Entera Bio Announces FDA's Acceptance of a Type D Meeting Review to Affirm Design of the Pivotal, Phase 3 Protocol for EB613 PTH Mini Tablets, as the First Oral Osteoanabolic Treatment of Post-Menopausal Osteoporosis

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- **Type D meeting protocol submission builds on concurrence reached with FDA following successful Type C meeting and supports potential Phase 3 initiation in H2 2023**

JERUSALEM, Feb. 15, 2023 (GLOBE NEWSWIRE) -- Entera Bio Ltd. (NASDAQ: ENTX), ("Entera" or the "Company") a leader in the development of orally delivered peptides and therapeutic proteins, today announced that a Type D meeting protocol review has been accepted by the U.S. Food and Drug Administration (FDA) to provide responses by March 30th, 2023. The pivotal, Phase 3 study protocol is entitled "A 24-Month Phase 3, Randomized, Double-Blind, Global Multicenter Study Comparing the Effects of Oral hPTH(1-34) (EBP05[EB613]) Daily Tablets vs. Placebo on Bone Mineral Density (BMD) in Postmenopausal Women with Osteoporosis." EB613 is the first oral, once daily mini tablet presentation of hPTH (1-34), (teriparatide). EB613 has a well-established mechanism of action, PK and safety profile and met primary (PD/biomarker) and secondary endpoints (BMD) in a placebo controlled, dose ranging Phase 2 study in 161 postmenopausal women with low bone mass and osteoporosis.

As part of its briefing documents for the Type D process, Entera has submitted its Phase 3 protocol which reflects (1) the agreement reached during the Company's September 2022 Type C Meeting discussion with FDA that a single 24 month Phase 3 *placebo-controlled* study could support a New Drug Application (NDA) submission under the 505(b)(2) regulatory pathway and (2) that *Total Hip Bone Mineral Density (BMD)* could serve as the primary endpoint for the registrational study. The objective of Type D meeting review is to confirm that the protocol fully meets FDA's expectations, including the analysis of the primary endpoint and the population PK evaluations, ahead of potential study initiation in H2 2023.

The FDA previously agreed on major design elements of the protocol including the primary endpoint, enrollment criteria, titration and 2:1 randomization plan, and that 400 or more patients on EB613 is consistent with ICH E1A to support safety for the NDA. The current protocol reflects a 667/333 patient randomization, a 24 month total study duration and a futility interim analysis to occur when the last of the 300 first randomized subjects have completed 12 months in the study. Furthermore, Entera has provided power calculations for its primary endpoint, the change in TH BMD vs. placebo and for its key secondary endpoint which is designed to evaluate the change in TH BMD versus published surrogate threshold effects (STEs) that are associated with fracture risk reduction (Eastell 2022[i]).

"We look forward to continuing our incredibly collaborative dialogue with the FDA concerning what we anticipate as the last critical step prior to potentially initiating our Phase 3 pivotal study in H2 2023. Since receiving FDA's End of Phase 2 minutes in January of 2022 which conveyed that the previously anticipated non-inferiority head-to-head design versus Forteo® Phase 3 design may not be favorable to the approvability of our program, the Company has undergone a massive leadership and operational shift to successfully pivot and align with FDA's recommendations and transition to become Phase 3 ready. To our knowledge, Entera stands as the first osteoporosis drug development company ever permitted to conduct a single placebo controlled registrational study with a BMD (NOT fracture) endpoint. This is unprecedented and we believe, speaks to the agency's partnership in this journey to find a viable treatment alternative to treat the millions of osteoporosis patients that, despite the guidelines and availability of highly efficacious anabolic agents, are simply unwilling to take the daily or monthly injections," stated Miranda Toledano, Chief Executive Officer of Entera.

About Entera Bio

Entera is a leader in the development of orally delivered macromolecules, including peptides and other therapeutic proteins. The Company focuses on significant unmet medical needs where a simple, oral mini-tablet peptide replacement therapy holds the potential to transform the standard of care. The Company's most advanced product candidates, EB613 for the treatment of osteoporosis and EB612 for the treatment of hypoparathyroidism, are in clinical development. EB613 is the first oral, once daily mini tablet presentation 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. A placebo controlled, dose ranging Phase 2 study of EB613 mini-tablets (n= 161) met primary (PD/biomarker) and secondary endpoints (BMD). In October 2022, the Company announced concurrence with FDA on a single, placebo controlled, BMD endpoint pivotal study design to support an NDA for EB613 tablets. 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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[i] Eastell R, Vittinghoff E, Lui LY, et al. Validation of the Surrogate Threshold Effect for Change in Bone Mineral Density as a Surrogate Endpoint for Fracture Outcomes: The FNIH-ASBMR SABRE Project. J Bone Miner Res. 2022;37(1):29-35.

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