Entera Bio Announces FDA Agreement for a Single Phase 3 Clinical Trial to Support an NDA for EB613 for the Treatment of Osteoporosis

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- Total Hip BMD Established as Primary Endpoint -

JERUSALEM, Oct. 06, 2022 (GLOBE NEWSWIRE) -- Entera Bio Ltd. (NASDAQ: ENTX), ("Entera" or the "Company") a leader in the development of orally delivered peptides and therapeutic proteins, announced today the successful conclusion of its Type C meeting and agreement from the U.S. Food and Drug Administration (FDA) that a single Phase 3 placebo-controlled study could support a New Drug Application (NDA) submission of EB613 (oral hPTH (1-34), teriparatide tablets) under the 505(b)(2) regulatory pathway. The FDA also agreed that Total Hip Bone Mineral Density (BMD) could serve as the primary endpoint for the registrational study of EB613 in post-menopausal osteoporosis patients.

The single pivotal Phase 3 clinical trial includes a 24-month placebo-controlled duration with change in Total Hip BMD assessed as the primary endpoint. The 2:1 randomization (EB613 vs. placebo) and planned 400 patients exposed to EB613 are expected to be sufficient to support both the safety and efficacy assessments for the NDA. Furthermore, the FDA agreed with Entera's proposed enrollment of post-menopausal women with osteoporosis based on a BMD T-score of ≤-2.5 to -3.0 and no major fracture history. This patient population is consistent with that studied during Entera's Phase 2 6-month dose ranging study of EB613, which met all primary and key secondary endpoints of biochemistry and BMD. Finally, Entera intends to submit relative PK data comparing its oral tablet form of teriparatide, EB613 versus the subcutaneous injection of teriparatide, Forteo® to support the 505(b)(2) pathway.

"This is a major milestone for Entera. We greatly appreciate the opportunity to work collaboratively with the FDA, which was essential for reaching concurrence on all critical elements proposed for the registrational path of EB613," said Miranda Toledano, Chief Executive Officer of Entera. "We have agreement with FDA to continue to treat the same patient population that significantly benefited from EB613 treatment during our Phase 2 study. These low BMD patients at high risk of fracture are often reluctant to initiate injectable anabolic (bone forming) therapy and represent a large unmet need; 40% of the 3 million currently treated patients across the United States, according to our market research. As the first daily tablet PTH osteoanabolic treatment, we believe EB613 could significantly impact the osteoporosis treatment paradigm. We look forward to advancing EB613 into Phase 3 and initiating patient enrollment during 2023," said Miranda Toledano, Chief Executive Officer of Entera.

About EB613 (a.k.a. EBP05)

EB613 is the first and most advanced oral, daily tablet formulation of synthetic hPTH (1-34), (teriparatide), consisting of the exact same 34 amino acid sequence as daily subcutaneous teriparatide injection, Forteo® which has been the leading anabolic treatment of osteoporosis since 2002 with peak sales of $1.7 billion in 2018 prior to patent expiration. Entera's Oral PTH formulations have been administered collectively to a total of 225 subjects in two Phase 1 studies and 3 phase 2 studies (including 35 in 2 phase 2 hypoparathyroidism studies). The most recent study was a dose ranging Phase 2 study in postmenopausal women with low bone mass. This study met primary and key secondary endpoints and was presented in a late-breaker oral presentation at the ASBMR 2021 conference. For the primary efficacy endpoint: a statistically significant increase in P1NP (a bone formation marker) at 3 months was achieved. A significant dose response was observed for 0.5, 1.0, 1.5 and 2.5 mg oral PTH doses on P1NP, Osteocalcin and bone mineral density (BMD). Subjects receiving the 2.5 mg dose of EB613 showed significant increases in dose-related BMD at the Lumbar Spine, Total Hip, and Femoral Neck at 6 months. Subjects receiving the 2.5 mg dose of EB613 daily for 6 months had a significant placebo adjusted increase of 3.78% in Lumbar Spine BMD ($p<0.008$) which is similar to the 3.9% increase in Lumbar Spine BMD seen with Forteo® in clinical studies reported in the literature. Increases in Total Hip and Femoral Neck BMD were greater than those previously reported with Forteo® at 6 months. EB613 exhibited an excellent safety profile, with no drug related serious adverse events. The most common adverse events included mild nausea, moderate back pain, moderate headache, and moderate upper abdominal pain.

About Entera Bio

Entera is a leader in the development of orally delivered macromolecules therapeutics including peptides and other therapeutic proteins, 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. 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.

Cautionary Statement Regarding Forward Looking Statements

Various statements in this press release 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 press release 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 press release. The information in this press release is provided only as of the date of this press release, 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.

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