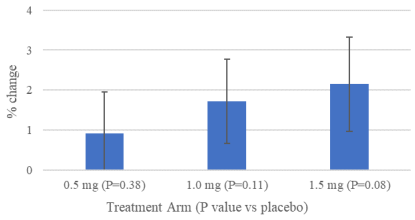
Entera Bio Ltd Announces Interim Data From Phase 2 Clinical Trial of EB613 in Osteoporosis and Second Quarter 2020 Financial Results

August 20, 2020 10:30 AM EDT

– 6-Month Interim Data Indicate EB 613 Has Meaningful and Positive Impact on Lumbar Spine Bone Mineral Density (BMD) in a Dose Dependent Manner –
– Company Expects to Complete Patient Enrollment in Q3:20 and Report Interim Biomarker Data from 2.5 mg Dose in Q1:21 with Final Data Expected in Q2:21 –
– Company to Host Conference Call and Webcast Today at 8:30 a.m. EDT –

BOSTON and JERUSALEM, Aug. 20, 2020 (GLOBE NEWSWIRE) -- Entera Bio Ltd. (NASDAQ: ENTX), a leader in the development of orally delivered large molecule therapeutics, announced financial and operating results for the quarter ended June 30, 2020 as well as 6-month interim biomarker and bone mineral density (BMD) data from the first 50% of the projected enrollment in the ongoing Phase 2 clinical trial of EB613. EB613, Entera's clinical compound, is an orally delivered human parathyroid hormone (1-34), or PTH, program positioned as the first potential oral bone building product to treat osteoporosis patients.

Difference in % change in Lumbar Spine BMD at Month 6: EB613 minus Placebo



The above graph shows the placebo adjusted change in Lumbar Spine BMD at 6 months for the EB613 Treatment Groups

Based on the 6-month data, EB613 generated a mean placebo adjusted increase in lumbar spine BMD of 2.15% (p = 0.08) for the 14 patients in the 1.5 mg treatment arm, as compared to 16 patients in the placebo arm. The placebo-adjusted increase was comprised of a mean BMD increase of 1.44% in the 1.5 mg treatment arm compared to a mean decrease of 0.71% in the placebo arm. An additional analysis of BMD changes in all EB613 treatment groups showed a significant dose-dependent trend in the percentage change in lumbar spine BMD. This dose response supports the use of a higher dose to potentially increase efficacy. As expected and consistent with published data from subcutaneous teriparatide, an analysis of BMD of the total femur and femoral neck did not show a significant effect from treatment with EB613. Increases in and maintenance of BMD are widely accepted by clinicians throughout the world as indicators of an overall improvement of osteoporosis and a change in lumbar spine BMD is typically accepted by the United States Food and Drug Administration as a phase 3 study efficacy endpoint for a novel oral formulation intended to treat osteoporosis using the 505 (b)(2) regulatory pathway. This is due to the fact that PTH (1-34) (teriparatide for injection) has been shown to reduce the risk of fractures.

The 6-month Placebo Adjusted Lumbar Spine BMD results are summarized below (mean, standard error):

https://www.globenewswire.com/NewsRoom/AttachmentNg/43b00428-a38a-41e8-a645-2627ad3fdd9a

"We are highly encouraged by the dose dependent improvement in lumbar spine BMD as seen in the interim data from the first half of the patients in the EB613 Phase 2 dose ranging clinical trial, especially given the small sample size of only 14 patients in the 1.5 mg treatment group. While the data reported today include favorable results from the 1.5 mg treatment arm, we believe that 1.5 mg may not be the maximum effective dose. This belief which is supported by the 3-month biomarker data we reported earlier this year, led us to amend the protocol in July to add a 2.5 mg treatment arm to the trial," stated Roger Garceau, MD, Director and Interim CEO of Entera. "Given the results we saw in the 1.5mg treatment group, we are very much looking forward to seeing the performance of the 2.5 mg treatment arm," continued Dr. Garceau.

6-Month Interim Results from Phase 2 Study of EB613 in Osteoporosis

The Phase 2 clinical trial of EB613 is a dose-ranging, placebo-controlled, study in postmenopausal female subjects with osteoporosis, or low BMD, and is being conducted at four leading medical centers in Israel. Phase 2 dose-ranging studies are utilized to determine the best dose to move into later stage clinical trials. Based on the three-month interim biochemical marker and safety data from the first 80 subjects randomized, the Phase 2 protocol was amended in July 2020 to discontinue the two lower doses (0.5 mg and 1.0 mg) and add a 2.5 mg dose of EB613. The clinical trial is currently enrolling subjects in the 2.5 mg, 1.5 mg and placebo groups, with completion of enrollment for the targeted 160 patients expected by the end of the third quarter. There are currently 131 subjects enrolled in the trial.

Of the first 80 subjects who were enrolled in the trial, 72 completed their 3-month visit and 68 completed their 6-month visit. Bone biomarker data at 6-months including P1NP, Osteocalcin and CTX were consistent with the results seen after three months of treatment at the 1.5 mg dose. There were no significant changes in any of these bone biomarkers after treatment with EB613 for 6 months, versus placebo. The demographics for the EB613

Phase 2 clinical trial such as age, BMI and baseline levels of bone markers were generally consistent with demographics from similar osteoporosis studies in the literature.

	N	Mean	Median
Age	72	61.10	61.00
Weight (Kg)	72	64.65	61.50
BMI	72	25.34	24.36

The placebo adjusted changes at 6-months in lumbar spine BMD for each treatment arm are summarized in the table below:

Difference in Mean % Change in Lumbar Spine BMD from Baseline at Month 6 (EB613 Treatment – Placebo) *

	Mean	Std Error	p-value
EB613 0.5 mg	0.9168	1.0370	0.38
EB613 1.0 mg	1.7218	1.0502	0.11
EB613 1.5 mg	2.1533	1.1820	0.08

**Number of subjects: Placebo (16), 0.5 mg treatment arm (19); 1.0 mg treatment arm (19); 1.5 mg treatment arm (14)*

"These interim data mark the first time Entera has evaluated the BMD effect of EB613, and we are pleased with the results to date. Given the small number of subjects evaluated and our estimate that the 1.5-mg dose may not be maximally effective, we did not expect to see statistically significant results, but were very pleased with the p-value observed in the high dose group. We were also pleased with the significant dose-dependent trend in the change in lumbar spine BMD. As potentially the first oral PTH to treat osteoporosis patients, we note that EB613 has a bone biomarker profile that is different from subcutaneous PTH," stated Arthur Santora, MD, PhD, Chief Medical Officer of Entera. "As a result, these interim lumbar spine BMD data are supportive of the 2.5 mg dose we recently added to the ongoing Phase 2 study. Based on guidance from the FDA, and given positive final results from the current Phase 2 trial, we anticipate one global pivotal Phase 3 505(b)(2) non-inferiority study of EB613 as compared to Forteo®, with a primary endpoint of a change in lumbar spine bone mineral density," continued Dr. Santora.

Second Quarter 2020 and Recent Highlights

- *Highly Encouraging Market Research Results Indicate Oral PTH's Potential to Significantly Expand a Multi-Billion Dollar Global Market:* Two primary market research studies of clinicians who treat osteoporosis patients were conducted by a third-party firm with a goal of gaining a better understanding of the perceived value and potential market penetration of an orally-delivered PTH product in the treatment of osteoporosis. Results included:
  - Approximately 85% of clinicians surveyed stated they were likely to prescribe oral PTH to treat moderate to severe osteoporosis
  - Oral PTH was described by clinicians as a potential game-changer that addresses a substantial unmet need with the possibility of improving patient compliance and comfort
  - More than half of clinicians are likely to increase usage of PTH to treat osteoporosis if an effective orally delivered product is available

- *Continued Development of EB612*: Following the conclusion of a successful Phase 2a study of EB612 in the treatment of hypoparathyroidism, Entera is developing formulations of the drug with different release profiles with the goal of selecting the optimal formulation to be used in a Phase 2b or Phase 3 clinical trial in patients with hypoparathyroidism in 2021.

- *Pipeline Update:* Entera is making progress towards its goal of building out two new targets each year for preclinical development based on its oral drug delivery platform. Several potential candidates are currently being evaluated, and Entera expects to provide an update on target selection by the end of 2020.

- *European Patent for Oral PTH:* The European Trademark Office granted Entera a patent titled "Methods and Compositions for Oral Administration of Proteins." This composition patent covers oral administration of proteins (up to 100kD) and specifically PTH, using Entera's oral delivery technology.

- *Amgen Collaboration Agreement:* Several studies have been completed using Entera's

technology to evaluate different formulations of Amgen's drug. While continuing to work with Amgen, Entera is actively evaluating additional business development opportunities to leverage the Company's technology platform.

"In the coming quarters, we expect to achieve several additional milestones in the clinical development of EB613 for the treatment of osteoporosis including the completion of patient enrollment for the Phase 2 study in the third quarter of 2020, efficacy results for the full three-month biomarker data in the first quarter of 2021, and efficacy and safety results for the full trial in the second quarter of 2021. We anticipate an End-of-Phase 2 meeting with the FDA in the middle of 2021, followed by the potential commencement of a global, pivotal Phase 3 study in 2021 or 2022. Given the highly encouraging results of two recent market surveys with clinicians who treat osteoporosis, we believe the value proposition of EB613 has been confirmed. An effective and safe oral PTH may significantly expand the osteoporosis treatment market, as only an estimated 5% of osteoporosis patients today are opting in for the currently available injectable products," added Dr. Garceau.

Financial Results for the Six Months Ended June 30, 2020

Revenues for the six months ended June 30, 2020 were $94,000 as compared to $74,000 in the first half of 2019, with revenues in both years attributable to R&D services provided to Amgen. The cost of revenues for the six months ended June 30, 2020 and 2019 were $73,000 and $62,000, respectively and were comprised of salaries and related expenses in connection with the R&D services provided to Amgen.

Operating expenses were $6.4 million for the six months ended June 30, 2020, compared to $5.1 million for the first half of 2019. Entera's operating loss was $(6.4) million for the six months ended June 30, 2020, compared to $(5.1) million for the first half of 2019.

Research and development expenses were $3.6 million for the six months ended June 30, 2020, compared to $3.4 million for the six months ended June 30, 2019. The increase was primarily due to an increase in consulting fees related to the preparation of an IND application for EB613 and an increase in clinical trial expenses relating to the Phase 2 clinical trial of EB613 which were partially offset by a reduction in material and production expenses due to significant manufacturing activities to support preclinical and clinical trials during the six months ended June 30, 2019 that were not repeated in 2020.

General and administrative expenses were $2.8 million for the six months ended June 30, 2020, compared to $1.7 million for the six months ended June 30, 2019. The increase was primarily due to increases in compensation related expenses, professional fees and insurance costs that were partially offset by a decline in investor relations and other expenses.

Net comprehensive loss was $(6.1) million for the six months ended June 30, 2020, or $(0.34) per ordinary share, compared to $(4.4) million, or $(0.38) per ordinary share for the six months ended June 30, 2019. The change in net loss is primarily due to the increase in overall operating expenses.

At June 30, 2020, Entera had cash and cash equivalents of $9.8 million, compared to $15.2 million at December 31, 2019.

Entera expects an operating loss of at least $11.4 million for the year ending December 31, 2020, and believes its current cash position will be sufficient to fund its operations into the second quarter of 2021.

Conference Call and Webcast Information

Entera's management will host a conference call on Thursday, August 20, 2020 at 8:30 a.m. EDT. A question-and-answer session will follow Entera's remarks. To participate on the live call, please dial (855) 547-3865 (US) or (409) 217-8787 (international) and provide the conference ID "5243229" five to ten minutes before the start of the call.

To access a live audio webcast of the presentation on the "Investor Relations" page of Entera's website, please click here. A replay of the webcast will be archived on Entera's website for approximately 45 days following the presentation.

About Entera Bio Ltd.

Entera is a leader in the development of orally delivered macromolecule 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 Phase 2 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.

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 interim data from the ongoing Phase 2 clinical 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; a possible suspension of the Phase 2 clinical trial of EB613 for clinical or data-related reasons; the impact of COVID-19 on Entera's business operations including enrollment in the Phase 2 clinical trial for EB613 in patients with osteoporosis and the ability to collect the necessary data from the Phase 2 trial of EB613; 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 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 so far 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 find a dose that demonstrates the comparability of EB613 to FORTEO

in the ongoing 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; 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; 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 Quarterly Report on Form 6-K for the quarter ended June 30, 2020, to be filed with the SEC in the third quarter of 2020. 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.

ENTERA BIO LTD.
CONDENSED CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS
(UNAUDITED)
(US$ in thousands, except share and per share data)

	Six months ended June 30		Three months ended June 30	
	2020	**2019**	**2020**	**2019**
REVENUE	$ 94	$ 74	$ 52	$ 74
COST OF REVENUE	73	62	31	62
RESEARCH AND DEVELOPMENT EXPENSES, NET	3,616	3,448	2,011	1,413
GENERAL AND ADMINISTRATIVE EXPENSES	2,827	1,684	1,537	628
OPERATING LOSS	6,422	5,120	3,527	2,029
FINANCIAL INCOME:				
Income from change in fair value of financial liabilities at fair value	(318)	(794)	(366)	(682)
Other financial expenses, net	6	35	29	19
FINANCIAL INCOME, NET	(314)	(759)	(337)	(663)
NET COMPREHENSIVE LOSS FOR THE PERIOD	$ 6,108	$ 4,361	$ 3,190	$ 1,366

	U.S. dollars		U.S. dollars	
LOSS PER ORDINARY SHARE:				
Basic and diluted	$ 0.34	$ 0.38	$ 0.17	$ 0.12
WEIGHTED AVERAGE NUMBER OF SHARES OUTSTANDING:				
Basic and diluted	18,142,016	11,601,289	18,234,191	11,742,797

ENTERA BIO LTD.
CONDENSED CONSOLIDATED STATEMENTS OF FINANCIAL POSITION
(US$ in thousands)

	June 30, 2020 (Unaudited)	**December 31, 2019** (Audited)
Cash and cash equivalents	$ 9,767	$ 15,185
Accounts receivable and other current assets	677	451
Property and equipment, net	199	202
Other assets, net	819	865
Total assets	$ 11,462	$ 16,703
Accounts payable and other current liabilities	$ 1,727	$ 2,148

Warrant liabilities		2,350		2,444
Total current liabilities		4,077		4,592
Total Non-current liabilities		156		192
Total shareholders' equity		7,229		11,919
Total liabilities and shareholders' equity	$	11,462	$	16,703

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