Entera Bio Receives FDA Agreement on BMD as Primary Endpoint for EB613 Registrational, Phase 3 Study in Post-Menopausal Women with Osteoporosis

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JERUSALEM, July 28, 2025 (GLOBE NEWSWIRE) -- Entera Bio Ltd. (NASDAQ: ENTX), a leader in the development of oral peptides and protein replacement therapies, announced today that in a written response to a Type A meeting request, the U.S. Food and Drug Administration (FDA) agreed with the Company's proposal that the NDA marketing application filing for EB613 would be supported by a single multinational, randomized, double-blind, placebo-controlled, 24 month phase 3 study in women with postmenopausal osteoporosis, where change in total hip BMD is evaluated as the primary endpoint, and incidence of new or worsening vertebral fractures is evaluated as the key secondary endpoint. This marks a shift from precedent placebo-controlled phase 3 studies of new osteoporosis drugs which required incidence of fracture as the primary endpoint.

"This regulatory update is a major milestone for Entera and the entire osteoporosis community," said Miranda Toledano, CEO of Entera. "Our alignment with the FDA reflects the strength of our data and collaborative discussions. Importantly, it allows us to advance our clinical development program without having to wait for FDA's qualification of the Study to Advance Bone Mineral Density as a Regulatory Endpoint (SABRE), which is still expected this year. We thank the FDA and the Review Team at the Division of Endocrinology for their constructive approach. We also thank the SABRE team for paving the path to innovation for osteoporosis treatment," said Toledano.

"Osteoporosis afflicts more women than heart attack, stroke and breast cancer combined. Over 200 million women globally are estimated to have osteoporosis and remain vastly undertreated, despite efficacious injectable anabolic (bone forming) treatments. One in two women over the age of 50 will suffer a fracture due to osteoporosis. No new drug for osteoporosis has been approved by FDA since 2019; and innovation has stalled for close to a decade due to the size, duration, cost and ethical constraints associated with fracture endpoint studies. In a silent disease, patient and clinician access to novel and alternative forms of validated mechanisms of action is important. We are developing EB613 as the first oral, once-daily anabolic tablet treatment to potentially serve this unmet medical need. EB613 is intended to increase skeletal mass, improve bone microarchitecture and reduce the risk of fracture," said Miranda Toledano, CEO of Entera.

About EB613

Substantial evidence supports the efficacy of anabolic therapies over bisphosphonates for lowering fracture risk in osteoporosis patients at high risk. However, all available anabolic therapies are administered by subcutaneous (SC) injection and used in a minority of eligible patients. EB613 (oral PTH (1-34), teriparatide), is being developed as the first oral, once-daily anabolic tablet treatment for osteoporosis. EB613 completed a phase 2, 6-month, 161-patient, placebo-controlled study that met all biomarker and BMD endpoints without significant safety concerns in women with postmenopausal osteoporosis or low BMD (JBMR 2024). EB613 produced rapid dose-proportional increases in biochemical markers of bone formation, reductions in markers of bone resorption, and increased lumbar spine, total hip, and femoral neck BMD. The effects of EB613 on trabecular and cortical bone using 3D-DXA showed increases with EB613 compared with placebo in a variety of indices, including integral volumetric BMD and trabecular volumetric BMD, cortical thickness, and cortical surface BMD. Mechanistically, the findings suggest that bone strengthening, and fracture resistance may occur rapidly with EB613. Furthermore, the data are consistent with those of published subcutaneous teriparatide at the 6-month time point. Further abstracts have been submitted to ASBMR and NAMS 2025 conferences.

About Entera Bio

Entera is a clinical stage company focused on developing oral peptide and protein replacement therapies for significant unmet medical needs where an oral tablet form holds the potential to transform the standard of care. The Company leverages on a disruptive and proprietary technology platform (N-Tab™) and its pipeline of first-in-class oral peptide programs targeting PTH(1-34), GLP-1 and GLP-2. The Company's most advanced product candidate, EB613 (oral PTH(1-34), teriparatide), is being developed as the first oral, osteoanabolic (bone building) once-daily tablet treatment for post-menopausal women with low BMD and high-risk osteoporosis. A placebo-controlled, dose-ranging Phase 2 study of EB613 tablets (n= 161) met primary (PD/bone turnover biomarker) and secondary endpoints (BMD). The EB612 program is being developed as the first oral PTH(1-34) tablet peptide replacement therapy for hypoparathyroidism. Entera is also developing the first oral oxyntomodulin, a dual targeted GLP1/glucagon peptide, in tablet form for the treatment of obesity and metabolic syndromes; and first oral GLP-2 peptide as an injection-free alternative for patients suffering from rare malabsorption conditions such as short bowel syndrome in collaboration with OPKO Health. For more information on Entera Bio, visit www.enterabio.com or follow us on LinkedIn, Twitter, Facebook, Instagram.

About SABRE

The Study to Advance BMD as a Regulatory Endpoint (SABRE) initiative, which started as a public private partnership sponsored by the FNIH in 2013, has amassed the strongest evidence to date that treatment-related gains in Bone Mineral Density (BMD) reliably and quantitatively predict fracture-risk

reduction. In November 2023, the SABRE team submitted a full qualification package to FDA's Biomarker Division as part of the Drug Development Tool Biomarker Qualification Pathway to potentially qualify BMD as a surrogate endpoint to fracture; in March 2024, the FDA Biomarker Division indicated to the SABRE project team that a decision would be issued within 10 months. The single most important predictor of osteoporotic fractures in postmenopausal women without a previous fracture is BMD. Treatment guidelines in the U.S. strongly recommend pharmacologic therapy for patients with a BMD T-score of -2.5 or lower in the spine, femoral neck, total hip. SABRE final FQP meta-analysis included data from 22 randomized, placebo-controlled trials (63,000 participants across seven drug classes) and showed that treatment-related gains in total-hip BMD explain 72% of the observed fracture-risk reduction. The R2 for this correlation was 0.73—double the correlation between blood pressure and stroke ($R^2 = 0.37$), which is the well accepted basis for the value of antihypertensive therapy.

Cautionary Statement Regarding Forward Looking Statements

Various statements in this presentation 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 presentation 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 may be contractually obligated to provide; 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 ability to establish and maintain development and commercialization collaborations; Entera's operation as a development stage company with limited operating history; Entera's competitive position with respect to other products on the market or in development for the treatment of osteoporosis, hypoparathyroidism, short bowel syndrome, obesity, metabolic conditions and other disease categories it pursues; 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 Statement 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 Entera'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 presentation. The information in this presentation is provided only as of the date of this presentation, 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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