disclosing the same information. Therefore, investors should look to the "Investors" section of our website for important and time-critical information.

The information contained in this Item 7.01, including in Exhibit 99.1 attached hereto, is "furnished" and not "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section. Such information shall not be incorporated by reference in another filing under the Exchange Act or the Securities Act of 1933, as amended, except to the extent such other filing specifically incorporates such information by reference.

Item 9.01 Exhibits

(d) Exhibits.

Exhibit Number	Exhibit
99.1	Entera Corporate Presentation August 2022
104	Cover Page Interactive Data File.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

ENTERA BIO LTD.

Date: August 1, 2022

By: /s/ Miranda J. Toledano
Name: Miranda J. Toledano
Title: Chief Executive Officer

Exhibit 99.1

Disclaimer

Various statements in this presentation are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. All statements (other than statements of historical facts) in this presentation regarding our prospects, plans, financial position, business strategy and expected financial and operational results may constitute forward-looking statements. Words such as, but not limited to, "anticipate," "believe," "can," "could," "expect," "estimate," "design," "goal," "intend," "may," "might," "objective," "plan," "predict," "project," "target," "likely," "should," "will," and "would," or the negative of these terms and similar expressions or words, identify forward-looking statements. Forward-looking statements are based upon current expectations that involve risks, changes in circumstances, assumptions and uncertainties. Forward-looking statements should not be read as a guarantee of future performance or results and may not be accurate indications of when such performance or results will be achieved.

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 is contractually obligated to provide, such as those pursuant to Entera's agreement with Amgen; 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 Oral Delivery of Therapeutic Proteins

We Focus on High Unmet Clinical Needs where Oral Delivery of a Protein Therapy Can Significantly Improve the Standard of Care

- Founded in 2009 (Jerusalem, Israel); IPO in 2018 (Nasdaq: ENTX)
- Proprietary 1st in Class Oral PTH Candidates with Demonstrated Clinical Efficacy in Phase 2 Studies
- External Strategic Partnerships to Diversify Pipeline and Revenue Streams (e.g. Amgen)

EB613 (oral PTH (1-34), teriparatide) First Oral Bone Forming / Anabolic Drug for Osteoporosis

- Phase 2 study met biomarker and 6-month BMD endpoints (ASBMR late-breaker oral presentation, 2021)
- 6-month lumbar spine BMD data in line with SC Forteo® injection; total hip and femoral neck BMD changes were greater than previously reported data with SC Forteo® injection
- FDA Type C Meeting based on revised Phase 3 protocol submitted (response expected in H2'2022)

EB612 First Oral PTH for Hypoparathyroidism - Granted Orphan Designation (US, EU)

- Pilot 4-month Phase 2 results presented (ASBMR 2015) and published in peer-reviewed journal (JBMR 2021)
- Phase 2 PK-PD study versus Natpara® presented (ASBMR 2019)
- Rapid decline in median serum phosphate levels and maintenance of target calcium levels throughout the study
- Novel formulation leverages Entera's 2nd generation peptide delivery platform (PK study expected in H1'2023)

Execution Oriented Leadership Team

Miranda Toledano, MBA, Chief Executive Officer	23 years of C-level leadership, principal investment and wall street/ transactional experience in the biotech sector	TRIGR THERAPEUTICS, ROYALTY PHARMA, FBR & Co
Art Santora, MD, PhD, Chief Medical Officer	35 years of special care, academic research, FDA in endocrinology focusing on osteoporosis and other diseases of bone and calcium metabolism; lead clinical physician for Fosamax®	MERCK, NIH, FDA U.S. FOOD & DRUG ADMINISTRATION
Dana Yaacov, CPA, MBA, Chief Financial Officer	15 years of finance management and accounting experience	pwc
Hillel Galitzer, PhD, MBA , Chief Operating Officer	21 years of biotech experience in clinical trial and supply chain operations support and early-stage R&D	Hadasit Bio-Holdings Ltd., האוניברסיטה העברית בירושלים THE HEBREW UNIVERSITY OF JERUSALEM
Anke Hoppe, BSc, VP of Clinical Operations	30 years of experience overseeing clinical operations across big pharma, small biotech, and CROs	COVANCE SOLUTIONS MADE REAL, gsk GlaxoSmithKline, Syneos Health
Gregory Burshtein, PhD, VP of R&D	18 years experience in oral drug delivery research, formulation and pre-clinical development	האוניברסיטה העברית בירושלים THE HEBREW UNIVERSITY OF JERUSALEM

Global Clinical & Scientific Advisory Board

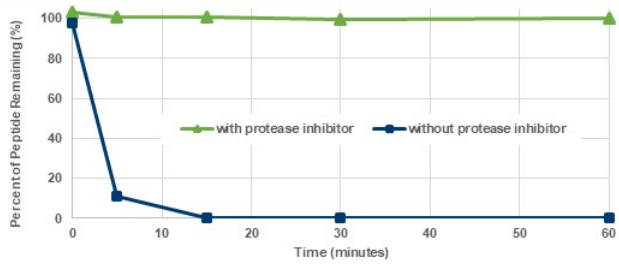
Professor John P. Bilezikian	Vice-Chair, Department of Medicine for International Research and Education; Chief, Emeritus, of the Division of Endocrinology; Director, Emeritus, of the Metabolic Bone Diseases Program at Columbia University Medical Center
Professor Maria Luisa Brandi	Professor of Endocrinology, 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 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

Entera Proprietary Oral Delivery Platform

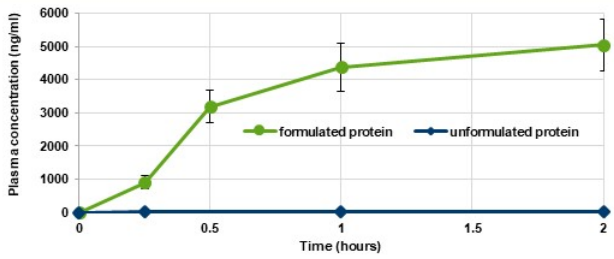
Synergistic Activity of Proteolysis Inhibition and Permeability Enhancement

Oral delivery of most therapeutic proteins is challenging due to poor absorption into the blood stream, enzymatic degradation within the gastrointestinal tract, and variable drug exposure

Stability of Peptide in Solution in presence of Trypsin



Absorption Enhancer Dramatically Increases Systemic Plasma Levels of Protein



Entera's Proprietary Technology - Synergistically Protects & Transports Large Molecules

1. Prevents the degradation of the therapeutic protein in the GI tract; maintains the integrity of the protein (stability)
2. Enhances peptide absorption by increasing transcellular transport (bioavailability)

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.

Internal Pipeline Focuses On Approved Injectable Proteins

Partnership Agreements Include Novel Undisclosed Targets

Program	Target	Preclinical	Phase 1	Phase 2	Phase 3	Partner	Next Milestone
EB613	Osteoporosis	PTH 1-34					Phase 3
EB612	Hypoparathyroidism *(Orphan Disease)*	PTH 1-34 (2nd generation)					Human PK
EB613	Non-Union Fractures	PTH 1-34					Internal Review
GLP-2	Short Bowel Syndrome						Undisclosed
hGH	GH deficiency						Undisclosed
Undisclosed	Anti-inflammatory					AMGEN	Undisclosed
Undisclosed	Various					Multiple	Undisclosed

Evaluating additional high value therapeutic proteins which could be developed as oral formulations to offer significant benefit to patients

EB613 (oral PTH (1-34), teriparatide)
Oral Bone Forming / Anabolic
for the Treatment of Osteoporosis

EnteraBio

EB613: First Oral PTH Drug Candidate for Osteoporosis

Indication

Osteoporosis: Skeletal disease characterized by low bone mass, micro-architectural deterioration of bone tissue and increased bone fragility leading to an increased susceptibility to fractures. Currently the vast majority of patients have a preference and are treated with oral therapy (bisphosphonates)

Molecule/ Drug Product

Parathyroid hormone (PTH) is an 84-amino acid hormone and the primary regulator of calcium and phosphate metabolism in bone and kidney. EB613 is an oral formulation of synthetic hPTH (1-34), (teriparatide), a peptide consisting of the first 34 amino acids of PTH (the functional region), developed with Entera's proprietary drug delivery technology which stabilizes the teriparatide and promotes absorption in the gastrointestinal tract. Subcutaneous Forteo® (teriparatide injection) has been the leading anabolic treatment of osteoporosis since 2002 (with U.S. peak sales of $960m)

Key Efficacy Profile

Phase 2 study met primary endpoint showing a statistically significant increase of P1NP*, a marker of bone formation, at 3 months; at 6 months of treatment with EB613, the increase in spine bone mineral density (BMD) was similar in magnitude to that previously reported with SC Forteo ® injections; Increases in total hip and femoral neck BMD with EB613 were greater than those previously reported with SC Forteo ® injections

Key Safety Profile

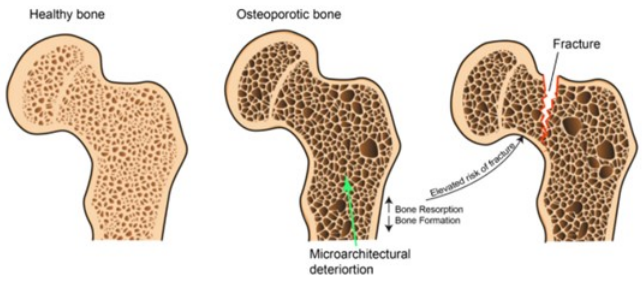
Favorable phase 3 safety profile similar to Forteo® and differentiated from oral bisphosphonates
The most common adverse events included mild nausea, moderate back pain, moderate headache, and moderate upper abdominal pain

End of Phase 2 Minutes: FDA suggested Entera explore a placebo-controlled study with BMD ASBMR-FNIH STEs as primary endpoint. Type C meeting expected H2'2022

*P1NP: amino pro-peptide of type 1 collagen

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

Bone Density Healthy vs. Osteoporotic

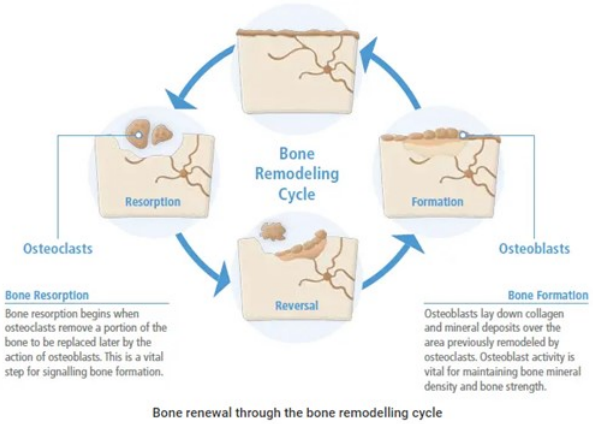


Osteoporosis is a disease associated with low bone mass and enhanced skeletal fragility and is most commonly caused by:

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

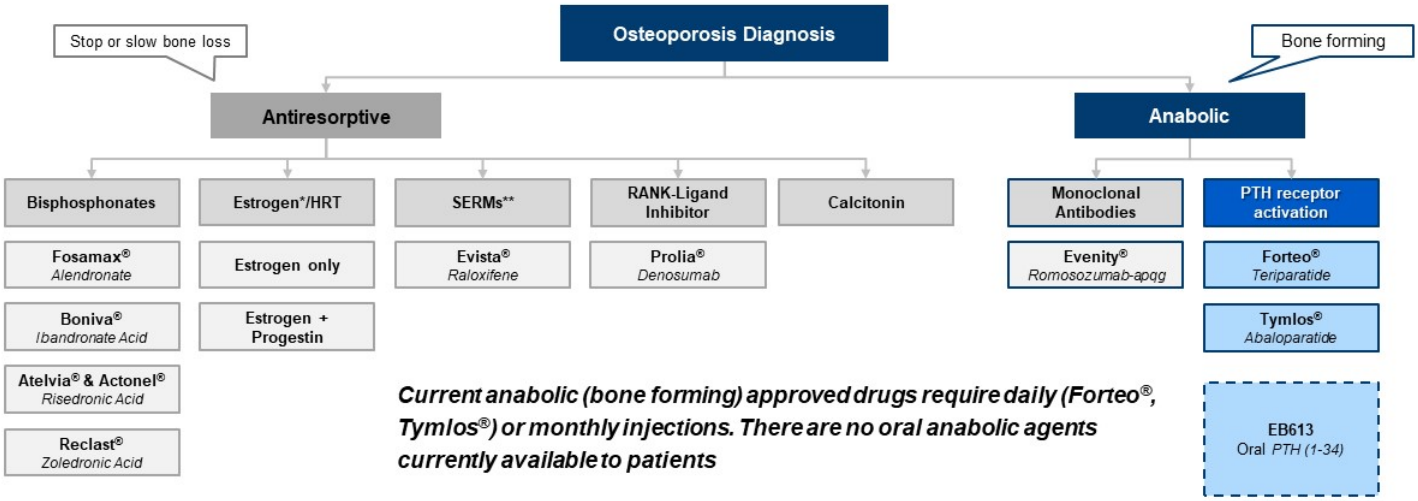
The Bone Remodeling Cycle can be separated into two distinct processes: **Resorption (osteoclasts) and Formation (osteoblasts)**



Bone renewal through the bone remodelling cycle

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

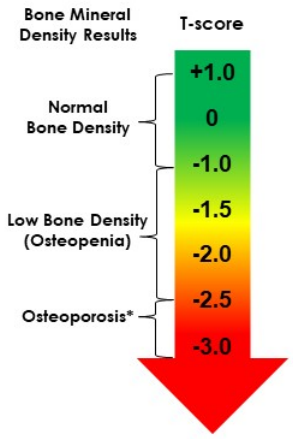
Current Osteoporosis Pharmacologic Treatment Is Segmented Into: Anti-Resorptive & Anabolic Options



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;.

Healthcare Providers Typically Use T-score BMD Classifications, Patient Fracture History and Preference To Drive Therapy Selection

T-Score Scale



Injections deter many patients from using PTH, contributing to a treatment gap in high-risk patients. An oral formulation of PTH with adequate bioavailability, similar safety and effects on BMD may address this unmet clinical need

Low BMD Category	Percent of Patients with low BMD		Initial Typical 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; limited Anabolic penetration
Very High Risk Osteoporosis *(T-scores ≤ -3.0 or ≤ -2.5 with prior fragility fractures)*	10%	23%	Bisphosphonates / Anabolic therapies

HCPs indicated most of their osteoporosis patients are:

Post-menopausal women (~70%)
Or older men (~15%)

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

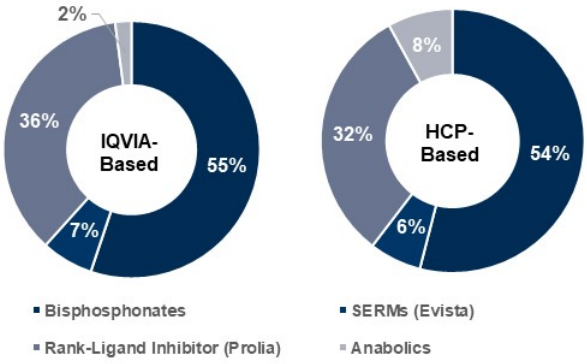
Anabolic Treated Patients Comprise Less Than 10% of Currently Treated Osteoporosis Patients

Estimated Treated Population by Class of Osteoporosis Medication

Population Treated by Class of Osteoporosis Medication (2021)

	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); TIG Primary Research Apr. 2022

EB613 Poised To Create A Paradigm Shift In The Treatment of Osteoporosis As The First Oral 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	✓	✓			✓*	✓

Bisphosphonates (oral daily pills) are the most common treatment of post-menopausal osteoporosis – **orally administered and inexpensive**, but many patients ***progress and have low tolerance***

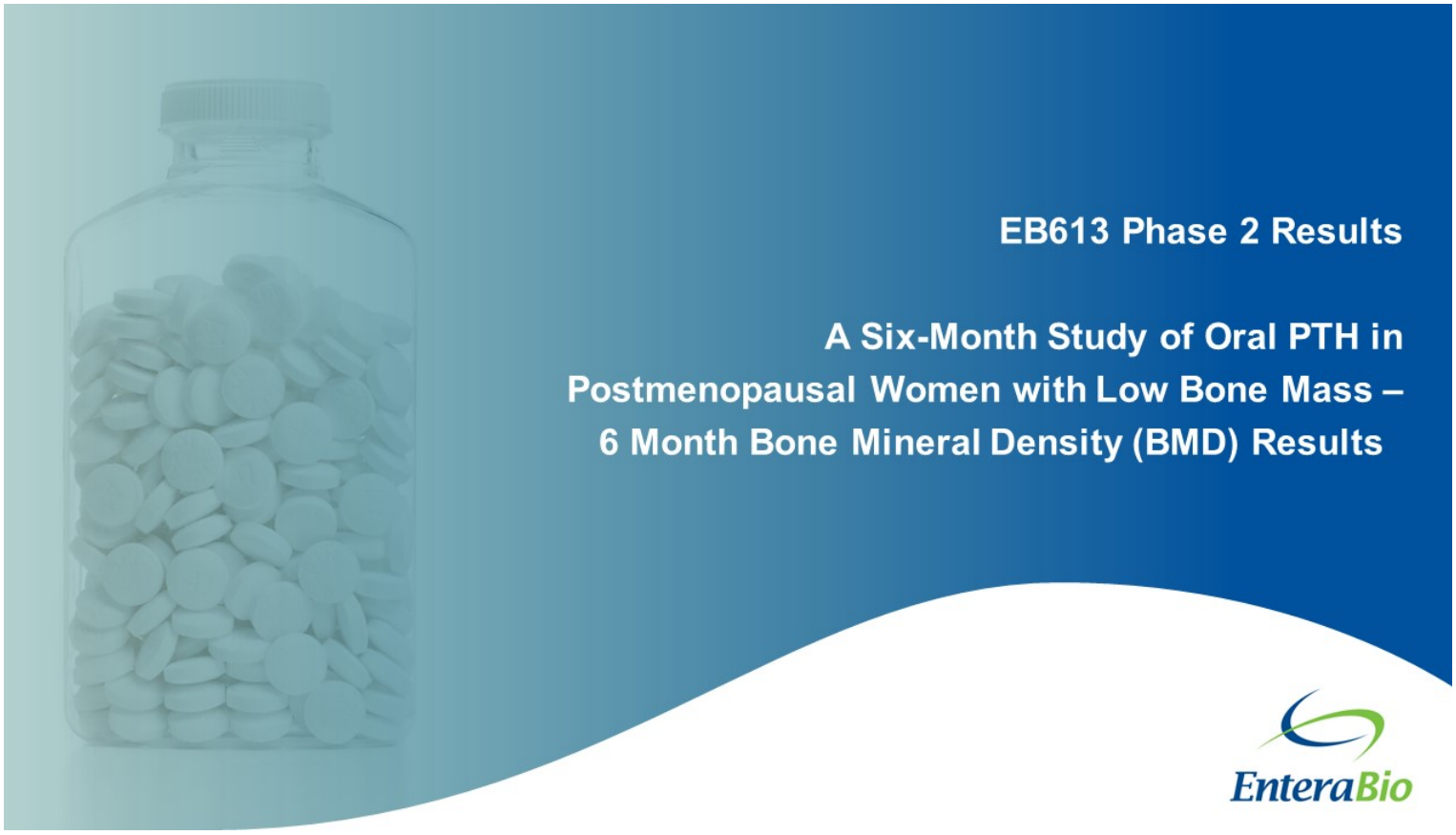
There have been no new oral drugs in >10 years

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

EB613 is positioned as the first potential oral anabolic PTH treatment for osteoporosis

Source: Triangle Insights Primary Research Apr. 2022

*Zoledronic acid is administered by intravenous administration



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

- 6-Month, Randomized Dose-Ranging Placebo-Controlled Study
- Conducted at 4 sites in Israel between June 2019 and May 2021; Final enrollment =161

Screening

Key inclusion criteria

- 50+ years old and 3+ years post menopause
- Low bone mass

Key exclusion criteria

- Osteoporosis treatment within last 2 years
- Known medical predisposition
- 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 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

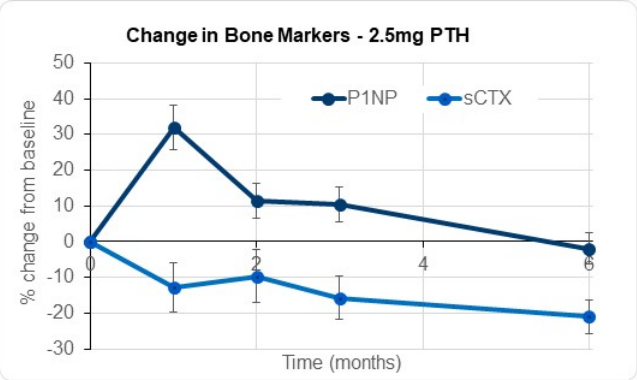
3 M Partial** & Final interim analysis of primary endpoint

6 M Final analysis / Topline data – All endpoints

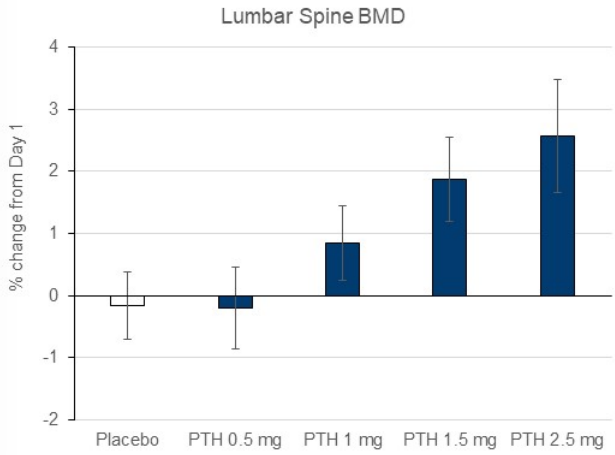
* Following an interim analysis, a 2.5mg arm was added and recruitment to the 0.5mg & 1.0 mg arms was stopped
** Following AEs typical of orthostasis additional subjects in the 2.5mg group received 1.5mg for 1 month, 2.0mg for the next month and 2.5mg during months 3 to 6 (Titrated).

EB613 Predictive Profile Of Bone Biomarkers and Significant Dose-Dependent Increases in BMD

2.5mg selected as Phase 3 dose – sustained "anabolic window" from Month 3 to Month 6 in patients treated with EB613. A significant dose response of 0.5, 1.0, 1.5 and 2.5 mg doses on Month 1 P1NP and Osteocalcin *(P<0.0001)*. Serum CTX decreased 21% from baseline at Month 6 (p<0.01) while P1NP was unchanged

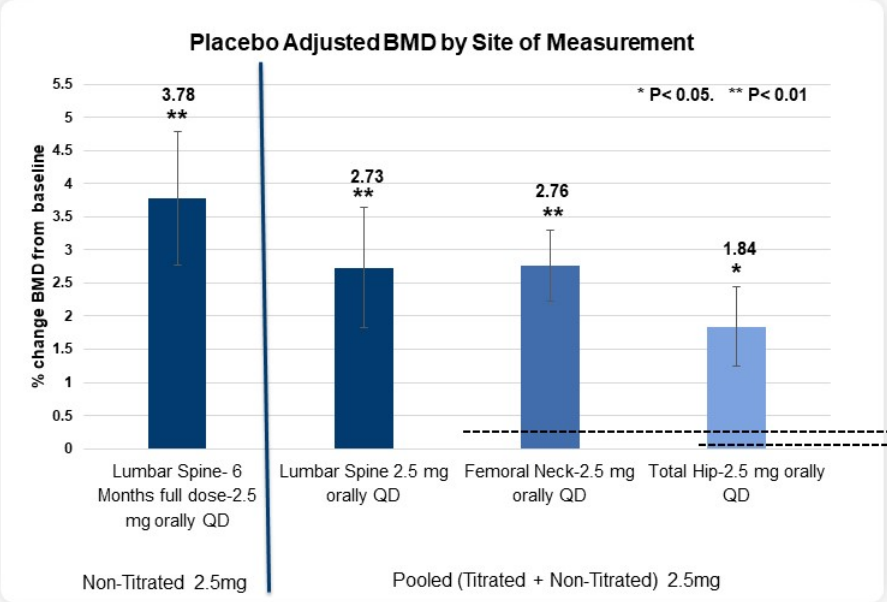


Oral PTH produced a statistically significant Dose Response in Lumbar Spine BMD (p<0.0001)



Presented at Late Breaker LB-1116 and Poster FRI-237– ASBMR 2021

EB613 Positively Impacts Lumbar Spine, Femoral Neck and Total Hip BMD at 6 Months, With Excellent Statistical Significance



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

EB613 appears to have a greater impact on femoral neck and total hip BMD than previously reported studies involving SC injection Forteo®[1,2]

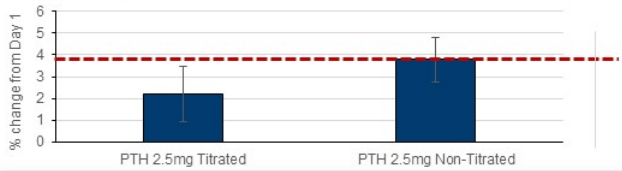
0.8% Placebo vs 1.1% Teriparatide
Difference = 0.3% at Femoral Neck[2]

0.4% Placebo vs 0.5% Teriparatide
Difference = 0.1% at Total Hip[2]

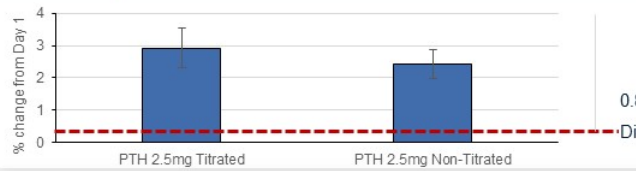
Notes: 1. Cosman, et al. Current Osteoporosis Reports (2021) 19:189–205; 2. Leder BZ et.al. JCEM (2015) (historical data from Abaloparatide vs. Forteo)

EB613: 6 Month Placebo Adjusted BMD by Site at 2.5mg Dose

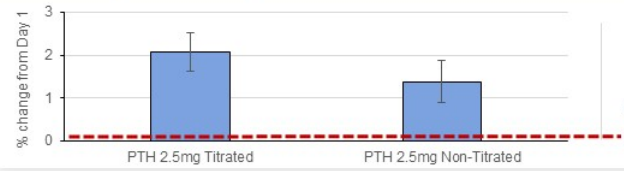
Placebo adjusted Lumbar Spine BMD



Placebo adjusted Femoral Neck BMD



Placebo Adjusted Total Hip BMD



At 6 months of treatment with 2.5mg EB613:

The increase in spine BMD was similar in magnitude to that previously reported with SC injection Forteo®

Increases in total hip and femoral neck BMD were greater than those previously reported with SC injection Forteo®

--- Historical data (Leder BZ et.al. JCEM 2015)

Presented at Late Breaker LB-1116 and Poster FRI-237– ASBMR 2021

EB613 Phase 2 Adverse Event Profile

Adverse event profile similar to that observed with Forteo®, and typical of orthostatic hypotension

EB613 not associated with serum calcium increases or hypercalcemia adverse events

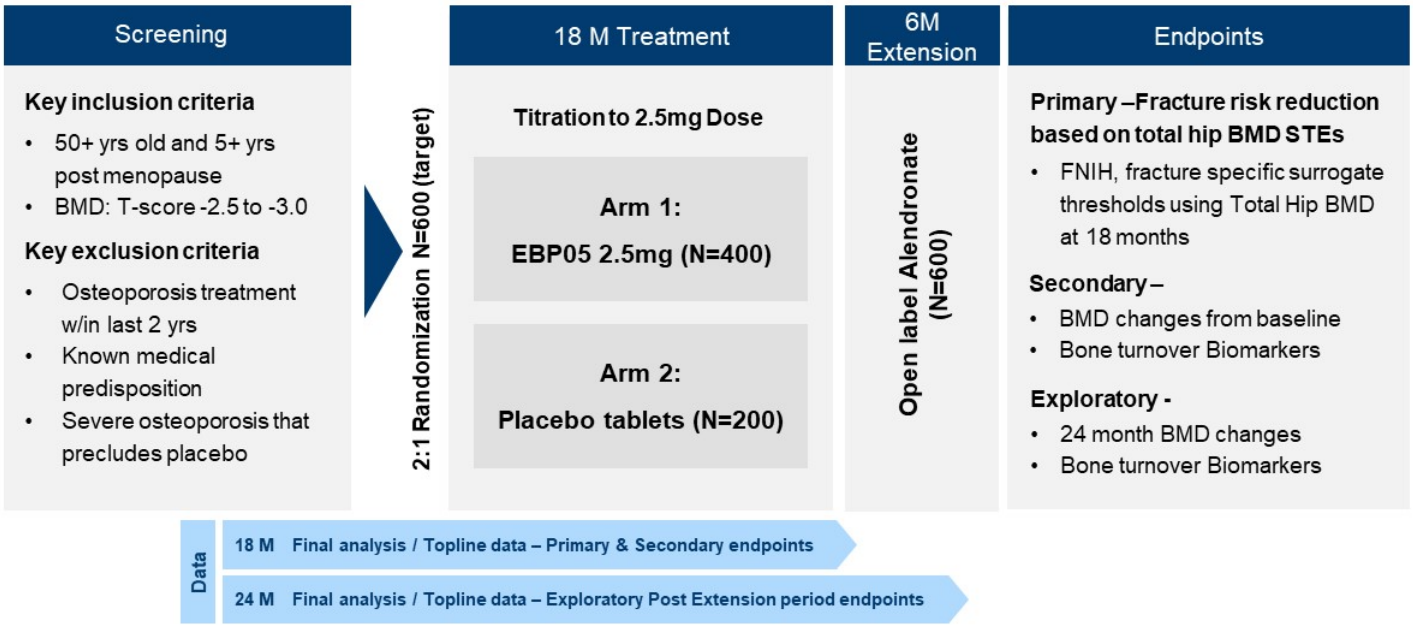
Greater than 90% of subjects tolerated the 2.5 mg dose well, after titration (1.5mg for 1 month, 2.0mg for the next month and 2.5mg during months 3 to 6)

AEs commonly attributed to vasodilatation with subcutaneous injectable PTH were observed - headache, nausea, presyncope and dizziness **There were no serious drug-related AEs**

Subject disposition	Placebo (N=43)		EBP05 0.5 mg orally QD (N=25)		EBP05 1 mg orally QD (N=29)		EBP05 1.5 mg orally QD (N=28)		EBP05 2.5 mg orally QD (N=19)		EBP05 2.5 mg titrated orally QD (N=17)	
	N	%	N	%	N	%	N	%	N	%	N	%
Randomized	43	100	25	100	29	100	28	100	19	100	17	100
Discontinued Before Month 3	3	7	3	12	2	6.9	4	14.3	7	36.8	1	5.9
Discontinued from Study Before Month 6	5	11.6	3	12	3	10.3	6	21.4	9	47.4	1	5.9

EB613 Proposed Phase 3 Clinical Trial Design

- A Global Phase 3, 18-Month, Placebo-Controlled Study (2:1), with a 6-Month Alendronate Extension
- Designed to address FDA suggestion - Placebo-Controlled study, BMD endpoint (ASBMR-FNIH Criteria)



Data

18 M Final analysis / Topline data – Primary & Secondary endpoints

24 M Final analysis / Topline data – Exploratory Post Extension period endpoints

ASBMR-FNIH BMD Regulatory Endpoint Backgrounder

- Message from the president of the ASBMR on 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**
- The FNIH collected data from over 50 randomized trials and individual data from over 170,000 patients
- The FNIH conducted a meta-regression of 38 placebo-controlled trials of 19 therapeutic agents[1] and a meta-regression analyses of 91,779 individual patient data from 23 randomized placebo-controlled trials[2]
- **The FNIH concluded that total hip (TH) BMD, as opposed to lumbar spine and femoral neck BMD, was found to be the best predictor of fracture risk reduction, at all sites (vertebral, non-vertebral and hip)**
- **FNIH's submission of the Full Qualification Package, for final approval by the FDA, is expected by the end of the year[3]**

ASBMR®
The American Society for Bone and Mineral Research

1. Bouxsein et. al. Journal of Bone and Mineral Research, Vol. 33, 2018, pp 1–11
2. Black et. al. Lancet Diabetes Endocrinol 2020; 8: 672–82
3. FNIH, June 1, 2022 press release https://fnih.org/news/announcements/fda-approves-biomarkers-qualification-plan-first-surrogate-endpoint-anti

EB613 Phase 3 Clinical Trial Design Background – ASBMR-FNIH STEs

- The primary endpoint proposed for EB613 Phase 3 is based on the ASBMR- FNIH's Surrogate Threshold Effect (STE) using Total Hip (TH) BMD as the predictor of significant fracture reduction for all different fracture types.
- Placebo adjusted TH 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.

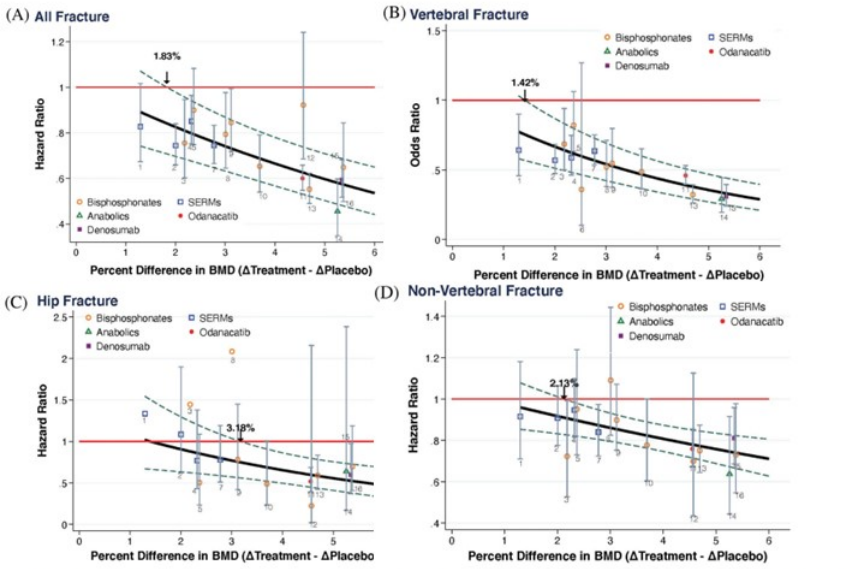
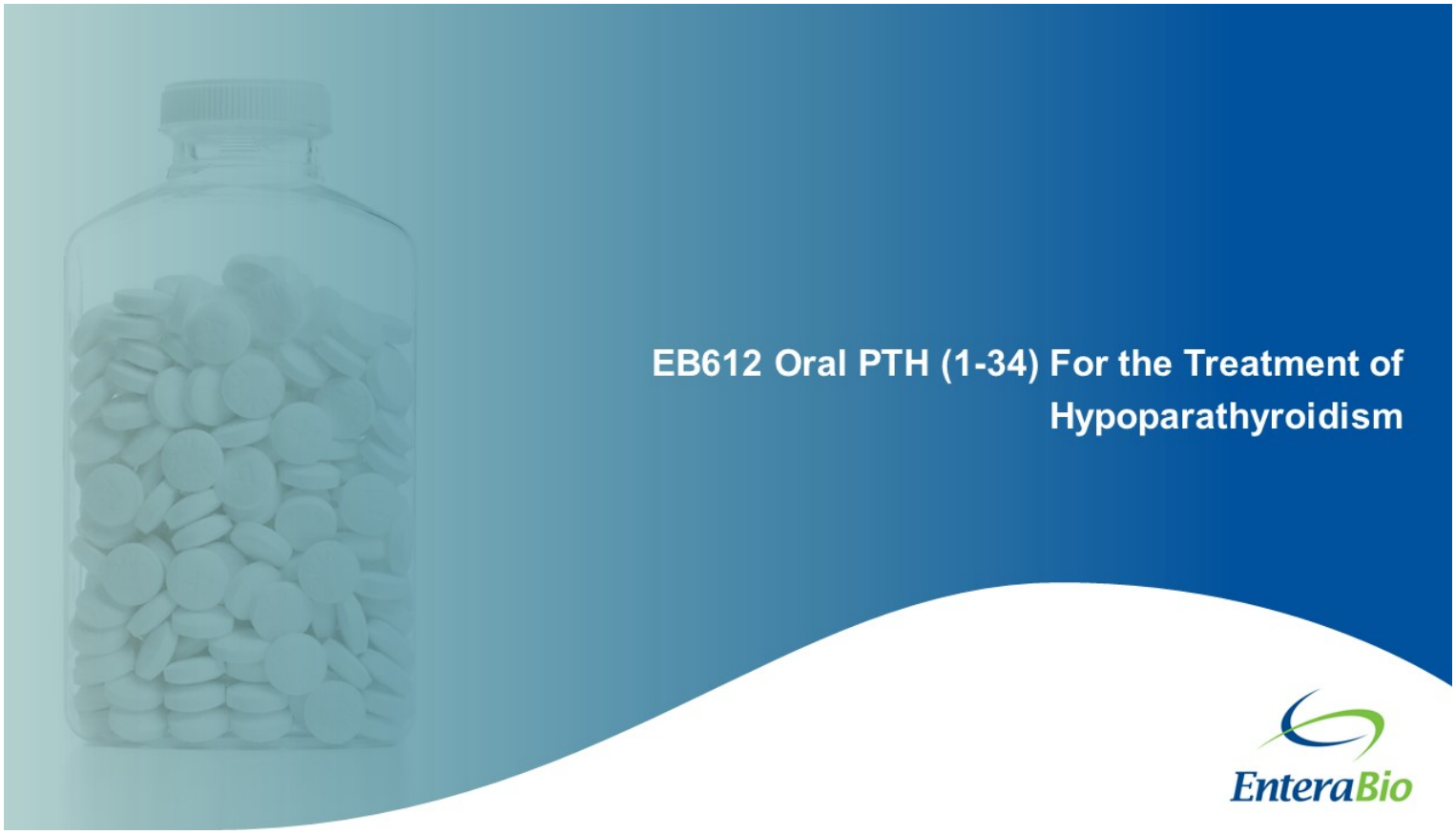


Fig 1. Relationship between difference in the change in total hip BMD between active and placebo groups at 24 months and the hazard or odds ratio of all, vertebral, hip and nonvertebral fractures. The red horizontal line is the ratio of 1 (no treatment effect) and the STE is the point where the upper 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. Journal of Bone and Mineral Research, 2021, pp 1–7

EB613 Positioning

- EB613, as a first in class *oral* PTH treatment, may potentially offer a viable anabolic (bone formation) therapeutic option to lower the risk of fracture for high risk (based on low BMD score or prior fracture history) osteoporotic patients
- ***PTH receptor activation is a mechanistically validated and key target in the treatment of osteoporosis (Forteo® and Tymlos®)***
- Based on third party research, many high-risk patients (approximately 35-40% of the estimated 3.2 million treated patients in the US) are reluctant to take daily injections and only turn to currently injectable anabolic drugs when their disease becomes very severe (with multiple fractures)
- EB613 Phase 3 design is in accordance with End of Phase 2 suggestion by FDA to explore a placebo-controlled study using the ASBMR-FNIH BMD Biomarker Tool
  - 18 month double blind placebo-controlled treatment phase followed by 6-month transition to alendronate adheres to a real-world treatment paradigm and ensures all patients will receive active treatment
- Based on recent third-party market research, healthcare providers would support the use of anabolics earlier in the treatment paradigm - yet hampered to date due to difficulty of administration (injectables) and price



EB612 Oral PTH (1-34) For the Treatment of Hypoparathyroidism

EnteraBio

Hypoparathyroism: 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 creates long term co-morbidities
- Natpara® (parathyroid hormone) injection was approved in 2015 and was withdrawn from US market in September 2019; Natpara® had sales of $230m in 2018, its 3rd full year of sales, before it was recalled. The recall was not connected to the safety or efficacy of parathyroid hormone
- TransCon PTH, an investigational once-daily long-acting prodrug of parathyroid hormone (PTH(1-34)) U.S. FDA regulatory submission on track for Q3 and EU MAA for Q4 2022, according to Ascendis

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)

EB612: First Oral PTH (1-34) 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:

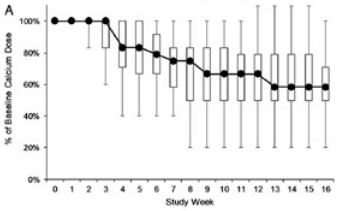
42% reduction (p=0.001) from baseline in median calcium supplement use

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 study

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

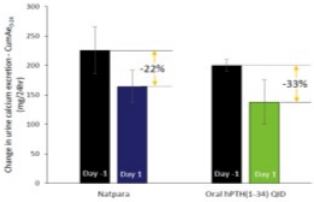
Efficacy: Oral hPTH (1-34) 2.25 mg QID for one day is associated with an increase in serum albumin-corrected calcium and 1,25(OH)2D and a decrease in serum phosphate

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

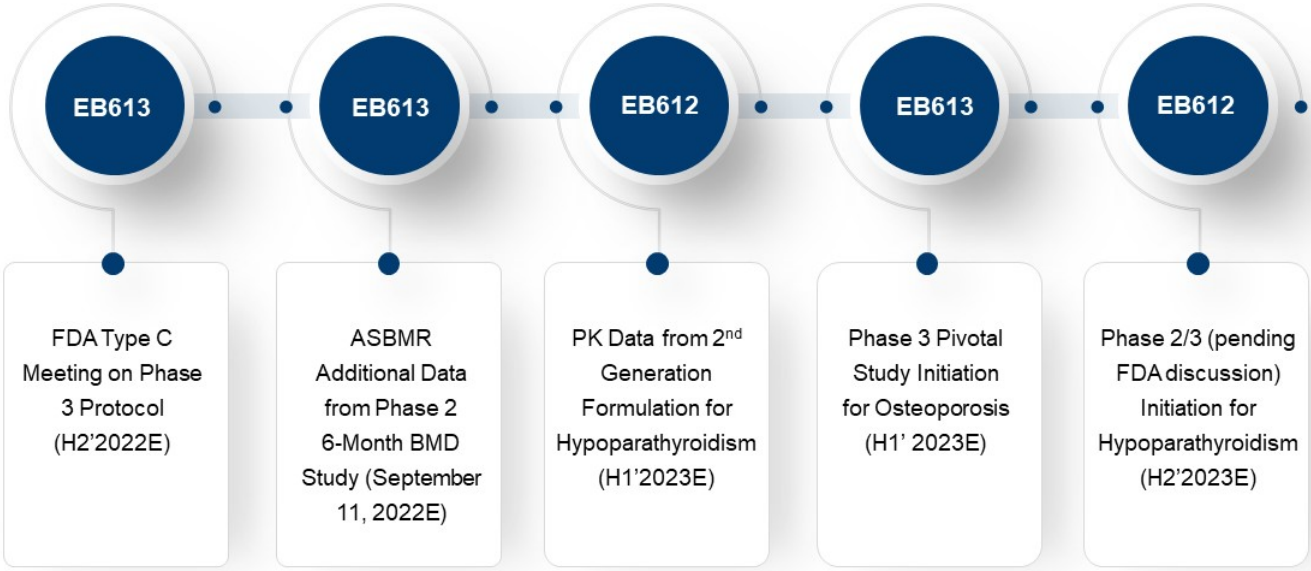
Improved/ Decreased Urinary Ca
Excretion Over a 24-Hour Period



EB612 Positioning

- EB613 is potentially the first oral PTH (1-34) 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 leverages Entera's 2nd generation peptide delivery platform (PK study expected in H1'2023)**

Key Short-Term Catalysts




EnteraBio
Thank You
Contact:
Entera Bio:
Ms. Miranda Toledano
Chief Executive Officer
Email: miranda@enterabio.com

Appendix

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EB613 Phase 3 Clinical Trial Design - FNIH

June 23rd, 2022 message from the president of the ASBMR (American Society for Bone and Mineral research) Dr. Ebeling reported on the FNIH progress and support from the ASBMR[1].

"Dear Colleagues:

I am very happy to announce that the US Food and Drug Administration (FDA) Biomarkers Qualification Program recently 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.

Indeed, this is the first qualification plan accepted by the FDA for a surrogate endpoint under the 21st Century Cures Act, a remarkable achievement for the Project Team. This team, including ASBMR members Dennis Black, Mary Bouxsein and Richard Eastell, now plans to submit a Full Qualification Package based on this approved plan for final approval by the FDA before the end of this year.

The ASBMR is proud to financially support this critical initiative. Achieving FDA approval to utilize BMD as a surrogate endpoint in future osteoporosis drug development trials could provide patients with more options to fight a disease that leads to debilitating fractures that cause disability, loss of independence and even death. It is also likely to attract more researchers to the musculoskeletal field, enabling a new horizon of discoveries to help our patients."

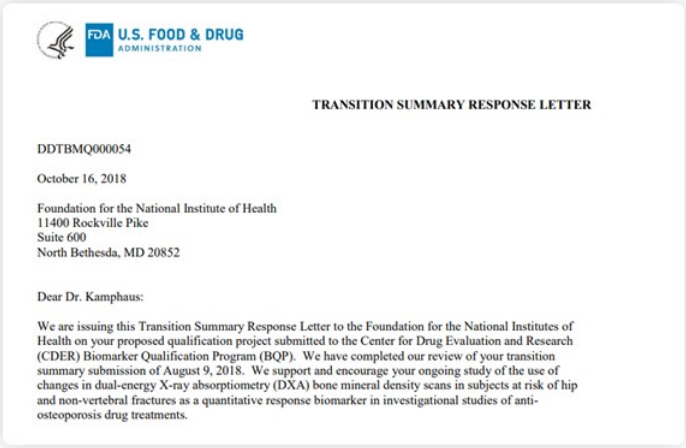
1. https://www.asbmr.org/about/council/presidents-corner-detail/message-from-asbmr-president-peter-ebeling-ao-frac-7

EB613 Phase 3 Clinical Trial Design Background - FNIH

- The Foundation for National Institutes of Health (FNIH) – Bone Quality Project (BQP), supported by the FDA and other public, private and academic partners has been evaluating the potential use of existing biomarkers such as BMD to enable the development of anti osteoporosis drugs since 2013.[1]
- The FNIH-BQP has been working closely with the FDA to ensure alignment with the FDA's requirements and expectations as evident from extensive correspondence between the FNIH and FDA.[2]

FDA responded to the proposed use of percentage change in BMD in our original Letter of Intent in 2016, stating that "Percentage change in DXA BMD should be the most appropriate measure as this metric would not be affected by the DXA machine type or normative database used. However, there may be a threshold of percent change in BMD, above which we are comfortable with stating fracture risk reduction has been demonstrated."

Aug. 2018 FNIH Status update to the FDA[3]



FDA U.S. FOOD & DRUG ADMINISTRATION

TRANSITION SUMMARY RESPONSE LETTER

DDTBMQ000054

October 16, 2018

Foundation for the National Institute of Health
11400 Rockville Pike
Suite 600
North Bethesda, MD 20852

Dear Dr. Kamphaus:

We are issuing this Transition Summary Response Letter to the Foundation for the National Institutes of Health on your proposed qualification project submitted to the Center for Drug Evaluation and Research (CDER) Biomarker Qualification Program (BQP). We have completed our review of your transition summary submission of August 9, 2018. We support and encourage your ongoing study of the use of changes in dual-energy X-ray absorptiometry (DXA) bone mineral density scans in subjects at risk of hip and non-vertebral fractures as a quantitative response biomarker in investigational studies of anti-osteoporosis drug treatments.

1. https://fnih.org/our-programs/biomarkers-consortium/programs/bone-quality-project 2. https://fda.force.com/ddt/s/ddt-project?ddtprojectid=97 3. file:///C:/Users/HILLEL-THINK/Downloads/265-FNIH-Legacy-project-transition-to-507-process_1.pdf

Entera Proprietary Oral Delivery Platform: Key Advantages and Validation

- ✓Significantly Increased Bioavailability of Macromolecules
- ✓Reduced Pharmacokinetic Variability
- ✓Versality Across Molecular Weight and Target Profile
- ✓Advantageous Stability versus Injectables
- ✓Controlled Onset of Action, Minutes to Hours
- ✓Simple Production Process Preserving API activity
- ✓IP Protection across existing and next generation of our platform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The combined effect of permeation enhancement and proteolysis inhibitio on the systemic exposure of orally administrated peptides: Salcaprozate sodium, soybean trypsin inhibitor, and teriparatide study in pigs

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