Entera Bio Presents Positive Phase 2 6-Month Bone Mineral Density Data for Oral PTH Formulation at Late Breaker ASBMR Conference Session

October 6, 2021 12:30 PM EDT

Increases in lumbar spine, femoral neck and total hip BMD demonstrated with EB613

Linear Dose Responses Seen in Biomarker and Bone Mineral Density Data

Pivotal Phase 3 registration study expected to commence 2022

BOSTON and JERUSALEM, Oct. 06, 2021 (GLOBE NEWSWIRE) -- Entera Bio Ltd. (NASDAQ: ENTX), a leader in the development of orally delivered large molecule therapeutics, presented the 6-month bone mineral density (BMD) data from its completed Phase 2 clinical trial of EB613, an oral formulation of human parathyroid hormone (1-34), or PTH, for the treatment of osteoporosis. The Late Breaking Presentation "A Six-month Phase 2 Study of Oral PTH in Postmenopausal Women with Low Bone Mass – 6 Month Bone Mineral Density (BMD) Results" was selected for a prestigious oral presentation, given by Entera's Chief Medical Officer, Dr. Arthur Santora. The oral presentation was given at 12:15 PM PDT at the American Society for Bone and Mineral Research (ASBMR) Annual Meeting in San Diego on Monday, October 4, 2021. Many scientific leaders in the field of Osteoporosis expressed great excitement with the data and the possibility of an oral osteoanabolic (bone building) agent which elderly osteoporosis patients would be willing to take.

This Phase 2 Dose Ranging study in Osteoporosis showed clinically significant changes in increases in BMD at the spine, femoral neck, and total hip. These BMD changes were associated with an increase in P1NP and a decrease in the serum CTX biomarker. A difference between the increase in P1NP, a marker of bone formation and the change in CTX, a marker of bone resorption, usually indicates an increase in bone mass, and is sometimes referred to as an "anabolic window."

Key secondary endpoints for the trial included changes in lumbar spine, femoral neck and total hip BMD, the bone markers P1NP, osteocalcin and serum CTX after 6 months of treatment.

The most important secondary objective in the study was the demonstration of a statistically significant increase in BMD of the lumbar spine. Patients receiving 2.5 mg oral PTH for 6 months had a placebo-adjusted increase of 3.78% in lumbar spine (LS) BMD ($p<0.002$). Additionally, there was a highly statistically significant dose dependent increase in LS BMD across all dose groups ($p<0.0001$). In previously published studies with subcutaneous injectable PTH(1-34) (Forteo®) no significant increases in BMD of the total hip and or the femoral neck were generally observed at 6 months. In contrast, EB613 showed dose-dependent increases in BMD at the total hip and femoral neck at 6 months, with the greatest increases in BMD observed in the 2.5 mg group. The increase in BMD at these sites has great clinical relevance as a high percent of osteoporotic fractures occur at the hip.

"We are really excited by these full 6-month BMD data which show that our oral PTH 1-34 (EB613) for the treatment of osteoporosis produced results comparable with results observed in previously published studies utilizing injectable PTH 1-34 (Forteo®)," stated Entera CEO Dr. Spiros Jamas. "The data provides an excellent foundation for our Phase 3 registration trial, which we expect to commence in 2022." He noted that there is an enormous clinical need for an oral agent to treat osteoporosis which can build bone and thereby reverse some of the decrease in bone strength caused by Osteoporosis. EB613 addresses this need.

Dr. Santora noted, "In this study, EB613 demonstrated reliable, consistent improvements in spine and hip BMD, overcoming a major challenge of earlier efforts to develop oral PTH agents. Additionally, EB613 performed comparably to injectable PTH 1-34 for increases in lumbar spine BMD, and also showed significant increases of BMD at the femoral neck and total hip. Change in BMD is the efficacy endpoint required for a 505(b)(2) approval pathway. Interestingly, a decrease in CTX, a marker of bone resorption, was robust and continued through six months. This contrasts with the large CTX increase typically observed with injectable formulations of PTH 1-34 currently available and may reflect a favorably lower bone remodeling rate with EB613."

The safety profile of EB613 was consistent with the known profile of subcutaneous PTH. The most common drug-related AEs were headache, nausea, dizziness and presyncope; all drug-related adverse events were either mild or moderate, and there were no serious drug-related AE. There were no treatment-emergent hypercalcemia AEs.

Osteoporosis, characterized by low bone mass and deterioration of bone tissue, leads to decreased bone strength and increased risk of fracture. EB613, an oral PTH, may address a major unmet clinical need for formulations that may facilitate treatment in high-risk patients who may not be willing to use daily or monthly injectable osteoanabolic therapeutics.

Phase 2 Six-Month Study Design and Results

Entera's Phase 2, 6-month, dose-ranging, placebo-controlled study evaluated EB613 in 161 postmenopausal women with low BMD. Subjects in the 2.5 mg group were either treated with 2.5 mg from Day 1 or titrated to 2.5 mg over 2 months. The primary endpoint of change in P1NP at 3 months was met and previously announced by Entera. The key secondary efficacy objective was the change in lumbar spine BMD vs. placebo at 6 months. Changes in biomarkers of bone turnover and change in proximal femoral BMD were evaluated through 6 months.

Six-month BMD and biomarker data are summarized below:

- Significant and dose-dependent increases in BMD of the lower spine, total hip, and femoral neck at 6 months (all $p<0.01$), with the greatest increases in the 2.5 mg EB613 treated group
- Subjects receiving 2.5 mg EB613 for 6 months had a placebo-adjusted increase of 3.78% in lower spine BMD ($p<0.008$); this group combined with the titrated 2.5 mg group showed lower

spine BMD increase of 2.73% (p<0.002)

- Pooled 2.5 mg EB613 group had significant placebo-adjusted 2.76% increase in femoral neck (p<0.002) and a 1.84% increase in total hip BMD (p<0.02) at 6 months. Significant decrease in serum CTX (of 21% from baseline at 6 months (P <0.01) while P1NP was unchanged
- The safety profile of EB613 was consistent with and similar to the known profile of injectable PTH (Forteo®)

About Entera Bio

Entera is a leader in the development of orally delivered large molecule therapeutics for use in areas with significant unmet medical need where adoption of injectable therapies is limited due to cost, convenience and compliance challenges for patients. The Company's proprietary, oral drug delivery technology is designed to address the technical challenges of poor absorption, high variability, and the inability to deliver large molecules to the targeted location in the body through the use of a synthetic absorption enhancer to facilitate the absorption of large molecules, and protease inhibitors to prevent enzymatic degradation and support delivery to targeted tissues. The Company's most advanced product candidates, EB613 for the treatment of osteoporosis and EB612 for the treatment of hypoparathyroidism are in clinical development. The Company recently completed the Phase 2 study for EB613. Entera also licenses its technology to biopharmaceutical companies for use with their proprietary compounds and, to date, has established a collaboration with Amgen Inc. For more information on Entera Bio, visit www.enterabio.com.

Forward Looking Statements

Various statements in this release are "forward-looking statements" under the securities laws. 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 our interpretation of the complete 3-month biomarker data from the recently completed Phase 2 clinical trial of EB613, the timing of data readouts from the recently completed Phase 2 clinical trial of EB613, the full results of the Phase 2 clinical trial of EB613, and our analysis of those full results, the FDA's interpretation and review of our results from and analysis of our Phase 2 trial of EB613, 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 impact of COVID-19 on Entera's business operations; the potential disruption and delay of manufacturing supply chains, loss of available workforce resources, either by Entera or its collaboration and laboratory partners, due to travel restrictions, lay-offs or forced closures or repurposing of hospital facilities; 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, if the FDA or other authorities are closed for prolonged periods, choose to allocate resources to review of COVID-19 related drugs or believe that the amount of Phase 2 clinical data collected are insufficient to initiate a Phase 3 trial, or a meaningful deterioration of the current political, legal and regulatory situation in Israel or the United States; the availability, quality and timing of the data from the Phase 2 clinical trial of EB613 in osteoporosis patients; the ability to find a dose that demonstrates the comparability of EB613 to FORTEO in the recently completed Phase 2 clinical trial of EB613; the size and growth of the potential market for EB613 and Entera's other product candidates including any possible expansion of the market if an orally delivered option is available in addition to an injectable formulation; the scope, progress and costs of developing Entera's product candidates including EB612 and GLP-2; 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 expectations regarding its expenses, revenue, cash resources, liquidity and financial condition; Entera's ability to raise additional capital; Entera's interpretation of FDA feedback and guidance and how such guidance may impact its clinical development plans; 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 "Special Note Regarding Forward-Looking Statements," "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" sections of Entera's annual and current filings which are on file with the SEC and available free of charge on the SEC's website at http://www.sec.gov. Additional factors may be set forth in those sections of Entera's Annual Report on Form 20-F for the year ended December 31, 2020, filed with the SEC in the first quarter of 2021. In addition to the risks described above and in Entera's annual report on Form 20-F and current reports on Form 6-K and other filings with the SEC, other unknown or unpredictable factors also could affect Entera's results. 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 in such forward-looking statements and estimates will be achieved.

All written and verbal forward-looking statements attributable to Entera or any person acting on its behalf are expressly qualified in their entirety by the cautionary statements contained or referred to herein. Entera cautions investors not to rely too heavily on the forward-looking statements Entera makes or that are made on its behalf. The information in this release is provided only as of the date of this release, and Entera undertakes no obligation, and specifically declines any obligation, to update or revise publicly any forward-looking statements, whether as a result of new information, future events or otherwise.

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