EnteraBio

Entera Bio Investor Presentation

August 17th 2021

Forward-Looking Statements

This presentation includes forward-looking statements that relate to future events or our future financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to differ materially from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. Forward- looking statements include all statements that are not historical facts and can be identified by words such as, but not limited to, "believe," "expect," "anticipate," "estimate," "intend," "plan," "targets," "likely," "will," "would," "could," and similar expressions or phrases. We have based these forward-looking statements largely on our management's current expectations and future events and financial trends that we believe may affect our financial condition, results of operation, business strategy and financial needs. Although the Company believes that its expectations with respect to forward-looking statements are based upon reasonable assumptions within the bounds of its existing knowledge of its business and operations, there can be no assurance that actual results, performance, or achievements of the Company will not differ materially from any future results, performance, or achievements expressed or implied by such forward-looking statements. Please refer to our SEC filings for a complete discussion of the risks associated with our business at www.sec.gov.

Entera Bio Investment Highlights

Platform for the Oral Delivery of Injectable Biologics and Proteins

- Two programs in clinical development
- Platform has been tested successfully on 8 molecules of broad characteristics and size
- Multiple business development opportunities; collaboration with Amgen signed in Dec 2018 around anti-inflammatory large molecule

Lead PTH program: EB613 for Osteoporosis Headed into Pivotal Phase 3

- Phase 2 study completed, met primary and key secondary endpoints; Preparing for End of Phase 2 meeting with FDA for planned pivotal one-year Phase 3
- Potential 1st oral bone building product; final data show dose dependent and positive impact on lumbar spine BMD
- US IND granted Dec 2020; FDA Guidance allows for use of 505(b)(2) approval pathway

Next internal PTH Program: Hypoparathyroidism EB612 (Orphan Disease)

- Phase 2 PK/PD data published in JBMR (Mar 2021); data helps define final formulations & Phase 3 pathway in 2022
- Orphan Disease Designation in both US & EU for hypoparathyroidism (HypoPT)

Large Target Markets with Significant Unmet Needs

- < 5% of osteoporosis patients are treated due to injectables' inconvenience/compliance issues; EB613 can further grow multi-billion $ osteoporosis market
- HypoPT market >$1 billion
- Future opportunities in other biologics, where oral delivery can grow multi billion $ markets

Management Team & Board with Capital Markets and Drug Development Expertise

Experienced Leadership Team & Board

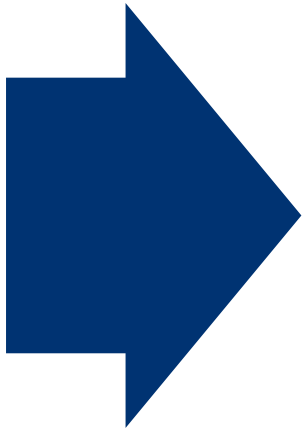
Jerry Lieberman CPA	**Chairman of the Board:** TEVA Board, formerly AllianceBernstein, Fidelity & Citicorp
Spiros Jamas Sc.D	**CEO**, formerly of AOBiome Therapeutics, Tempero Pharmaceuticals, Enanta Pharmaceuticals, and Alpha-Beta Technology
Phillip Schwartz MSc, PhD	**President of R&D** formerly of Serono, Endo Pharmaceuticals
Roger Garceau MD	**Director and Chief Development Advisor** formerly CMO of NPS Pharma (acquired by Shire plc for $5.2 B) - led Natpara® approval
Arthur Santora MD, PhD	**Chief Medical Officer** formerly of Merck, lead clinical physician for Fosamax®, FDA & NIH
Hillel Galitzer MBA, PhD	**Chief Operating Officer** formerly of Optivasive Inc. and Hadasit Bio-Holdings
Dana Yaacov MBA, CPA	**Israel Chief Financial Officer** formerly of PricewaterhouseCoopers
Ramesh Ratan	**US Chief Financial Officer** formerly of AOBiome, Xcellerex, Enanta, Repligen, Bristol-Myers
Steve Engen MBA	**Head of Business Development** formerly of Locust Walk, Shire, Solasia and Mundipharma

Oral Delivery of Large Molecules is Challenging

~30% of all FDA drug approvals between 2015 and 2018 were biologics (>$20 B+ annual sales); however biologic molecules cannot be orally formulated due to low bioavailability and high variability

Large molecules are broken down and degraded in the GI Tract - The human GI tract is uniquely designed to digest large molecules such as proteins and peptides

Large molecules are difficult to absorb - The weight, size and charge of intact large molecules inhibit absorption



Loss of activity

Poor absorption

Significant variability in drug exposure

Historically, most technologies have focused on either enhancing absorption or protecting the molecule; Entera has developed two technologies which function in tandem to deliver known API's

Our Solution: Protect and Enhance Absorption of Known Products

Protection of Proteins and Peptides

Combination of protease inhibitors and chemical entities protect proteins and peptides

Customized formulations for individual molecules or API's

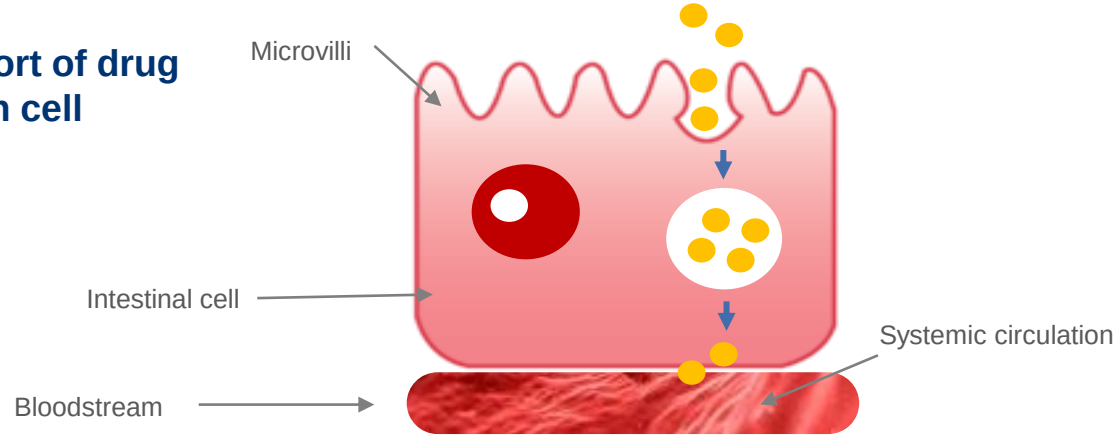
Just as the human gastro-intestinal track digests food, biological molecules such as PTH are also digested

Absorption Enhancement

A novel molecular entity induces endocytosis of itself and associated molecule

Transport via vesicles is specific and safe: no bacteria or other contaminants

Transport of drug through cell

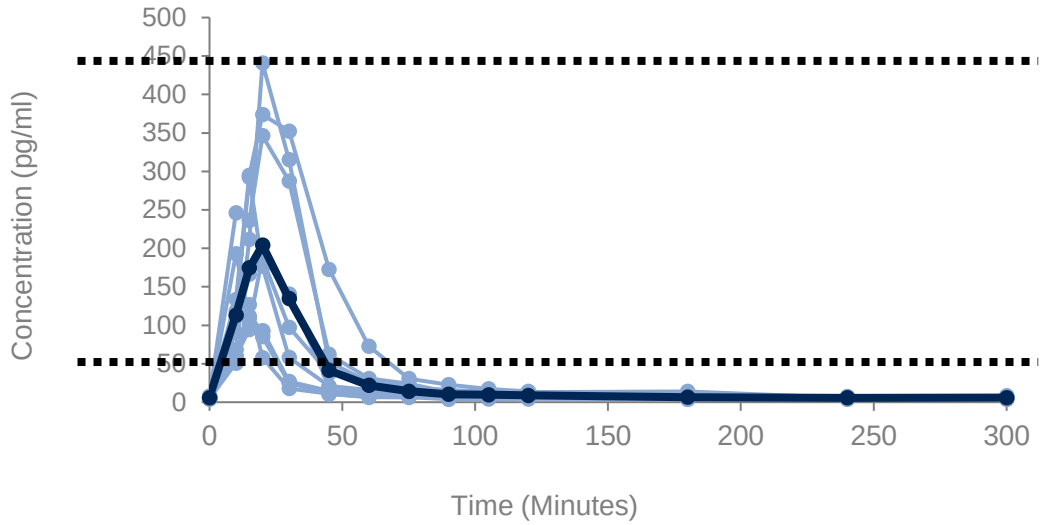


Entera's technology platform acts synergistically to transport and protect large molecules, while preserving and leaving the API untouched, providing rapid clinical and regulatory advantages

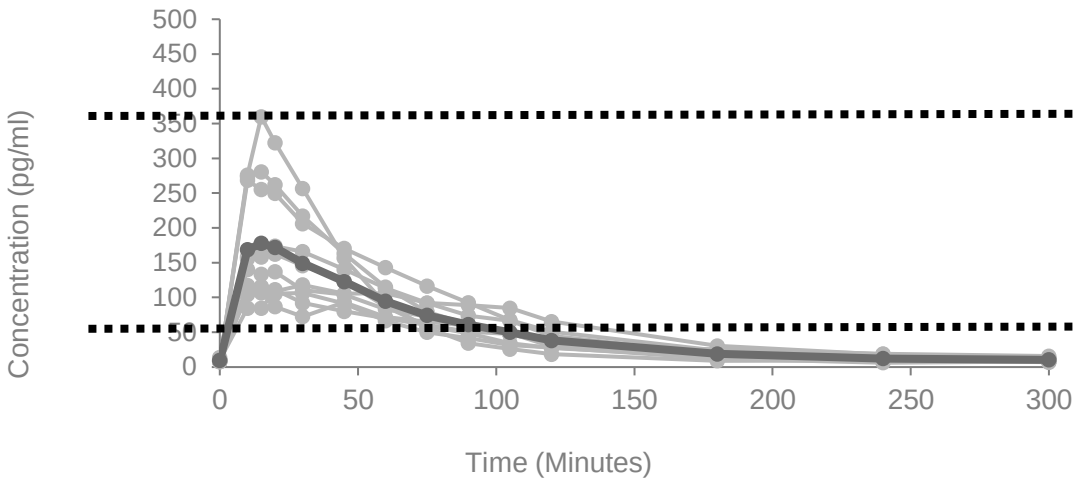
Highly Predictable Delivery and Reduced Variability

Oral delivery of large molecules has been plagued by variability and lack of specificity. Entera's technology addresses this major technical hurdle in the oral delivery of proteins

EB613 Oral PTH (1-34)



Injectable PTH (1-34)



Dark line is the mean of the observed release profiles.

Formulation	Participants	Cmax (pg/ml)	Tmax (min)	Coefficient of Variation (%)
EB613 Oral PTH	10	235.6 ± 36	16.5 ± 1.2	48
Injectable PTH	10	184.2 ± 26	16 ± 1.8	45

Oral formulation development: Theoretical assessment to PK study in humans

Theoretical assessment of the oral delivery feasibility based on the physicochemical parameters and pharmacology of the target molecule

→ Pharmacokinetic study in animals

→ Simulation of the human PK profile of a target molecule based on the PK data of the injectable formulation and results of animal PK study

→ Pharmacokinetic study in humans

Development of oral formulation of GLP2

GLP2 analogs are suitable for oral delivery with ENTX platform ✓

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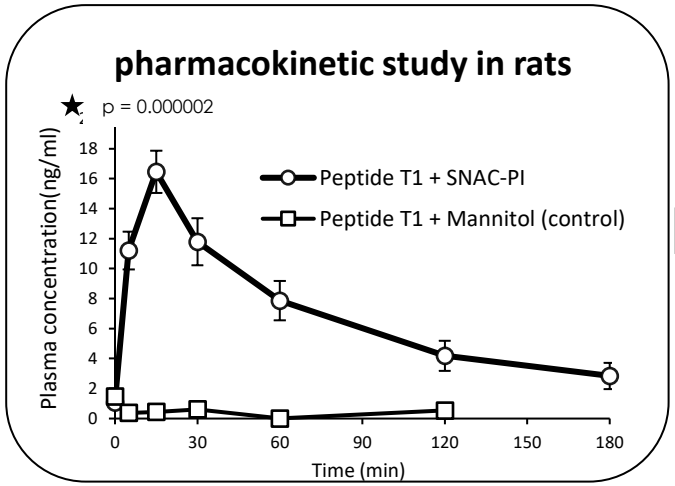

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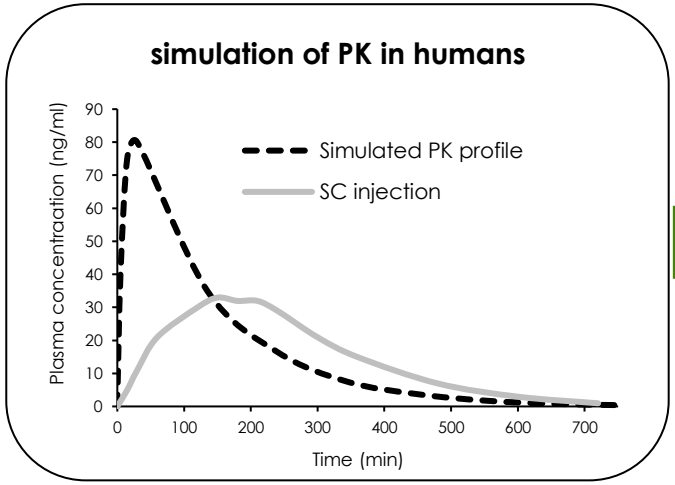

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NASDAQ: ENTX

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Entera's Pipeline Focuses on both Internal Development of Approved Injectable Therapeutics, as well as External Collaborations

~90% of current blockbuster products are injectable biologics[1], Entera's platform may be applicable to 1/3 of all biologic macromolecules

Program	Target	Preclin / Phase 1 / Phase 2 / Phase 3	Partner	Current Class Sales ($)	Next Milestone
PTH	Osteoporosis	EB613 PTH 1-34 505b2		$7.5 B+	End-of-Phase 2 Meeting with FDA H2 2021
PTH	Hypoparathyroidism (Orphan)	EB612 PTH 1-34 BLA		<$1.0 B+	Phase 2b/3 Start 2022
PTH	Non-union fractures	EB613 PTH 1-34		$1.0 B+	Phase 1/2
GLP-2	Short bowel syndrome			$574 M	Large animal studies
hGH	GH deficiency			$3.7 B+	Large animal studies
Undisclosed	Anti-inflammatory		AMGEN	$5.0 B+	Undisclosed
Undisclosed	Various			Multi-billion $	Undisclosed

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1. https://www.alcimed.com/en/press-releases/oral-delivery-of-macromolecules-big-pharma-keep-searching-for-the-holy-grail/

Osteoporosis Incidence & Health Care Burden

WHAT IS OSTEOPOROSIS?

Systemic skeletal disease characterized by low bone mass, deterioration of bone tissue and increased bone fragility and susceptibility to fractures

High Levels of Incidence in the US & WW [1,2]

- Osteoporosis affects 200 million people worldwide
- 54 million Americans have osteoporosis or low bone mass which places them at an increased risk for developing osteoporosis
- One in two women and one in four men >50 years old will break a bone due to osteoporosis

High Costs & Burden of Disease [1,2]

Osteoporosis is costly[2]

- 2 million broken bones and $19 billion in related costs each year; estimated to reach 3 million broken bones & $25 billion in costs each year by 2025

Osteoporosis is a silent and multifactorial disease[1]

- Many patients don't feel sick, can't feel the bones weakening
- Several other diseases or treatments can increase the likelihood of osteoporosis – autoimmune or hormonal disorders, or even common drugs such as antacids or steroids

1. National Osteoporosis Foundation. nof.org
2. International Osteoporosis Foundation. iofbonehealth.org/facts-statistics

High Incidence, yet Greatly Underdiagnosed and Undertreated

The first oral once daily tablet will grow the market substantially

- Benefits of bone building PTH and convenience of a daily oral tablet
- Significant cost advantages to price attractively for the 95% of patients NOT treating this disease; oral tablets are a fraction of the cost of injectables
- Patients, Physicians, Payers and Providers seeking more cost-effective solutions

Today's $4 B+ Market: The most effective drugs for severe osteoporosis require injections

- Annual injections cost ~$20-$30K
- Forteo® (Lilly) is a daily injection with 2019 sales of ~$1.4B[1]
- Prolia® (Amgen) had sales of ~$2.2B in 2019[2]

Yesterday's $3 B Market: Bisphosphonates are anti-resorptive agents without the ability to directly induce new bone synthesis

- Inexpensive and convenient (oral daily pills) but not so effective - many patients continue to get worse on bisphosphonates
- GI disturbances and the risk of osteonecrosis of the jaw
- The leading bisphosphonates, Fosamax® (Merck) and Reclast® (Novartis), had peak sales of $3.2B (in 2005)[3] and $1.5B (in 2010)[4] respectively. No new oral drugs in over a decade

Strategy - Grow Total Addressable Market (TAM) by Treating <u>All</u> Patients

- Multi billion $ opportunity for new patients: realizable opportunity for 10% market penetration at 25% of today's injectable price = $20 B + market, and potential to take share from the 50,000 patients treated with injectables

1. Lilly YE 2019 Earnings Release
2. Amgen YE 2019 Earnings Release
3. http://www.merck.com/finance/annualreport/ar2005/pdf/Merck_2005_Financial_Section.pdf Page 23
4. https://www.novartis.com/sites/www.novartis.com/files/novartis-annual-report-2010-en.pdf page 161

Entera Competitive Advantages: Bone Building, Inexpensive Daily Oral PTH Pill

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

Product Metrics **						Target
Annual WW Sales	$1.4 B	$175 M	$2.6 B	$350 M	$300M	↗
Annual Treatment Price	~$35K +	~$20K +	$3-5K	~$21K	generics	Flexible
% of Market	~1%	<1%	3-4%	<1%	<5%	Growth
Cost of Goods Sold	High	High	Moderate	High	Low	Low

Costs & convenience grow the market substantially – Entera has a competitive advantage

** *Based on publicly available information & management estimates*

EB613: Lead Program in Osteoporosis – De-risked Pathway

Product Overview

- Oral formulation of synthetic PTH (1-34) for treatment of osteoporosis
- Absorption profile is similar to Forteo® by Eli Lilly
- Strong IP including issued composition patents in major markets and additional provisional patent applications filed in US with claims specific to the treatment of osteoporosis

Clinical and Regulatory Overview

- Received IND "May Proceed" from FDA in December 2020
- 2018 & 2019 FDA guidance: 505(b)(2) pathway, and biomarker / BMD endpoints
- Phase 2 dose ranging study in Osteoporosis completed
  - **Study meets primary and key secondary endpoints**
- Phase 3 pivotal 12-month head-to-head study vs. Forteo® to support a 505(b)(2) submission
  - **Clinical trial design:** non-inferiority (+/- 25% margin)
  - **Primary endpoints**: lumbar spine bone density
  - **Safety:** hypercalcemia, hypotension, GI disturbances

EB613 Positioned to be the first oral bone building agent for the treatment of osteoporosis

- Phase 2 study met primary and key secondary endpoints
- Primary efficacy endpoint: a statistically significant increase in P1NP (a bone formation marker) at 3 months was achieved
- A significant dose response was observed for 0.5, 1.0, 1.5 and 2.5 mg PTH doses on P1NP, Otseocalcin and bone mineral density (BMD)
- Subjects receiving the 2.5 mg dose of EB613 showed significant dose-related increases in BMD at the lumbar spine, total hip, and femoral neck at 6 months
- Subjects receiving the 2.5 mg dose of EB613 for 6 months had a significant placebo adjusted increase of 3.78% in lumbar spine BMD ($p<0.008$) - the most important BMD endpoint
  - This is the primary endpoint for the 505(b)(2) pathway as was described by the FDA in Entera's pre-IND meeting
  - Increase in lumbar spine BMD expected to continue with duration of treatment
  - Similar to Forteo, EB613 expected to significantly reduce bone fractures relative to placebo by 50% or more
- EB613 exhibited an excellent safety profile, with no drug related serious adverse events
- An End of Phase 2 Meeting with the FDA to review Phase 3 protocol per 505(b)(2) pathway is expected in H2/2021

Multiple Phase 2 & Phase 3 Milestones for EB613 in Osteoporosis

Milestone		Time
Phase 2	Completed Study Enrollment	Nov 2020
Regulatory	US IND "May Proceed" granted by FDA	Dec 2020
Phase 2	Efficacy Results: Full 3-Month Biomarker Data	Mar 2021
Phase 2	Efficacy Results: Full 6-month Bone Mineral Density Data	Jun 2021
Phase 3	End-of-Phase 2 FDA Discussion & Phase 3 Plan	H2:2021
Phase 3	Commence Patient Enrollment	2022

High Disease Burden in HypoPT

72%

of patients experience 10+ symptoms daily[1]

Heavy Burden of Illness

Symptoms include weakness, muscle cramps, headache, brain fog[1,2,3]

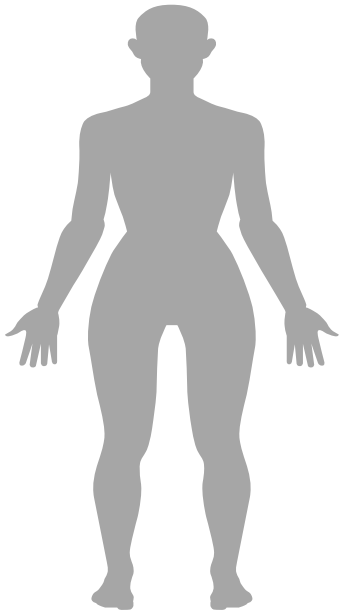
78%

of working patients miss work regularly due to symptoms and many are unemployed[1]

High Economic Impact

Hospitalization and ER visits for seizures and cardiac abnormalities[1]

Condition and Ca + Vitamin D Treatment Lead to Long-Term Consequences



Cardiovascular

Heart failure, blood vessel calcification[3]

Neurologic

Cognitive impairment, basal ganglia calcification[1,2]

Renal

Kidney stones, renal failure[1,3]

Skeletal

Reduced bone turnover[1,2]

~60k insured HypoPT patients in the US

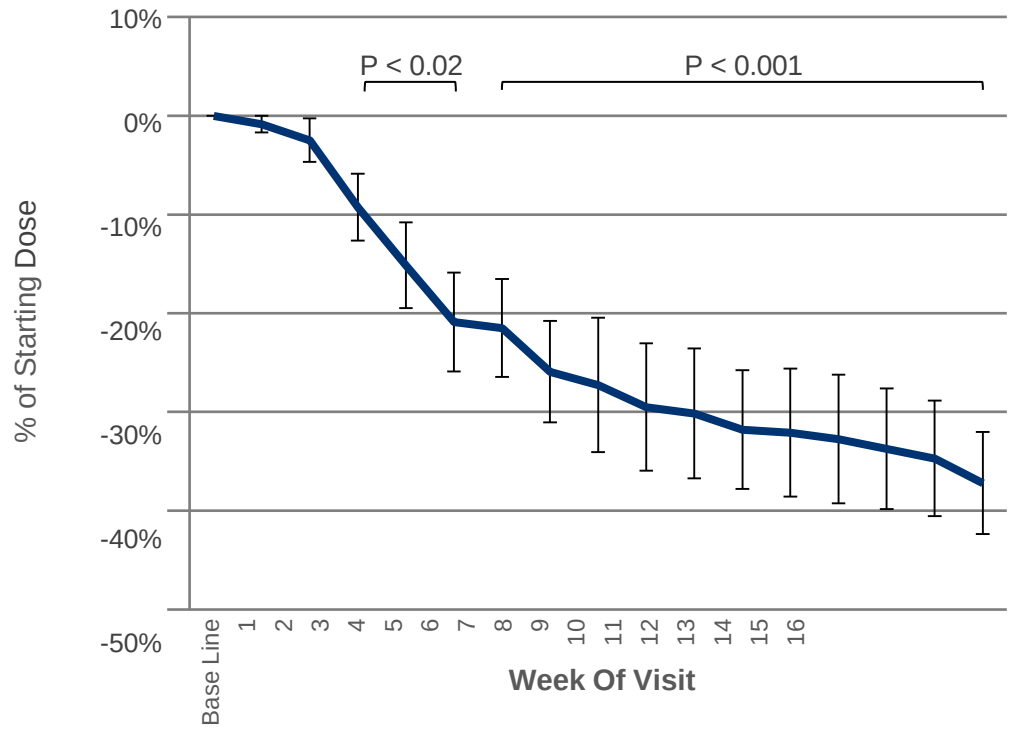
Natpara® reserved for most severe patients

1. Hadker N, Egan J, Sanders J, et al. *Endocr Pract.* 2014.
2. Bilezikian JP, Khan A, Potts JT, et al. *J Bone Miner Res.* 2011.
3. Shoback D. Hypoparathyroidism. *N Engl J Med.* 2008.

EB612: Phase 2a Study: Published in JBMR March 2021

Multicenter, Open-label Clinical Trial in HypoPT Patients [1]

Oral Calcium Intake
ITT Analysis (N=17)



Study Met All Primary Endpoints

- 42% reduction (p=0.001) from baseline in median calcium supplement use
- Maintenance of median ACa levels above the lower target level for HypoPT 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
- Median decrease of 21% (p=0.07) in 24-hour urine calcium excretion between the first and last treatment days
- Improvement in quality of life (p=0.03) from baseline to the end of the treatment period

[1] H. Galitzer, et al. "Safety and Efficacy of Oral Human Parathyroid Hormone (1-34) in Hypoparathyroidism: An Open-Label Study," JBMR, March 2021

Validating our Platform: Internal R&D / External Collaborations

Target collaborations and further R&D efforts where we create sustainable innovation around validated biology

Business Development & Collaboration Opportunities

1. **Pharmaceutical companies need a new oral solution. We can help collaborators stave off biosimilars and patent expirations, OR save development projects that would otherwise be shelved:** Technology tested successfully in 8 molecules of different characteristics and sizes
2. **Lead PTH Programs (EB 613 and 612):** Engaging commercial partners today following Phase 2 data read-outs
3. **Select Regional deals in Asia:** China market is large and growing with substantial interest in novel technologies; substantial interest in endocrine diseases in Japan
4. **New Opportunities in GLP-2 and human growth hormone:** New findings show oral absorption and bioavailability in preclinical studies

Initial Validation: Amgen Dec 2018 Collaboration: *$270 m total deal value, active preclinical work underway*

Intellectual Property & Know-How

Entera has a broad family of patents filed worldwide covering both actives and key excipients of our formulations, expiry dates starting in 2028 to 2035

- The underlying technology patents for oral delivery of large molecules/ proteins gives basic protection to all formulations utilizing this technology
- Patents related to specific formulations for the treatment of specific diseases adds a second level and allows for patent life extension
- Patents related to key improvements and understanding of the principles for correct use of technology represent a third level of protection and may be the most significant barrier to entry
- Entera controls certain critical raw materials and excipients, along with methods and validation packages for regulatory submissions

Leading Oral Delivery Technology Platform:

Two oral PTH programs: one headed into Phase 3 (EB 613 for osteoporosis) and one at Phase 2 (EB 612 for HypoPT)

Announcing new programs in 2021

Milestones:

*EB 613 – **Phase 2 Study Met Primary and Key Secondary Endpoints***

EB 613 – Present Phase 2 results at Medical Conferences in H2:21

EB 613 – FDA end-of-Phase 2 meeting; Phase 3 design in H2:21

EB 612 – Formulation for Phase 2b/Phase 3 in 2021

EB 613 – Phase 3 commencement of patient enrollment expected in 2022

Potential Business Development Collaborations:

Lead program commercial rights and new proprietary compounds, similar to Amgen

Strong Balance Sheet: >$28 M of Cash on August 8th 2021; Cash runway through end of Q4 2022

~28 M shares O/S (primary); ~31 M shares (FD)

Experienced management team & board