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Q2 20 Update Septmber 1, 2020

D.N.A (TLV:DNA)

Entera Bio (NASDAQ:ENTX) ,subsidiary of D.N.A, announced, as expected on its interim data from the ongoing Phase 2 clinical trial of EB613 in osteoporosis; price target is unchanged

Sector: Healthcare

Industries: Biotechnology and Medical Devices

Stock Target Price: NIS 2.62

Closing price: 0.50 NIS

52 Week Range: 0.46-1.22

Market cap: NIS 15.0 M

# of shares: 30.3M

Stock performance (3 mos.): -35%

Dr. Tiran Rothman - Lead Analyst

Frost & Sullivan
Research & Consulting Ltd.
A: Abba Even 1, Herzliya Pituach
T: +972 (0) 9 950 2888
E: equity.research@frost.com
W: www.frost.com/equityresearch

Conclusion

Entera Bio: Entera Bio's platform technology enables oral therapies based on molecules that would otherwise undergo gastric degradation and have limited or no bioavailability. By transforming injectable drugs to oral drugs, the treatment becomes more 'user friendly' which may lead to higher patient and physician acceptance. Furthermore, as an oral drug, various treatment regimens become possible that enable personalized care.

On its second quarter report the company announced the following:

- 6-Month Interim data indicate that EB 613 has meaningful and positive impact on lumbar spine bone mineral density (BMD) in a dose dependent manner, hence the company decided to add a 2.5 mg treatment arm to the trial
- Company expects to complete patient enrollment in Q3 2020 and report interim biomarker data from 2.5 mg dose in Q1 2021 with final data expected in Q2 2021

In July, the company published results from two primary market research studies of clinicians who treat osteoporosis patients in order to gain a better understanding of the perceived value and potential market penetration. The responses to the prospect of prescribing an oral PTH were overwhelmingly positive, driven by expected improvements in patient compliance; ease of administration, and without injection site discomfort. Physicians also considered reduced costs to patients and payers to be important features.

In our view and based on our July Initiation Report of Entera, Entera bio seeks potential partnerships with 1) leading injectable franchises that are now facing a growing threat from biosimilars 2) biologics and proteins that may prove to be complementary to Entera's oral delivery platform, as demonstrated by the strategic research collaboration Entera signed with Amgen in 2018 3) opportunities to license EB613 or EB612 globally, or in certain regions.

On August 10, Entera also announced that its Board of Directors has appointed Roger Garceau as Interim Chief Executive Officer.

Financially, we assume Entera will have to raise additional capital by early 2021. **We maintain our target price.**

Executive Summary

Entera

Entera has witnessed an emerging interest within various healthcare market segments for administration of injectable drug solutions through novel oral means that are considerably more consumer friendly, and consequently more profitable. The medical world has experienced prolific growth in the number of experiments taking place to discover oral solutions to drugs that had only been effective when administered intravenously or intramuscularly. Oral administration has many inherent advantages over injections including self-administration, and suitability for those sensitive to injections. Consequently, the treatment tends to be more receptive among patients. The market potential for orally ingestible alternatives is lucrative. A table of recent activity among leading market players is detailed in the table below.

Investor (Country)	*Investee (Country)*	*Amount*	*Product*	*Date*
Johnson & Johnson (US)	Protagonist Therapeutics (US)	$50M	Inflammatory Bowel Disease injectables in pill form	June 2017
Hefei (Sinopharm) (CN)	Oramed (IL)	$50M	Orally ingestible Insulin	Nov. 2015
Google Ventures, Novartis, AstraZeneca and many others (US)	Rani Therapeutics (US)	$70M	General platform, including; TNF-alpha inhibitors, interleukin antibodies, insulin and GLP-1	Feb. 2016
25 major financial institutions (US)	Chiasma (US)	$26.4M (as of August 30, 2017)	Developing and commercializing oral therapies - Phase III clinical trial for the treatment of acromegaly	Via Nasdaq in 2017
Sources: (1) (Business Insider Australia, 2017); (2) (Reuters, 2015); (3) (BioSpace, 2016); (4) (NASDAQ, 2017).				

The company's main focus is applying its technology to develop an oral formulation of human parathyroid hormone (1-34), or PTH. PTH has been approved in the U.S. and EU for more than 15 years in injectable form, for the treatment of osteoporosis and currently generated revenue in excess of $1.6 billion/ year.

PTH is critical in maintaining mineral balance in the body (magnesium, phosphorus and calcium), while its main function is to increase calcium levels when they are too low[1]. Their lead oral PTH candidates are EB613 for the treatment of osteoporosis and EB612 for the treatment of hypoparathyroidism (Figure 1). The company has strategically chosen to develop tablets comprising biological substances that today are given as injections, with a proven therapeutic and side effect profile, and are thus well positioned to 'go to market'.

- ***EB613 for Osteoporosis***: The company aims to use the 505(b)(2) regulatory pathway, which is less expensive and a much faster route to approval.
- ***EB612 for Hypoparathyroidism***: Entera Bio successfully completed a phase 2a clinical trial in Hypoparathyroidism. A pharmacokinetic/pharmacodynamic (PK/PD) cross over study of EB612 versus Natpara (*orphan drug designation*) will be reported later this year with the next planned step for clinical development being a phase 2b/3 pivotal study.

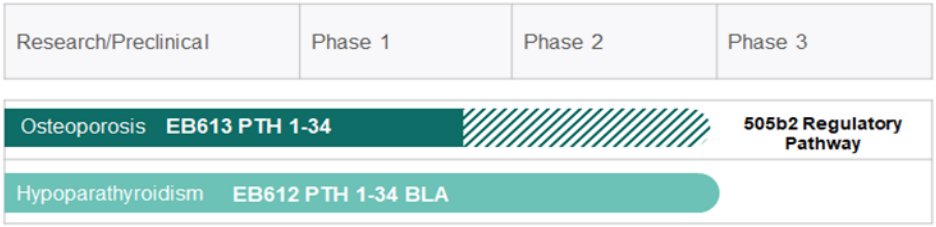
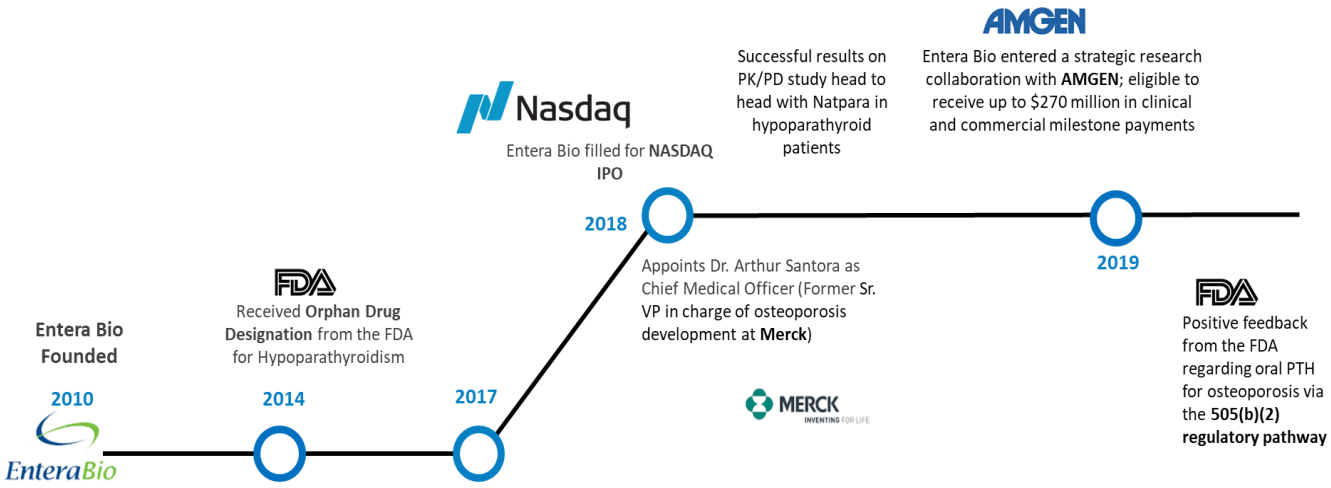


Figure 1: Entera Bio LTD. Lead candidates (Source: Investors presentation 2019)

[1] https://selfhacked.com/blog/parathyroid-hormone-pth/



On December 11th 2018, Entera Bio announced a research collaboration and license agreement with Amgen in the area of inflammatory disease and other serious illnesses. Entera will use its proprietary drug delivery platform to develop oral formulations for one preclinical large molecule program that Amgen has already selected. Amgen also has an option to select up to two additional programs to include in the collaboration.[2] Entera will be eligible to receive up to $270 million in milestone payments, for the development of three different molecules.

The company received positive feedback from the FDA regarding the use of the 505(b)(2) regulatory pathway to develop their osteoporosis treatment, and additional positive feedback regarding the use of bone mineral density (BMD) rather than fracture incidence as a primary endpoint in their phase 3 clinical trial. This feedback is testimony of the shorter and more efficient development process that the company will need to implement as well as of the market potential.

Entera Bio's clinical development and promising results along with the Amgen agreement emphasize the potential commercial opportunities that exist for the company. Entera's orally delivered PTH hormone may substituted the current injectable hormone, providing a combination of efficacy, tolerability, and convenience. Furthermore, the company could be the first oral bone-building therapy for Osteoporosis and the first to receive orphan designation in both the US & EU for hypoparathyroidism, granting 7 years of market exclusivity. Alongside this, Entera's long-term pipeline is set to develop solutions for indications that presently lack treatment and to license its technology to other companies.

[2] https://investors.enterabio.com/news-releases/news-release-details/entera-bio-and-amgen-enter-strategic-research-collaboration

Entera Bio - Upcoming Potential Catalysts

Program	Indication	Event	Significance	Timeline
EB613: PTH (1-34)	Osteoporosis **505(b)(2)**	IND submission	Medium	H1 2020
		Initiation of phase 2a trial- dose ranging study	High	**Achieved**
		Dose ranging study- bone marker data	High	Mid-2020
		Dose ranging study- bone mineral density (BMD) data[3]	High	H2-2020
		Report interim biomarker data from 2.5 mg Dose	HIgh	H2-2021
		End of phase 2 meeting with the FDA	High	H2-2021
		Pivotal phase 3, multicenter study BMD endpoint study comparing Oral PTH with Forteo®	Medium	H1 2021
		Expected commencement of sales by partner	High	H1-2023
EB612: PTH (1-34)	Hypoparathyroidism **Orphan Drug**	PK/PD study head to head with Natpara in hypoparathyroid patients	Medium	**Achieved**
		PK/PD study completion	Medium	**Achieved**
		Submit IND Multi National Study	Medium	H2 2020
		Dose ranging study	Medium	H1-2021
		Phase 2b/3 clinical trial	High	H1-2021
		Expected commencement of sales	High	2023

Sources: Frost & Sullivan Analysis; DNA Biomedical Solutions Ltd.

[3] Based on the three-month interim biochemical marker and safety data, 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.

Credit to Expert: Chen Yakar

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For further inquiries, please contact our lead analyst:
Dr. Tiran Rothman T: +972 (0) 9 950 2888 E: equity.research@frost.com

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