Entera Bio Reports Positive Results from a Phase 2 PK/PD Study of Oral PTH (1-34) in Patients with Hypoparathyroidism

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- Results of a Phase 2 PK/PD study of Oral PTH (1-34) in patients with hypoparathyroidism were presented at the American Society for Bone and Mineral Research Annual Meeting
- Data suggest favorable pharmacologic and pharmacokinetic profiles of Entera's Oral PTH formulation with a flexible oral dosing regimen vs. an injectable form of PTH
- Data will inform the Phase 2b/Phase 3 clinical development strategy

JERUSALEM and BOSTON, Sept. 23, 2019 (GLOBE NEWSWIRE) -- Entera Bio Ltd. (NASDAQ: ENTX) today announced the presentation of positive results from its pharmacokinetic (PK) and pharmacodynamic (PD) study in patients with hypoparathyroidism treated with its oral parathyroid hormone (PTH) drug [Oral hPTH(1-34)]. The results were presented at the American Society for Bone and Mineral Research (ASBMR) Annual Meeting in Orlando, Florida on September 22, 2019.

"Entera's previous Phase 2 study in hypoparathyroid patients presented in 2016 showed that four times daily (QID) dosing of oral hPTH (1-34) had a positive effect on serum calcium, a reduction in serum phosphate and a reduction in urinary calcium. The goal of this new PK/PD study was to compare twice-daily (BID), three times daily (TID) and QID dosing regimens and dose strengths of Entera's Oral hPTH (1-34) over a 24-hour period. The results showed that the largest changes in PD endpoints were found with QID dosing, with moderate changes in PD endpoints generally found with BID and TID dosing. In addition, the QID dosing decreased urine calcium over 24-hours, which indicates that it may be able to reduce urinary calcium in hypoparathyroid patients with hypercalciuria during long-term treatment," stated Professor Sofia Ish-Shalom, a principal investigator at the Endocrine Research Center at Lin Medical Center in Haifa, Israel. "As investigators, we were pleased to see that Oral hPTH (1-34) had a positive impact on PD parameters, an increase in serum calcium, a decrease in serum phosphate and an increase in active vitamin D (1,25-dihycroxyvitamin D) synthesis. Importantly, these data again show the ability of Entera's oral formulation to deliver PTH to the bloodstream at concentrations that produced the anticipated PD effect. Furthermore, this well controlled study included the highest approved dose of hPTH (1-84) (Natpar®) 100 micrograms as an active control."

"The data from this study suggest that our Oral PTH delivered at different frequencies, and with different doses, can be used effectively to customize the therapy of individual patients. For example, some patients with elevated urinary calcium might be well served with more frequent dosing three or four times daily, while patients who have milder disease might be adequately served by less frequent twice-a-day dosing. We as clinicians find the severity of disease is a continuum that is best treated by custom titration calcium and each drug to each patient's needs," stated Dr. Arthur Santora, Chief Medical Officer of Entera. "Both PK and PD data from this study will be very valuable in helping optimize the formulation of Oral hPTH (1-34) for hypoparathyroidism, as well as designing long-term studies of a diverse hypoparathyroid population. Importantly, for our ongoing dose ranging study in osteoporosis that employs a single daily dose of oral hPTH (1-34) each morning, the PK profile of the morning dose of oral hPTH (1-34) from this PK/PD study further supports our belief that the blood levels after a single daily morning dose of oral hPTH (1-34) may be sufficient to increase bone formation markers and BMD."

PK/PD Study Design

The Phase 2 PK/PD Study was open-label, and employed a 2-period partial crossover design to evaluate the PK and PD profiles of two doses, 0.75 mg and 2.25 mg, and three regimens (BID, TID and QID) of Oral hPTH (1-34) and included subcutaneous Natpar® [hPTH (1-84)] 100 µg once daily. The study was conducted in sixteen patients with hypoparathyroidism at the Hadassah Clinical Research Center in Jerusalem, Israel. Twelve patients were allocated to receive two treatments each and four patients were allocated to receive four treatments each. All patients continued to receive their usual therapy (calcium supplements plus alfacalcidol or calcitriol).

Preliminary results from Part 1 of this study, were reported by Entera Bio in a press release in November 2018. The full study data analyses presented at the ASBMR meeting demonstrated a positive impact of Oral PTH on three metabolic parameters - serum calcium, phosphate, and 1,25-dihydroxyvitamin D ("active" vitamin D) - in patients with hypoparathyroidism treated with oral hPTH (1-34) 2.25 mg QID. There was also a decrease in 24-hour urine calcium.

The full data set is being prepared for publication in a leading medical journal, and the poster presentation is available on the "Events" section of Entera Bio website.

The conclusions of the poster presentation indicate that:

- Oral hPTH(1-34) 2.25 mg QID for one day is associated with an increase in serum albumin-corrected calcium and $1,25(OH)_2D$ (1,25-dihydroxyvitamin D), a decrease in serum phosphate, and a decrease in urinary calcium in patients with hypoparathyroidism. The patients also received calcium supplements and either alfacalcidol or calcitriol.

- Oral PTH produced similar biological effects to Natpara® 100 µg QD, the highest dose of hPTH (1-84) currently indicated for use in patients with hypoparathyroidism, on serum calcium, phosphate and Vit D. Additionally, Oral hPTH (1-34) effected a decrease in urinary calcium. These changes in serum PD parameters were sustained over the 24-hour period of observation from time zero.

- BID, TID and QID 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 for those patients suffering from less severe hypoparathyroidism.

- Treatment with Oral hPTH (1-34) dosed at multiple times during the day has the potential to reduce calciuria generally associated with maintenance of serum calcium within the normal range using calcium supplements and calcitriol analogs alone.

- There were no treatment-emergent adverse events of hypercalcemia, as well as no treatment-emergent Serious Adverse Events reported in the study.

About Hypoparathyroidism
Hypoparathyroidism is a rare condition in which the body produces insufficient amounts of PTH. Individuals with a deficiency of PTH typically exhibit abnormally low levels of calcium in the blood, or hypocalcemia, and high levels of phosphate in the blood, or hyperphosphatemia. Hypoparathyroidism is estimated to affect approximately 77,000 individuals in the United States. Historically, the treatments for hypoparathyroidism have been calcium supplements and active vitamin D (calcitriol or alfacalcidol). Phosphate binders and thiazide diuretics that reduce urine calcium are occasionally added. It is often difficult to titrate the dose of active vitamin D without producing increased urine calcium or hypercalcemia with tissue calcification during chronic use, which can result in significant costs to the healthcare system. Natpara®, a once-daily injectable form of PTH, has been approved by the FDA and EMA for the treatment of hypocalcemia in patients with hypoparathyroidism.

*Natpara® is the brand name used in United States for Natpar® which is sold by Takeda in Europe. Natpar® was used in this Phase 2 clinical trial.

About Entera Bio Ltd.
Entera Bio is a clinical-stage biopharmaceutical company focused on the development and commercialization of orally delivered large molecule therapeutics for use in orphan indications and other areas with significant unmet medical needs. The Company is initially applying its technology to develop an oral formulation of a human parathyroid hormone analog, Oral PTH (1-34), for treatment of hypoparathyroidism and osteoporosis.

Entera has developed a proprietary platform technology that enables oral delivery of biologicals and large molecule drugs, which are typically delivered via injections and or other non-oral pathways. However, oral drug delivery is the easiest method for self-administering medications, offers patients greater dosing flexibility, and has the highest patient acceptance and compliance rates as compared to all other routes of drug administration. The Company employs this technology for its own pipeline products and may enter into licensing agreements with biopharma companies for application of the technology to their proprietary compounds, such as the Amgen strategic research collaboration. For more information on Entera Bio, visit www.enterabio.com.

Forward Looking Statements
This press release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Words such as "may," "should," "could," "would," "predicts," "potential," "continue," "expects," "anticipates," "future," "intends," "plans," "believes," "estimates," and similar expressions, as well as statements in future tense, often signify forward-looking statements. 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. Forward-looking statements are based on information that the Company has when those statements are made or management's good faith belief as of that time with respect to future events, and are subject to risks and uncertainties that could cause actual performance or results to differ materially from those expressed in or suggested by the forward-looking statements. Those risks and uncertainties, include, but are not limited to, the timing and conduct of our clinical trials, the clinical utility of our product candidates, the timing and likelihood of regulatory filings and approvals, our intellectual property position, and our financial position. For a discussion of these and other risks that could cause such differences and that may affect the realization of forward-looking statements, please refer to the "Special Note Regarding Forward-Looking Statements" and "Risk Factors" in the Company's Annual Report on Form 20-F and other filings with the Securities and Exchange Commission (SEC). Investors and security holders are urged to read these documents free of charge on the SEC's web site at http://www.sec.gov. The Company assumes no obligation to publicly update or revise its forward-looking statements as a result of new information, future events or otherwise.

Entera Bio Ltd. **INTERNATIONAL INVESTOR RELATIONS**

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