October 9, 2017

Initiation of Coverage

DNA Biomedical Solutions Ltd.: The company and its holdings can become a major force in the osteoporosis care market, pending success in next year's clinical trials.

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Symbol: DNA

Sector: Healthcare

Sub-sector: Biotechnology (Holdings)

Stock Target Price: NIS 0.83

As of October 3, 2017:

Closing Price: 0.47 NIS

Market Cap: 60.5 million NIS

of Shares: 132.3 million

Stock Performance (TTM): 60%

Average Daily Trading Volume: NIS 317.5K

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Company Overview

Israeli holdings firm **DNA Biomedical Solutions** Ltd. ('DNA' or 'DNA Biomed') was founded in 2004 and went public on the Tel Aviv Stock Exchange (TASE: DNA) in 2007. DNA has two key holdings, respective 35% and 40% stakes (both fully diluted) in biomedical companies - *Entera Bio* and *BeamMed*.

Entera Bio is a drug development company, founded in 2009 by DNA and Oramed (TASE/NASDAQ: ORMP), the latter from whom it has licensed a unique drug delivery platform for oral administration of pharmaceutically active large molecule proteins that are nowadays injected. *Entera* is conducting clinical trials for two candidate drugs treating three indications: hypoparathyroidism, osteoporosis and non-union fractures.

BeamMed, and its global subsidiaries, are medical device companies that deliver an ultrasound based screening solution for determining a patient's risk of developing osteoporosis, with unique additional product features. They have established themselves in the screening stage of the osteoporosis therapy value chain. Their product utilizes ultrasonically measurable parameters as the basis of a patient's risk factor. After initial success in East Asia, they are now looking to expand their US sales

HighlightS

- As an investment target, DNA's key advantage is in its holdings in two companies with divergent revenue cycles and business models. DNA's portfolio diversity is central to its investor attractiveness.
- We view the investment in DNA as an opportunity in the short term, mainly given the potential identified in BeamMed's entrance to the US market.
- In the long term, we assume Entera will see clinical success in its pivotal trial planned for next year. This will position Entera as a leading player in the hypoparathyroidism domain.
- Strategically speaking, DNA and its holdings can become, pending successful clinical phases, a major force in the Osteoporosis care market.
- In view of these considerations, the value of DNA is estimated at, \$30.9M/NIS 110.0M; a stock target price of \$0.23/NIS 0.83.

Stock overview YTD (Source: TASE website)



Executive Summary

Investment Thesis

DNA Biomedical Solutions Ltd. (TASE: DNA; hereinafter "DNA") is an Israeli publicly-traded company with holdings in biomedical and medical device companies *Entera Bio Ltd* and *BeamMed Ltd* (hereinafter either Entera or BeamMed respectively). According to DNA, their two portfolio companies collectively address markets with an accumulative value of \$10.4 billion.

As an investment target, DNA's key advantage is in its holdings in two companies with divergent revenue cycles and business models. Their portfolio diversity is central to their investor attractiveness. On the one hand, Entera is a classic biomedical company with no revenues and exorbitant levels of R&D investment in its initial years, and which, pending the results of clinical trials, will grow exponentially once it is approved for market, and subsequently begins revenueyielding operations.



DNA Companies' Market Sizes and CAGRs (2017-2021) (Transparency Market Research, 2017) (Transparency Market Research, 2015) (DNA Biomedical Solutions Ltd, 2017) (Grandview Market Research, 2017)

On the other hand, BeamMed operates under a commercialy-driven business model. Its regulatory process is rather minimal, meaning BeamMed's product reaches the market quickly. The company is now in growth stages, having begun R&D in the late 1990s they have been generating revenues from sales for several years now.

The synergy, from an investor's perspective, between the two companies lies in their activity in the osteoporosis value chain. As illustrated below, BeamMed sits squarely at the start of the Osteoporosis Care Market's value chain, in the screening segment (pre-diagnosis). BeamMed's device is also utilized for ongoing monitoring. Meanwhile, Entera is developing an orally ingestible treatment for patients diagnosed with osteoporosis, placing them at the top of the value chain. In other words, though they operate in the same market, they provide totally different value to patients. Moreover, BeamMed addresses a much wider audience, 'those at risk' of developing osteoporosis, while Entera addresses only those with a confirmed diagnosis. Whilst the former population is more numerous than the latter, this does not necessarily correspond to profitability. Those with confirmed diagnoses will almost certainly seek treatment, however those 'at-risk' may not necessarily get themselves screened.



Entera's unique platform for turning large molecules into orally ingestible medications is exclusive to them and the licensor, and is central to their competitive advantage over firms offering such Hypoparathyroidism and Osteoporosis solutions exclusively by way of injections. The medical community generally prefers orally administered solutions. Furthermore, *Entera*'s long-term pipeline is set to develop solutions for indications that are presently without treatment in any form.

BeamMed provides value through three key product features:

- 1. A patient's qualitative data (demographics) are stored in a database alongside the measurements obtained ultrasonographically. This database is at the core of the company's competitive advantage and is central to the accuracy of their screening.
- 2. Quantitative ultrasound is far less invasive than the alternatives. This has seen an end-user preference for their device, especially in markets such as China where invasive procedures are often avoided due to cultural sensitivities.
- 3. By sheer virtue of being a screening solution, *BeamMed*'s product is positioned to reap the benefits of several market trends. These are primarily demographic, including a growing geriatric population in wealthy countries, and bureaucratic, especially the favor upon which regulatory and reimbursement authorities alike view preemptive detection technologies.

Thus, we view the investment in DNA as an opportunity in the short term, mainly given the potential identified in BeamMed's entrance to the US market. In the longer term, success in the pivotal trial planned for next year will have a significantr impact on the value of Entera and can position the company as a leading player in the Hypoparathyroidism domain. We believe that the chances of success are high, based upon safety profile and indications of improved clinical effects compared with an available, well-characterized injection treatment for Osteoporosis containing the same active substance. However, due to lack of data disclosure from Entera, we follow our conservative approach and apply the relevant statistical success rate for similar companies of 40% in the valuation. In conclusion, we believe that DNA and its holdings can become, pending successful clinical phases, a major force in the Osteoporosis Care Market.



Timeline of DNA Biomedical's significant milestones

Searce: DMA likenedical locations Annual Report for year anding 23 December 2016. p.8.

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Upcoming Potential Catalysts

| Company | Program | Indication | Event | Significance | Timeline |
|--|---------------------|----------------------------------|---|--------------|----------|
| | | L- Hypoparathyroidism | Initiation of pivotal Phase 2b/3 | Medium | Q4-2017 |
| | | | Topline data expected | High | H1-2019 |
| .0 .0 .0 .0 .0 .0 .0 .0 .0 .0 .0 .0 .0 | 34 | | Expected submission of NDA/BLA to FDA | Medium | Q4-2019 |
| | | | Expected commencement of sales | High | H1-2021 |
| EB613 | | EB613: PTH 1- Osteoporosis 34 | Phase 2a Initiation | Low | Q4-2017 |
| | | | IND submission | Low | Q1-2018 |
| | EB613: PTH 1- 34 | | Pivotal phase 2b/3 with strategic partner | High | Q3-2018 |
| | | | Expected commencement of sales by partner | High | H1-2025 |
| BeamMed | - | Osteoporosis | Signing distribution agreements in the United States. | High | H1-2018 |

| Upside scenarios | Downside scenarios |
|--|---|
| Success in reaching Entera's pivotal trial endpoints will significantly affect the company's value. We estimate this probability at 40%. | Failure to reach pivotal trial endpoints will significantly affect Entera's value. |
| Entera has witnessed an emerging interest within various healthcare market segments for administration of injectable drug solutions through oral means. | |
| BeamMed has a quality product with (currently) minor competition, which can accelerate sales by next year. | <i>BeamMed</i> 's milestones among quality controllers and reimbursement bodies alike are accelerating their penetration of the US market |
| Insurance companies have generally shown favor to screening solutions given the long-term cost savings. These achievements incentivize the end-user or his employer to purchase BeamMed products. Thus, sales can increase rapidly after closure of 1-2 deals in the US. | <i>BeamMed</i> 's products can be imitated relatively easily. Thus, with success may come similar solutions, especially in Asia. |

Valuation Methodology

R&D company valuations are challenging due to a non-cash valuation with a long time-to-market in most cases. Methods typically used for company valuations, such as asset valuation or multiplier methods, are incompatible with the valuation of R&D companies. In such companies, the current status of business cannot be analyzed by the capital in the balance sheet, and in most cases cannot be compared to similar companies due to their uniqueness, in both technological and financial aspects.

As part of a discounted cash flow (DCF), the accepted method used in financial valuations, there are several modifications to an R&D company's valuation. In general, there are three primary methods within the DCF method:

- 1. **Real Options** valuation method designated for pre-clinical and early-stage clinical programs/companies where the assessment is binary during the initial phases, and based upon scientific-regulatory assessment only (binomial model with certain adjustments).
- 2. Pipeline assessment valuation method used for programs/companies prior to the market stage. The company's value is the total discounted cash flow plus unallocated costs and assessment of future technological basis. The assessment of the future technological basis is established based on the company's ability to "produce" new clinical and pre-clinical projects and their feed rate potential.

3. **DCF valuation** - similar to companies not operating in the life sciences field, this method applies to companies with products that have a positive cash flow from operations.

Entera's valuation was conducted under the "Pipeline assessment" method, suitable for the development stages of the company's products. The company's valuation is calculated by examining the company as a holding company visà-vis existing projects, with Risk-adjusted Net Present Value (rNPV) capitalization to the net present value, including weighting of several scenarios. These primarily include analysis of the company's income, evaluated in accordance with scientific/technological assessment, based on various sources and estimates relating to the market scope, the degree of projected market success, and regulatory risk.

The weighted average of company revenue in the pharmaceutical and medical equipment market is based on the following data:

- Total Market market potential for the product/product line
- Market Share the company's ability to penetrate the market during the forecast period
- Peak Sales peak sales of the company/product during the forecast period
- <u>Annual Cost of Treatment</u> estimated annual cost per patient, based on updated market studies
- <u>Success Rate</u> chances for success of clinical trials and transition to the next phase in the examined sub-field.

Valuation of Entera's "technological basis" is, in fact, a valuation of the company's "residual value". This valuation was conducted using the Feed Rate methodology that is common in the field of Life Sciences, rather than using the conventional terminal value, normally used by non-Life-Science companies.

BeamMed's valuation was conducted using the DCF method as the company already has sales and cash flows.

Valuation Summary

Entera Bio

The company has two leading indications: EB 612 (Hypoparathyroidism) and the EB 613 (Osteoporosis):

- Hypoparathyroidism We adopt the company's decision to take the drug to market without a strategic partner. Thus, managerial focus will be on sales and forming a sales team; in parallel, a higher profit margin will be derived from revenues yielded. We assume the above based on the company's projected timeline, aimed at going to market in 2021.
- Osteoporosis the company plans on partnering with a large pharmaceutical company, whereby the partner
 will conduct a phase 2b/3 pivotal trial, regulatory approvals, registrations and commercialization. The
 potential agreement with the partner would include milestone payments and annual royalty payments from
 sales of the drug (expected by 2025).

Valuation of Entera's main indications and technological platform:

Pipeline Analysis (\$K)

Source: Frost & Sullivan analysis

The equity valuation elements are presented in the table below:

| Pipeline Analysis | | <u>rNPV (\$K)</u> |
|------------------------------------|--------------------|-------------------|
| EB 612 | Hypoparathyroidism | 96,411 |
| EB 613 | Osteoporosis | 21,728 |
| Total rNPV Pipeline | | 118,139 |
| Unallocated Costs | | -40,820 |
| Terminal Technology Value | | 10,037 |
| Enterprise Value | | 87,357 |
| Non-operational assets/liabilities | | -2,783 |
| Equity Value | | 84,574 |

Sensitivity Analysis

The table below presents Entera's equity value in relation to the capitalization rate. We set a range of 0.5% change from our CAPM model (see Appendix B).

Sensitivity Analysis - Capitalization Rate vs. Equity Value

| <u>Cap. rate</u> | <u>Equity Value (\$K)</u> |
|------------------|---------------------------|
| 20.6% | 74,135 |
| 20.1% | 79,216 |
| 19.6% | 84,574 |
| 19.1% | 90,225 |
| 18.6% | 96,188 |

We estimate Entera's equity value to be in the range of \$79.2M - \$90.2M; a mean of \$84.6M.

BeamMed

Valuation - Key points:

- According to the company's executives, they have, as of 2017, signed agreements with three leading US distributors: McKesson, Henry Schein and Medline. Thus, in forthcoming years we believe sales will increase both in the US and in Asia. We set our valuation for the next five years, until 2022.
- As of June 30, 2017, the company holds \$2.1M in cash and an owner's loan totalling \$400k.
- The discount rate of 18.7% is based on our CAPM model (see appendix B).

Equity value analysis:

| Enterprise Value (EV) | \$K |
|--|-------|
| EV - 2017-2022 | 3,403 |
| EV - Terminal value | 3,599 |
| EV - Company | 7,002 |
| | |
| Non-operational assets/liabilities | |
| Cash | 2,151 |
| Loans | -394 |
| Total Non-operational assets/liabilities | 1,757 |
| | |
| Equity Value | 8,759 |

Sensitivity Analysis

The table below presents BeamMed's equity value in relation to the capitalization rate. We set a range of 0.5% change from our CAPM model (see Appendix B).

Sensitivity Analysis - Capitalization Rate vs. Equity Value

| <u>Cap. rate</u> | Equity Value (\$K) |
|------------------|--------------------|
| 19.7% | 8,330 |
| 19.2% | 8,538 |
| 18.7% | 8,759 |
| 18.2% | 8,994 |
| 17.7% | 9,243 |

We estimate BeamMed equity value to be in the range of \$8.5M - \$9.0M; a mean of \$8.8M.

DNA Biomedical Solutions

DNA is a holding company, which holds, based on the company financial reports, 35% in Entera and 40% in BeamMed (fully diluted).

In a recent capital raising dated 8, October 2017, Entera completed fund raising of \$10.2M (based on a \$97M equity value, fully diluted). This represents DNA share (35%) as \$34M.

It is worth mentioning that Entera's capital structure is currently undergoing changes prior to their IPO (Initial Public Offering), which is expected in the next coming months.

Thus, we calculate DNA's equity value as follow:

| \$K | 100% | DNA % share | DNA \$K share |
|--|---------|-------------|---------------|
| Entera rNPV | 84,574 | 35% | 29,601 |
| BeamMed – rNPV | 8,759 | 40% | 3,504 |
| | | | |
| DNA - Pipeline Value | 33,105 | | |
| | | | |
| DNA General and Administrative Expenses | (2,498) | | |
| Non operational assests/liabilities | | | |
| Cash | 287 | | |
| Total non operational assests | 287 | | |
| Equity Value | 30,894 | | |

Based on the above, we evaluate DNA's equity value at \$30.9M/NIS 110.0M; a stock target price of \$0.23/NIS 0.83.

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Company Structure

DNA Biomedical Solutions was founded in 2004, and went public in 2007 on the Tel Aviv Stock Exchange (TASE: DNA), on which the Company currently trades 62% of its shares. The remaining stakes in the company are held by various and other stakeholders. Notable stakeholders include: Zeev Bronfeld (14.0%); *Oramed* (7.88%); Raphael Menachem (5.48%); and the bulk of founder's equity is held by Yonatan Malcha (5.25%).

DNA has two key holdings, 40% and 35% respective stakes (both fully diluted) in biomedical companies *BeamMed* and *Entera Bio. BeamMed* acquired *Sunlight Medical Asia Ltd* (heretofore "Sunlight") in 1998 and this subsidiary forms the basis of the company's operations in East Asia, particularly Mainland China. *Sal-Med* (a BeamMed subsidiary) is based out of *BeamMed*'s headquarters in Israel and doesn't differ in any notable way from its parent company. *BeamMed Inc.* is based in Florida and was established in 2011 as part of the parent company's accelerated effort to expand their market reach in the United States. Finally, as opposed to the 100% held subsidiaries above, in September 2015 *BeamMed* acquired a 51% majority stake in Spanish company BCPIS (Business Consulting Platform in Spain).

Sources: DNA Biomedical Solutions: Annual Report for 2016. p.5; TASE Website: DNA Biomedical Solutions Ltd - Company Information; DNA Biomedical Solutions: Annual Report for 2015. p.167.

Company Structure – BeamMed

| BeamMed Corporate Structure | | Fully-diluted Holding |
|--|-------------------------|-----------------------|
| DNA Biomedical Solutions | | 40.00% |
| Total Others | | 60.00% |
| Others | Tal Marom (CEO) | 5.00% |
| | Shenhav Trustees | 5.00% |
| | Third parties (Foriegn) | 40.00% |
| | ESOP Trust Management | 7.85% |
| | Employee Options | 2.15% |
| (DNA Biomedical Solutions Ltd, 2017) p.38. | | |

Company Structure - Entera

| Entera Bio Corporate Structure | | Non-diluted | Fully-diluted |
|---|--------------------------------|-------------|---------------|
| DNA Biomedical Solutions | | 69.6% | 35.16% |
| | Total Others | 30.4% | 64.84% |
| | Phillip Schwartz | - | 5.02% |
| Others | Pontifax and other CLA holders | - | 14.99% |
| | Private Investors and VCs | 28.4% | 38.75% |
| | Others including ESOP | 2% | 6.08% |
| Source: (DNA Biomedical Solutions Ltd, 2017). | | | |

Entera and BeamMed Overview

Entera Bio has licensed a unique platform to orally deliver large molecule proteins, by way of a tablet, which can replace injectable alternatives. The company has chosen to initially focus on indications with a lack of in drugs or solutions. They are about to initiate mid-late stage clinical trials for hypoparathyroidism (phase 2b/3), osteoporosis (phase 2a), and non-union fractures (phase 2a). The platform utilized by *Entera* is licensed from cofounder and stakeholder *Oramed Pharmaceuticals*, and its primary aim is to optimize a patient's intake of the aforementioned molecules; this is the core value *Entera* brings to market. In July 2017, the company announced its intention to list on the NASDAQ.¹

BeamMed, and its global subsidiaries, deliver ultrasound-based screening solutions for determining a patient's risk of developing osteoporosis. Their technology was acquired from Sunlight with IP rights in 2006, and since then BeamMed has expanded their product portfolio. BeamMed operates in the Bone Densitometers industry, is most active in China, and is looking to push further into other markets, specifically the US. The proliferating geriatric population, particularly in developed economies, is a key market driver. The company's push into the US is supported by favourable reimbursement rates for early detection, which minimizes long-term costs of treating the disease.

Entera Bio

Company Overview

Entera was founded in 2009 and commenced operations in the following year with financing from DNA and Oramed, as well as scientific support from the latter, from whom its technology is licensed. The company's mission is to develop oral delivery of large molecules to address undertreated diseases, which are currently treated by injections. Oral administration offers increased patient comfort, compliance and cost effectiveness, and is therefore the preferred method of drug administration. Entera's oral delivery platform may be applied to an array of molecular drugs. The company has strategically chosen to develop tablets comprising biological substances given as injections, with a proven therapeutic and side effect profile, and are thus well positioned to 'go to market'. Currently, its platform is applied to the development of a formulation of recombinant Parathyroid hormone (PTH 1-34), an important hormone in bone remodeling, as a foothold to show the platform's feasibility. The first two products in the company's pipeline are geared towards hypoparathyroidism and osteoporosis indications, both based on PTH 1-34 as an oral drug.

The company holds orphan drug designation for the hypoparathyroidism indication from the FDA (US) and EMA (Europe) since April 2014 and June 2016, respectively, accelerating market penetration for this product. For the most part, rare-disease treatments are considered an attractive market because the relatively small patient population allows for dramatic price increases. The advent of an orally ingestible alternative will only further these, already lucrative, monetization possibilities. The company is set to begin phase 2b/3 clinical trials of its product for hypoparathyroidism, and phase 2a of its second product for osteoporosis by the end of 2017. Another indication in the second product's pipeline addresses non-union fractures, an indication that currently has no proven treatment solution. Phase 2a initiation is expected at the beginning of 2018. Additional programs based on their platform are currently under development.²

¹ Entera Bio Investor Presentation. (2017).

² Ibid.

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(Entera Bio Investor Presentation, 2017)

Success in the approval process for the hypoparathyroidism drug candidate may have positive implications for the clinical and business development of the other drug candidate treating Osteoporosis, as both deal with the same active ingredient and the same technological wrapping, although they differ in the formulation, dosage and treatment regimen. Although hypoparathyroidism has a smaller market potential, its accelerated regulatory pathway will eventually provide a market-stamp for safe and efficient use of the drug, and will open doors for other drug candidates with larger indications and markets.

The company plans to develop the product for hypoparathyroidism and bring it to market. Alternatively, for the osteoporosis product, Entera intends to recruit a strategic partner after completion of phase 2a (expected by Q3-2018), for the rest of the clinical development and commercialization, based on payments and future royalties.

Market, Standard of Care and Unmet Needs

Entera develops oral delivery of large molecules to address underattended clinical demand. *Entera*'s oral delivery platform can be applied to an array of molecular and therapeutic substances such as, peptides and proteins that are currently given as injectable alternatives. Peptides and proteins have great potential as therapeutics, compared with the typical small-molecule drugs that currently make up the majority of the pharmaceutical market, as they are highly selective.³ Peptides can be designed to target a broad range of molecules, offering multiple advantages in fields such as oncology, immunology, infectious disease and endocrinology. Also, there is a lot of interest in the development of systems allowing for the oral delivery of peptide and protein therapeutics, as oral delivery improves patient compliance.⁴

Unfortunately, oral bioavailability of peptides is limited by degradation in the gastrointestinal (GI) tract, as well as their inability to cross the epithelial barrier. These therapeutics tend to have a high molecular weight, low lipophilicity and charged functional groups that hamper their absorption.⁵ These characteristics lead to the low

³ Craik, D. J. et al., Chem. Biol. Drug. Des. (2013). 136–147.

⁴ Maher S, et al., Drug Discovery. Today. Technol. (2012) 9(2), 113-119.

⁵ Aungst B, et al. J. Control. Release. (1996) 41(1), 19–31.

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bioavailability of most orally administered peptides (<2%) and short half-lives (<30 min).⁶ Moreover, even after the drug is absorbed, first-pass metabolism, known as the first-pass effect, can greatly reduce the fraction of a drug that reaches the systemic circulation through the liver. The liver metabolizes the drug, reducing the amount of the active, parent compound that enters systemic circulation.⁷ Other considerations are related to the food effect which might change the rate and extent of absorption if the drug is administered before or after a meal or under fasting conditions. These might determine how the oral drug will be used and for what indication.⁸

Intravenous (IV), Intramuscular (IM), subcutaneous (SC), intrarectal, transdermal and pulmonary delivery routes of these therapeutics overcome the issue of absorption through the GI, and avoid or minimize the first-pass effect (Brunton L). However, these administration routes are limited by other factors including systemic proteases, rapid metabolism, opsonisation, conformational changes, dissociation of subunit proteins, non-covalent complexation with blood products and destruction of labile side-groups.⁹ As well, the use of injections on a daily basis during long-term treatment has obvious drawbacks in contrast to the oral route which offers the advantages of self-administration with a high degree of patient acceptability.

Methods to improve the bioavailability of protein therapeutics through oral administration can be broadly classified into categories of structural modifications, enzyme inhibitors, absorption enhancers and carrier systems.

- **Structural modifications,** including cyclization, PEGylation, fusing therapeutic proteins to vitamin B12, protein lipidization, stapled peptides, substitution of natural L-amino acids with d-amino acids
- Enzyme inhibitors such as soybean trypsin inhibitor and Aprotinin (Trasylol)
- Absorption enhancer, including chitosans, medium-chain fatty acids, lectins, certain toxins, cell-penetrating peptides (CPPs) and surfactants
- **Carrier systems**, including hydrophilic mucoadhesive polymers, thiomers, polymer matrices, nanoemulsions, hydrogels, liposomes and nanoparticles (NPs).

Despite these advancements, realization of orally administered biologicals with its accompanying advantages remains an elusive goal.

Entera Bio's platform for oral delivery of biological macromolecules

Entera's platform technology consists of an oral capsule that facilitates effective oral administration and absorption of intact proteins through the gastrointestinal (GI) tract. Its technology was proprietary to Oramed, of which Entera was formerly a subsidiary. The technology is based on co-administration of therapeutic proteins within a capsule carrier that consists of two components. The first is a proprietary combination of protease inhibitors and chemical entities that protect the therapeutic

Entera Bio Investor presentation (2017)

proteins from enzyme degradation and consequent drug breakdown in the stomach and intestine. Each "cocktail" is customized for the drug molecules candidate. The second is an absorption enhancer that enables molecular transport of large molecules through the intestinal wall by endocytosis induction. Endocytosis is a natural transport mechanism of molecules via vesicles, which is considered to be specific and safe.

⁷ Pond SM, et al.,. Clin. Pharmacokinet (1984) 9(1), 1–25.

⁶ Borchardt T, et al., Adv. Drug Deliv. Rev. (1997) 235–256.; Bruno, B.et al., Therapy Delivery. (2013) 4(11), 1443–1467.

⁸ Kidron, M., et al., J Diabetes Sci Technology (2009) 3(3), 562-567.

⁹ Torchilin, V. et al., Therap. Deliv. (2009) 5(2-3),1443-1467.

Preclinical data in animals supports oral delivery and has been successful in various biological molecules of different sizes, from small molecules (1.6kD) to larger compounds (10kD). PK/PD profile seem favorable for multiple daily oral dosing, administered by individualized titration.

The first two products in the company's pipeline are based on a formulation of recombinant parathyroid hormone (PTH 1-34), an important hormone in bone remodeling. The drug is identical to a portion of the human parathyroid hormone (PTH), consisting of the first (N-terminus) 34 amino acids, which is the bioactive portion of the hormone. It is an effective anabolic (i.e., bone growing) agent used in the treatment of some forms of osteoporosis.¹⁰ Its intermittent use activates osteoblasts more than osteoclasts, which leads to an overall increase in bone mass.

Entera Bio has not disclosed any other technical information regarding the content of its platform carrier aside from the aforementioned. It is important to note that oral delivery of biological molecules by Entera's platform is not straightforward for each biological drug candidate, and success with one product does not guarantee that of the others. Each drug substance needs to be ustomized and tested for its delivery extent.

Market Overview

Entera's strategy to initially focus on rare diseases to prove its technological capability has strong market precedent. This is further substantiated by the drastic marginal revenue that can be yielded from rare-disease treatments, and specifically so from hypoparathyroidism, which is currently only treated by injection.¹¹ The company's long-term addressable market, simply as a provider of oral solutions for injectable medications, has the potential to reach up to 10% of the pharmaceutical industry in its entirety. Yet, capturing this market is subject to clinical trial and error.

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 ingested intravenously or intramuscularly.¹² 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 ¹³ |
| Hefei (Sinopharm) (CN) | Oramed (IL) | \$50M | Orally ingestible Insulin | Nov 2015 ¹⁴ |
| 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 ¹⁵ |
| 25 major financial institutions (US) | Chiasma (US) | \$26.4M (at 30.8.17) | Oral therapies for acromegaly (Phase III). | Via Nasdaq in 2017 ¹⁶ |

¹⁰ Saag KG, et al., The New England Journal of Medicine (2007) 20, 357

¹¹ SHIRE Pharmacuticals. Annual Report Q2-2015. (2015).

¹² DNA Biomedical Solutions. Financial Report for 2016. (2017).

¹³ https://www.businessinsider.com.au/protagonists-oral-peptides-pill-versions-of-blockbuster-drugs-2017-6?r=US&IR=T.

¹⁴ http://www.reuters.com/article/oramed-china-idUSL8N13O0AO20151130.

¹⁵ http://www.biospace.com/News/bay-area-startup-rani-therapeutics-tops-70-million/409783.

¹⁶ NASDAQ Website. (2017)

Hypoparathyroidism Drugs Market

Market Size

The hypoparathyroidism drugs market is extraordinarily condensed, and prior to the technological advent of oralbased solutions, consisted of a single player, SHIRE Pharmaceuticals. The PTH injection to treat hypoparathyroidism (hereinafter referred to by its trade name, *Natpara*) was developed by NPS (acquired by Shire for \$5.2B in 2015), and is currently only available in the US. In 2016, the drug generated revenues of \$85.3M, a significant increase of more than 350% from 2015.¹⁷ Such volatile growth is not expected in the long-term. Having said that, it is important to note that the FDA only approved the drug in 2015. Nevertheless, the US market size in 2016 can be roughly estimated at \$85.3 million, and is forecasted to reach \$441.31 million by 2022, a CAGR of 31.51%.¹⁸ Importantly, these figures exclude the 120,000 patients outside the US, where SHIRE does not supply the drug. The company estimates the global market at approximately \$1B with a CAGR of 3.3% until 2021.¹⁹

Drivers and Constraints

- General patient preference for oral solutions
- Despite the high costs of rare disease treatment by injection (\$100K annually per patient), insurers are usually willing to cover the costs because the patient population is relatively small and the condition can be life-threatening.
- Reimbursement policy for an orally ingestible solution would only be more favourable given the lowered risk, and lower practitioner costs due to the safe self-administration of oral alternatives.
- Despite *Natpara* receiving landmark approval from the FDA as the first regulated hormone replacement in treating the condition, the FDA warned that once-a-day treatment was far less effective than treatment several times per day (Food and Drug Administration, 2014). The latter preferred dosage will only be easily administered if the substance can be ingested orally.
 - Orphan drug designation, an accelerated pathway with benefits. A regulatory classification granted to unique FDA approval candidates being developed to address insufficiently met medical needs for diseases affecting a relatively small share of the population (up to 200,000 people in the United States). The program is designed to incentivize pharmaceutical firms to develop drugs for rare medical conditions.
 - Benefits include: taxation benefits, grants, government R&D subsidies, higher prices, barriers to entry for production of generic drugs, and most importantly, seven years of market exclusivity (even if the patent period ends, the company can continue operating monopolistically).

¹⁷ Shire Pharmacueticals Plc. Annual Report 2016. (2017).

¹⁸ Evaluate Pharma, (2017).

¹⁹ Entera Bio Investor Presentation. (2017); Transparency Market Research. Thyroid Gland Disorders Treatment Market - Global Industry Analysis, Size, Share, Growth, Trends and Forecast 2015 – 2023. (2015).

Osteoporosis Drugs Market

Market Size

The Osteoporosis Drugs Market was valued at \$8.5B in 2017,²⁰ and is set to grow at a CAGR of 3.3% (2015-25) to \$9.7B by 2021. The osteoporosis therapeutics market is an emerging one. Some treatments are available, and many are under development by pharmaceutical companies. The International Osteoporosis Foundation estimates that 200 million people suffer from Osteoporosis worldwide. The principal driver of this market size is the increasing patient population, this in turn a product of geriatrics comprising an increasingly dominant share of the population. Approximately 75 million patients worldwide live in Europe, the US or Japan, widely considered to be the most easily penetrable geographies.²¹

Recently, experts have cited increased incidence rates among women who contract the condition during menopause. Moreover, the geriatric correlation is also significant among females: 67% of 90-year-old women; 40% of 80-year-old women; 20% of 70-year-old women; and 10% of 60-year-old women suffer from the disease. In addition, 33% of women over age 50 will experience at least a single osteoporotic fracture.²² Whilst relative incidence among males is lower, real growth in the number of patients in general, and the male share in particular, is driving the market. This increase can be partially attributed to lifestyle factors that are statistically more prevalent among men and which are known to deteriorate bone health. Such factors include alcohol abuse, a sedentary lifestyle, and tobacco use. The foremost among these has a particularly significant correlation with Osteoporosis patients, and is perhaps the most influencial growth factor for the number of male patients.²³ Incidence among men for medical conditions is generally lower due to a known trend whereby men are far less likely to seek medical assistance than women. Recent awareness programs to address this issue will see higher reporting rates among men and will increase their incidence numbers, increase in both real terms and relative to the number of female patients.

Geographic Segmentation

As of 2015, North America dominates overall market share, driving many strategic partnerships and investments by major corporations to further their market reach. In practice, the bulk of these efforts are aimed at enhancing R&D capabilities and improving/maintaining high standards of care. On the consumer side, demand is arising both out of these new innovations and the growing disease burden. The Asian-Pacific market is also expected to grow significantly in the coming years, with enlarging upper-middle classes and rapid upgrades in local healthcare infrastructure being the leading market accelerators. Alongside, efforts to commercialize both original and generic treatments at price points accessible to the wider population, will further expand market reach. The Asian market

²⁰ DNA Biomedical Solutions. Financial Report for 2016. (2017).

²¹ Ibid

²² https://www.iofbonehealth.org/facts-statistics#category-19.

²³ Grandview Market Research. Osteoporosis Drugs Market Analysis By Product (Branded, Bisphosphonates, Parathyroid Hormone Therapy, Calcitonin, Selective Estrogen Inhibitors Modulator (SERM), Rank Ligand Inhibitors, Generics), And Segment Forecasts, 2014 – 2024. (2015).

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will also exhibit market growth due to worldwide trends such as biotechnological innovation and an increased focus on osteoporosis care in emerging economic giants, India and China.²⁴

Market Drivers and Constraints

- Unanimous preference for orally ingestible alternatives by all major players in the market: patients, physicians and reimbursers.
 - Oral administration has many inherent advantages over injections including self-administration and suitability for those sensitive to injections (e.g. those with fragile skin or those with psychological aversion).
 - The medical world has experienced prolific growth in the number of experiments taking place to find oral solutions to drugs that are currently only effective when ingested intravenously or intramuscularly.²⁵
- Low levels of awareness, treatment, and diagnosis, due to the asymptomatic nature of the condition.
- Complex drug-taking regimen, patient compliance with this regimen and the frequency of dosage.
- Lack of long-term clinical data.
- Declining reimbursement rates for DEXA scans in the US could lead to fewer diagnoses and thus less patients seeking treatment despite their suffering from the condition.
 - On the other hand, technological development of alternative diagnosis and screening solutions which are reimbursed favorably may sufficiently mitigate this constraint.
- In the US, Osteoporosis treatment is invariably reimbursed generously because it is medically critical.
 - Although out-of-pocket costs for Osteoporosis patients are generally low, their variance is high, ranging between \$5 and \$150 depending on the treatment and the insurer's policy with respect to that treatment.²⁶

Company's Products

In June 2010 Oramed entered into an exclusive out-licensing agreement with Entera to develop oral delivery for drugs of certain indications. The out-licensed technology differs from Oramed's main delivery technology, used for its oral insulin and GLP-1 analog and is subject to different patent applications.

Entera's oral delivery capsule is a drug carrier platform that can be applied to an array of molecular and biological solutions. The company addresses large biological substances with proven therapeutic and side effect profiles that are commonly given as injections for underattended diseases, in an attempt to provide even greater efficacy to the injectable alternative. Their carrier platform consists of two key product features, the first being a molecular protection system preventing drug breakdown and elongating the half-life of the therapeutic drug delivered into the gut, and the second component being a synthetic chemical complex facilitating large molecular transfers through intestinal barriers.

Osteoporosis Drugs Market

by Geography 2016-26

(Vision Gain Market Research, 2017)

²⁴ Grandview Market Research, 2017; Vision Gain Market Research. Osteoporosis Drugs Global Market 2016-2026. (2017).

²⁵ DNA Biomedical Solutions Ltd. Q2-2017 Financial Report. (2017).

²⁶ US Department of Health. National Health and Nutrition Examination Survey. (2017).

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The first two products in the company's pipeline are targeted towards hypoparathyroidism and osteoporosis indications, both based on a formulation of recombinant parathyroid hormone (PTH 1-34), an important hormone in bone remodeling. The company is set to begin phase 2b/3 clinical trial of its product for Hypoparathyroidism, and phase 2a of its second product for osteoporosis by the end of 2017. A third indication in the pipeline, based upon the second product, addresses non-union fractures, an indication currently without an established conclusive clinical treatment. Phase 2a initiation is expected at the beginning of 2018.

As of December 2016, the company submitted eight new patents related to formulation as well as relevant treatment areas based on the company's platform technology of PTH (1-34) for hypoparathyroidism, osteoporosis and union fractures. Five of these patents are under PCT (The Patent Cooperation Treaty) application (international filing) with other patents pending for submission. The company has patents in the US, Australia, China, Japan, New Zealand, Canada, Israel and Russia. The company's patents for hypoparathyroidism and osteoporosis expire in 2029.²⁷

EB612 (PTH 1-34) for Hypoparathyroidism

Hypoparathyroidism is an uncommon condition in which the parathyroid glands in the neck are either missing entirely, or secrete abnormally low levels of parathyroid hormone (PTH). PTH is key to regulating and maintaining a balance of two important minerals - calcium and phosphorus. The level of calcium in the blood is sensed through the calcium-sensing receptor in the parathyroid chief cells that secrete the parathyroid hormone in accordance. Magnesium is required for PTH secretion as well. PTH acts on several organs to increase calcium levels: it increases calcium absorption in the bowel; prevents calcium excretion; increases phosphate release in the kidney; and in bones, increases calcium through bone resorption.

The main symptoms of hypoparathyroidism result from low blood calcium levels, which interfere with normal muscle contraction and nerve conduction, often causing cramping and twitching of muscles or tetany (involuntary muscle contraction), peripheral neuropathies, electrolyte imbalances, and can be fatal in severe cases. Risk factors for contracting the condition may include family history, recent neck surgery (particularly if involving the thyroid), and certain autoimmune or endocrine disorders.²⁸ The diagnosis is made with blood tests, and other investigations such as genetic testing depending on the results.

A healthy diet, as well as calcium or vitamin D replacement can ameliorate the symptoms, but can increase the risk of kidney stones and chronic kidney disease. Severe hypocalcaemia, a potentially life-threatening condition, is treated with intravenous calcium (e.g. as calcium gluconate). Overall, the treatment of hypoparathyroidism is limited as the only available approved drug treatment is a daily injection of a recombinant complete parathyroid hormone (PTH-184), which was developed by NPS (acquired by Shire in 2015), and has since traded under the brand name Natpara. It is usually administered in more severe cases of low blood calcium levels. Pump delivery of synthetic PTH 1-34 provides the closest approach to physiologic PTH replacement therapy.

Hypoparathyroidism is considered a heavy burden illness, with 72% of patients experiencing more than ten symptoms on a daily basis.²⁹ It has a high economic impact as 78% of the patients report six days absent from work/yr and many are unemployed. Chronic Hypoparathyroidism affects approximately 180,000 patients worldwide. Of those, approximately 60,000 are in the US: approximately 18% of patients are classified as severe, 39% as moderate and 43% as mild. Entera estimates that its drug candidate will extend the treatment to a broader range of patients, and can treat patients across the spectrum of severity.

²⁷ DNA Biomedical Solutions, Financial Report for 2016. (2017)

²⁸ http://www.mayoclinic.org/diseases-conditions/hyperparathyroidism/symptoms-causes/dxc-20319888

²⁹ Hadker N, et al., Endocr Pract. (2014) 20, 671-679

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Entera Bio Investor Presentation. (2017).

The company holds orphan drug designation for Hypoparathyroidism from the FDA (US) and EMA (Europe) since April 2014 and June 2016, respectively, to develop the oral drug of PTH 1-34. Orphan drugs are a regulatory classification granted to unique FDA approval candidates being developed to address insufficiently met medical needs for diseases affecting a relatively small share of the population (up to 200,000 people in the US). The program is designed to incentivize pharmaceutical firms to develop drugs for rare medical conditions. Such benefits include: taxation benefits; grants; government R&D subsidies; higher prices; barriers to entry for production of generic drugs; and most importantly, seven years of market exclusivity (even if the patent period ends, the company can continue operating monopolistically). Without such incentives, drug companies would be dissuaded from developing solutions with relatively high development costs, and which appeal to only a small consumer market. Accordingly the company can take advantage of the benefits above-mentioned, to drive their product to market and maximize its profitability.

Clinical Data for EB612

Entera Bio completed multicenter, open-label, phase 2a clinical trial in Hypoparathyroidism with EB612, administered three to four times daily in parallel to a baseline regimen of calcium and vitamin D. The trial included 17 hypoparathyroidism patients, and was carried out in Israel.³⁰ The trial results met the primary endpoints including reduction in calcium supplements and plasma levels, demonstrating a promising safety profile. As well, phosphate levels decreased overall and consistently following each dose. Importantly, PTH 1-34 is well studied, and has been administered as an injectable drug with the brand name Forteo to millions of osteoporosis patients for more than a decade, which further strengthens its safe use. PTH pulsed throughout the day better mimics endogenous hormone levels. Moreover, clinical evidence supports multiple daily dosing; NIH studies have shown that multiple doses daily are superior to one dose a day (QD). All in all, phase 2a results demonstrate the potential for an improved profile to the phase 3 pivotal trial findings versus Natpara.

Upcoming milestones for the clinical development of EB612 include pharmacokinetic/pharmacodynamic (PK/PD) cross over study of EB612 versus Natpara, which is intended to inform and optimize the design of the EB612 pivotal trial initiated afterwards. The phase 2b/3 pivotal trial will include 120-160 patients with EB612 individually titrated to patients, with data planned to be available by H2-19. Like Natpara, it should only need one pivotal trial, conducted with the same KOLs/PI sites. In parallel to the pivotal study, a head-to-head study is planned in the US versus Natpara to show EB612's potential to be superior to Natpara and accelerate its market acceptance. These milestones are defined to follow an efficient and well established pathway on the way to receiving regulatory approval for marketing EB612.

³⁰ Entera Bio Official Website.

The forecasted clinical development timeline of EB612 for hypoparathyroidism

Source: DNA Biomedical Solutions. Financial Report for Q2-2017. (2017).

EB613 (PTH 1-34) for Osteoporosis

Background

Osteoporosis is a progressive systemic skeletal disease, characterized by a reduced bone mass and poor bone quality. The decrease in bone density results from loss of minerals from the bone, primarily of calcium. Consequently, bone strength decreases, resulting in fragile bones and increased risk of bone fractures. Osteoporosis itself has no symptoms, until a fracture actually occurs. Osteoporotic fractures occur in areas where healthy people would normally not break a bone, most commonly in the hip, wrist or spine. These fractures increase dramatically with age, and often cause rapid deterioration in health, resulting in death. Sometimes this phenomenon runs in families as it is inherited. Due to the asymptomatic nature of the condition, many mild-to-moderate patients are hesitant to take currently available therapies, or may not even know that they are at risk.

About 200 million people worldwide are affected by osteoporosis – about 80% are women. Over 10 million patients are affected in the US. Every second woman and every fifth man over 50 years of age suffers an osteoporotic fracture.³¹ Caucasian (white) and Asian women, especially those who are post-menopausal, are at highest risk. The global annual cost of osteoporosis was estimated at \$8.5 billion in 2016.

The parathyroid hormone (PTH) is one of the two major hormones modulating calcium and phosphate homeostasis in the body. It is an anabolic agent, in which therapy with it results in new bone formation. Intermittent administration of recombinant human PTH has been shown to stimulate bone formation. The first 34 amino acids (the bioactive portion of the complete hormone molecule containing 84 amino acids)-are already used in the treatment of some forms of osteoporosis by the drug Teriparatide (brand name Forteo) since 2002, given as an injection. The drug is also occasionally used off-label to speed fracture healing.

Entera's EB613 utilizes PTH 1-34, the same active molecule as Forteo, but for oral treatment of osteoporosis.

³¹ http://www.iofbonehealth.org/facts-statistics.

Clinical Data for EB613

Entera Bio completed phase 1 initiated in 2014 for oral administration of EB613 to treat Osteoporosis in more than 40 subjects. The results of the trial demonstrated a favorable pharmacodynamic profile in Osteoporosis. To the best of our understanding, the safety profile and indications of clinical effect were also demonstrated. As EB613 consists of PTH 1-34, the same molecule as Forteo, the pharmacokinetic and pharmacodynamic profiles for both are highly predictive. From this perspective, the results seem promising, as an injection of Forteo is a well-characterized treatment for osteoporosis.

The company intends to initiate a multi-center, open label phase 2a clinical trial in Q4-2017; end points will include bone density and other bone markers. Following its completion, expected in Q3-2018, the company intends to engage with a strategic partner for late-stage clinical development and commercialization. The company estimates that the product will be available by 2025.

The forecasted clinical development timeline of EB613 for osteoporosis

Source: DNA Biomedical Solutions Ltd. Annual Report for 2016. (2017)

EB613 for Non-Union Fractures

An additional indication in pipeline, that makes use of EB613, addresses non-union of fractures, an indication which currently has no proven treatment solution. Non-union of fractures occur when normal bone healing is interrupted and a fracture does not heal properly, if at all. This complication may results from a fracture's movements, poor blood supply or infection. The most common reported risk factor is an open fracture.

Failure of bone healing occurs in 5-10% of all fractures.³² More than 300,000 people in the US annually experience fractures that fail to heal properly.³³ These are primarily fractures of the pelvis and hip, which involve extended hospital stays and result in very high costs to patients.

Numerous animal studies and off label use of Forteo suggest that PTH both accelerates bone healing and strengthens bone fusion.³⁴ Entera is preparing for a phase 2 clinical trial to address the clinical potential of oral PTH as a treatment for stress fractures and possibly prevention. Stress fractures refer to overuse injuries to bones caused by increased load or increased repetitions, often characterizing a military marching or training athletes. Phase 2a

initiation is expected at the beginning of 2018 in an academic institution abroad in collaboration with its local military. 35

Competitive analysis

Companies which s are attempting to develop oral carrier systems that will be able to deliver a variety of therapeutics with minimal modification include; Emisphere (USA), Evonik (Germany), Alkermes (Ireland), Anesta Corp. (US), Generex Biotechnology (US) and Alza Corp (US). As an example, Emisphere's Eligen system has the

³² Zura R, et al. JAMA Surg. 2016

³³ American Academy of Orthopaedic Surgeons. orthoinfo.aaos.org

³⁴ Coppola C, et al.Transl Med UniSa.2015

³⁵ Entera website.

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potential to deliver therapeutics from 0.5–150 kDa by a drug–carrier system known as SNAC.³⁶ A second such system is the gastro intestional mucoadhesive patch system (GI-MAPS) of Evonik;³⁷ the backing of Eudragit L100 is made of ethyl cellulose, while the surface layer is made of an enteric, pH-sensitive polymer.³⁸

Competative Landscape - Osteoporosis:

The current osteoporosis treatment landscape is mostly antiresorptive comprising five principal classes of agents: bisphosphonates (Reclast, Fosamax, Bonviva), estrogens (Premarin), selective estrogen receptor modulators (Viviant, Evista), calcitonin (Miacalcin), and monoclonal antibodies (Prolia). Each of these act by reducing loss of bone mineral. The second type of treatment includes PTH therapy, which results in new bone formation (anabolic agent).

Bisphosphonates are oral drugs with proven antifracture efficacy and a good safety profile that inhibits the bone resorption process, and are the most widely used first-line antiresorptive therapy.³⁹ However, bisphosphonates are characterized by GI disturbances and the risk of osteonecrosis of the jaw. The leading bisphosphonates, Fosamax and Zometa, had peak sales of \$3.2B (in 2005) and \$1.5B (in 2010) respectively. In 2007 the total worldwide sales of the top ten bisphosphonate products reached almost \$8 billion, but dramatically decreased to about \$2 billion by 2015.⁴⁰

The two most effective osteoporosis drugs on the market today are injections. The most recent entrant-Prolia (Denosumab) is a monoclonal antibody that blocks a cascade of signals causing bone breakage, given as an injection every 6 months to prevent bone loss. In 2017, its sales reached approximately \$2 billion, and are expected to increase further. The second type of drug, Forteo, developed by Eli Lilly, is the only anabolic osteoporosis agent on the US market. It is a recombinant form of PTH, administered by daily subcutaneous injections and is recommended for people with osteoporosis who are at high risk for fractures. 2017 worldwide sales of Forteo were \$1.7 billion. The following table presents the total worldwide market value of the top 10 available products:

| | 2016 | 2017 | 2018 | 2019 | 2020 | 2021 | 2022 |
|---------------------------------------|-------|-------|-------|-------|-------|-------|-------|
| Prolia (AMGN) | 1,635 | 1,944 | 2,165 | 2,375 | 2,567 | 2,756 | 2,927 |
| Forteo (LLY) | 1,500 | 1,668 | 1,692 | 1,301 | 1,036 | 860 | 729 |
| Reclast (NVS) | 326 | 364 | 394 | 421 | 450 | 477 | 508 |
| Viviant (PFE) | 133 | 206 | 277 | 340 | 393 | 443 | 489 |
| Premarin (PFE) | 488 | 470 | 463 | 456 | 447 | 439 | 430 |
| Pralia (Daiichi Sankyo) | 166 | 193 | 227 | 272 | 315 | 342 | 369 |
| Caltrate (PFE) | 313 | 320 | 326 | 333 | 339 | 346 | 352 |
| Edirol (Taisho) | 209 | 223 | 235 | 244 | 254 | 258 | 263 |
| Edirol (Chugai) | 246 | 266 | 280 | 292 | 250 | 242 | 242 |
| Abaloparatide SC (Undisclosed Partner | | | 43 | 100 | 163 | 205 | 240 |
| Sales) | | | | | | | |
| Other | 2,043 | 1,883 | 1,876 | 1,999 | 2,165 | 2,229 | 2,345 |
| Total | 7,060 | 7,536 | 7,979 | 8,133 | 8,378 | 8,597 | 8,893 |

Source: Evaluate Pharma. All Financial data in US \$ (mln)

³⁶ http://www.emisphere.com

³⁷ http://healthcare.evonik.com

³⁸ Bruno BJ, et al., Ther Deliv. (2013) 4(11), 1443–1467

³⁹ Chen JS, et al., Nat Rev Endocrinol. (2011) 6;8(2), 81-91

⁴⁰ Evaluate Pharma

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Source: Evaluate Pharma

Except for the commercially available drugs for treatment of osteoporosis, there are numerous drugs under development. Our search identified 29 drug candidates from stage I to late clinical or pre-registration stages.⁴¹

Other than Entera, several other companies are developing oral delivery treatments of osteoporosis. Among them, RGB-10 is a biosimilar of teriparatide (PTH) given as a subcutaneous injection, under development by Gedeon Richter (Hungary) for the treatment of osteoporosis, currently at pre-registration stage.

Ostora is a recombinant oral salmon calcitonin (rsCT) once-daily tablet at a preregistration stage, under development by Tarsa Therapeutics for the treatment of osteoporosis. It was previously under development by Unigene Laboratories, Inc., a biopharmaceutical company in the US, which develops oral and nasal drug delivery technologies.⁴²

Lasofoxifene is the lead compound in a series of partial estrogen agonists based upon Ligand's intracellular technology research, developed by Pfizer, for the treament of postmenopausal osteoporosis. It was also under development for vaginal atrophy. Currently on Phase III clinical stage.

K-5211 (LGD-4033) is a novel selective androgen receptor modulator (SARM), under development by Ligand for the treatment of sarcopenia, muscle wasting, cachexia and osteoporosis. The drug was licensed to Viking Therapeutics, and currently on phase II.

Competative Landscape – Hypoparathyroidism:

The Hypoparathyroidism drugs landscape consists of a sole player -Natpara , developed by NPS which was acquired by Shire Pharmaceuticals. The drug was FDA approved in 2015, and is presently only available in the US. In 2016 the drug brought in revenues of \$85.3 million,⁴³ and the US market is forecasted to reach \$441.31 million by 2022.⁴⁴ Entera's orally delivered PTH hormone is intended to substitute the current Natpara solution. Moreover, the company estimates that its drug candidate will extend the treatment to a broader range of patients, and can treat moderate to severe patients, as well as mild.The market for rare-disease treatments is considered attractive, despite

⁴¹ Pharmaprojects-a drug development database

⁴² https://www.bloomberg.com/research/stocks/private/snapshot

⁴³ Shire PLC. Annual Report 2016. (2017).

⁴⁴ Evaluate Pharma, 2017

a small number of patients, because companies can increase prices dramatically. Despite the high cost (\$100k annually), insurers are usually willing to pay for the therapies because they have few members who need them and the drugs can be life saving.⁴⁵

The total worldwide market value for Natpara is shown at the table below:

Source: Evaluate Pharma

BeamMed

Company Overview

BeamMed is a medical device company offering unique ultrasound based solutions for Bone Health assessment and determining a patient's risk of developing osteoporosis. BeamMed was founded in 2004 and is headquartered in Israel. Its technology was acquired from Sunlight with IP rights in 2006. Ever since, BeamMed has extended its product line offering greater portability and userfriendliness; MinOmni is their most recently developed portable product, whilst the Omnisence 9000 is the latest product to go to market.

The company develops, manufactures and markets its products. Its products enable physicians to provide early assessment, diagnosis and monitoring of Osteoporosis with relation to a patient's risk factor. The technology is largely patented and based on quantitative ultrasound which has been proven effective as a screening tool for Osteoporosis.

Additionally, the company possesses an exclusive embedded database categorized by ethnic group (Caucasian, Asian, Chinese, North American, Latin American) and by sex/age (male, female and children), which compares the physical measurement with those in the relevant group to improve clinical accuracy. This database in conjunction with the preparatory algorithm is a non-patented asset which gives the company added value.

The company operates in the Bone Densitometers industry, and is mostly active in China. BeamMed operates in other territories as well such as Europe, Canada and the United States. Thousands of devices are already in use in clinics, physician offices, HMOs, research centers, hospitals, check-up centers and pharmacies around the world. The company's push into the United States is asserted by favourable demographics and by the favorability shown to 'screening' solutions by reimbursement bodies which minimizes long-term costs of treating the disease.

⁴⁵ DNA Biomedical Solutions, Financial Report for 2016. (2017)

Market, Standard of Care and Unmet Needs

Background

BeamMed's Sunlight product range utilizes their proprietary quantitative ultrasound-based technology, for early assessment of osteoporosis. Osteoporosis is a progressive systemic skeletal disease that is accepted as a major public health problem, with increasingly high associated costs.

When the level of calcium and phosphate decreases, bone density does so alongside. During a human lifespan, older bones are reabsorbed and new ones are created. The human skeleton is replaced approximately every 10 years. If the bone density does not remain balanced between older and newer bones, loss of bone structure occurs. The bone loss occurs silently and progressively, and there are often no symptoms until the first fracture occurs.⁴⁶ Finally, bone loss can lead to osteoporosis, a condition reducing bone mass and bone quality. Osteoporosis-related fractures increase dramatically with age and they often cause rapid deterioration in health, resulting in death. Sometimes this phenomenon runs in families and is inherited.⁴⁷ According to the International Osteoporosis Foundation (IOF), hundreds of millions of people worldwide are affected by osteoporosis, including approximately 80% of women. Every second woman and every fifth man over 50 years of age suffers from an Osteoporotic fracture. By 2050, the worldwide incidence of hip fracture is projected to increase by 310% for men and 240% for women.⁴⁸

Osteoporosis cannot be reversed. However, it can be effectively managed by early diagnosis of bone mass loss and by prevention of further loss. Osteoporosis assessments are used to diagnose and measure bone density, as these indicators can prevent further osteoporosis deterioration and fracture risks in older adults.

Osteoporotic bone

BeamMed. BeamMed Corporate Presentation. (2017)

Technologies for Osteoporosis Detection

Diagnosis of Osteoporosis consists of central and peripheral skeleton screening methods. Commonly, central Dual Energy X-ray Absorptiometry (DXA), an X-ray-based imaging approach, is used as the first-in-line diagnostic tool to detect osteoporosis. Traditionally, DXA technology is used for bone density tests measuring the minerals levels in bones. Bone Mineral Density (BMD) loss provides an indication of bone status. DXA is the gold standard for osteoporosis diagnosis in postmenopausal women, particularly those aged 65 and older.⁴⁹ The technology utilizes a beam of radiation with a common and sustained energy level, which gets absorbed or passed through tissues, depending on their density. The central DXA test is usually taken on the lower spine and hips to measure bone loss. When testing cannot be done on the hip and spine, a central DXA test of the radius bone in the forearm is taken. Other central technologies for diagnosis are based on MRI (Magnetic Resonance Imaging) and CT (Computerized Tomography).

More recently, peripheral screening tests have been developed to measure bone density in the lower arm, wrist, finger, and heel. Screening tests can help identify seemingly healthy people who are most likely to benefit from

⁴⁶ http://www.iofbonehealth.org/facts-statistics.

⁴⁷ Holick, MF. The American Journal of Clinical Nutrition 80.6. (2004). 1678S-1688S.

⁴⁸ http://www.iofbonehealth.org/facts-statistics.

⁴⁹ Hardy, K. Radiology Today V.14 No.10. (2013).

further bone density testing. They are also useful when a central DXA is not available. These tests are often conducted at health fairs or medical offices.

There are several types of peripheral tests, including pDXA (peripheral dual energy x-ray absorptiometry), pQCT (peripheral quantitative computed tomography) and QUS (quantitative ultrasound), the lattermost being that performed by BeamMed devices.

BeamMed's quantitative ultrasound bone screening technology

BeamMed's Sunlight screening devices (the Omnisense catalogue) utilize Omnipath Axial Transmission technology, which is based on quantitative ultrasound. Omnipath is a unique, patented, proprietary axial transmission technology based on the speed of ultrasonic waves propagating along the bone, i.e. Speed of Sound (SoS), in m/sec. Axially transmitted SOS correlates with bone strength since multiple bone properties, such as microstructure, elasticity, cortical thickness and bone density are accounted for in the result.

Technically, the ultrasonic wave propagation times are used by a proprietary algorithm to determine the bones SOS, independent of soft tissue thickness. The frequency of acoustic waves used by Omnisense's line of products are 1.25MHz. Omnisense precision error is 0.6% at the radius, one of the highest precision ratings in the industry. Based on Omnisense's high precision levels, the FDA approved it for use in monitoring bone changes in the most relevant age group: pre- and post-menopausal women, 50-65 years of age. The output of measurement with Sunlight devices is expressed as a Z-score and a T-score, in addition to SoS in m/sec. A T-score bone density compares the specific bone density to that of a healthy adult at age 30. With this score, the physician is able to diagnose Osteopenia or Osteoporosis and determine if the patient has a greater risk of fracturing or breaking a bone. A Z-score compares the bone density to the relevant age group and body size. Additionally, BeamMed's exclusively embedded database categorized by ethnic group (Caucasian, Asian, Chinese, North American, and Latin American), whilst distinguishing between children/adults and between genders, assigns the physical measurement to the relevant group. All results are depicted graphically in a report that can be stored and printed. The software includes patient history and scheduling features, which enable efficient tracking of measurement history. It has a convenient USB-port connectivity to Windows, ideal for use in any physician's office or medical clinic, pharmacy, or annual checkup center. Finally, the technology also has the potential to serve as the basis for collaborative partnerships with OEMs.

Market Overview

BeamMed has been manufacturing and selling ultrasonographical medical devices for more than a decade. The International Osteoporosis Foundation estimates that 200 million people suffer from osteoporosis worldwide. The principal driver of this growth is the increasing geriatric share of the world's population. Osteoporosis is both an underdiagnosed and undertreated disease with therapy costs exceeding those of, for instance, breast cancer. Perhaps a reason behind this surprising fact is that the latter has a well-established screening market (Solomon, 2014). The diagnosis of osteoporosis in its early stages can improve people's quality of life and lower direct and indirect costs. Traditionally, central Dual Energy X-ray Absorptiometry (DXA), an X-ray-based imaging approach, is used as the first-in-line diagnostic tool to detect osteoporosis. BeamMed and other peripheral screening providers are positioned at the start of the Osteoporosis Care Market's value chain, dominating the screening segment (prediagnosis), addressing healthy patients 'at risk' of developing osteoporosis Care Market's value chain, BeamMed's products are not substitutes for DXA, which is still considered to be the gold standard.

Market Drivers & Consolidators

• **Demographic trends**. The geriatric share of the world's population is increasing. Every second woman and every fifth man over 50 years of age suffers an Osteoporotic fracture. Approximately 75 million of the total 200 million

worldwide patients live in Europe, the US or Japan, widely considered to be the most attractive markets due to high retirement savings, pension rebates and propensity to pay.⁵⁰

- Insurance Reimbursement. Favourable policy towards screening solutions in general, and those for Osteoporosis in particular, appeals to end-users. Positive results from regulatory agencies, which determine the favorability of reimbursement policies, have been awarded to BeamMed by both public and private authorities across key global markets.
- Market Need. The International Osteoporosis Foundation estimates that more than 70% of those at risk have never been diagnosed or screened. This indicates a pressing need for easy, cost-effective and safe early assessment tools.
- **Technological Drive.** The ultrasound industry is currently seeking innovative avenues to perform decisive, non-invasive diagnostic testing. The technological upgrades of ultrasonographic devices coupled with their reproducibility are driving this trend by ensuring better clinical output alongside increased affordability. BeamMed is part of this transformation as the leader in multi-site ultrasound-based Osteoporosis screening.⁵¹
- Market education. While those with fractures are likely to get themselves diagnosed, and those with a confirmed diagnosis will almost certainly seek treatment, without sufficient market education, there is no guarantee that those at risk will get themselves screened. Fortunately, from the BeamMed's perspective, their view of this practice as a market flaw is asserted by key actors in the healthcare supply chain.

Bone Densitometers Market

Market Value

The Global Bone Densitometers Market is set to grow at a CAGR of 3.1% (2016-24) to \$1.1B by 2024 (Transparency Market Research, 2017). Within this market, BeamMed's activities fall under the Peripheral Bone Densitometry segment, and their product competes as a quantitative ultrasound solution.

Market Size

Recently, experts have cited an increase in incidence rates among women who contract osteoporosis during menopause. Moreover, the geriatric correlation is also significant among females with 67% of 90-year-olds, 40% of 80-year-olds, 20% of 70-year-olds and 10% of 60-year-old women suffering from the disease. In addition, 33% of women over age 50 will experience at least a single osteoporotic fracture.⁵² Whilst relative incidence among males is lower, the real growth in the number of male patients is also driving the market. This increase can be partially attributed to lifestyle factors that are statistically more prevalent among men and which are known to deteriorate

⁵⁰ http://www.grandviewresearch.com/industry-analysis/osteoporosis-drug-market;

http://www.transparencymarketresearch.com/bone-densitometers-market.html; DNA Biomedical Solutions. Annual Report for 2016. (2017).

⁵¹ Frost & Sullivan. BeamMed - Best Practice Award. (2015).

 $^{^{52}\} https://www.iofbonehealth.org/facts-statistics\# category - 19.$

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bone health, including: a sedentary lifestyle, alcohol and tobacco abuse.⁵³ Incidence among men for medical conditions is generally lower as they are far less likely to seek medical assistance than women. Recent awareness programs to address this issue will see increased incidence numbers in both real terms, and relative to females.

Geographic Segmentation

Prior to their recent push into the US market, *BeamMed*'s core focus had been in East Asia, particularly Mainland China. This strategy reflects the market demand in terms of patient numbers. The region is the world's most populous, and the geriatric share thereof is growing, most rapidly in China. By 2050, 50% of all osteoporotic hip fractures will occur in Asia.⁵⁴ Much like in other geographies, healthcare reimbursors favor screening solutions as early detection may reduce long-run treatment costs. China's elderly are disproportionately situated in rural areas, and therefore a small, portable, affordable and yet reliable screening tool is necessary to reach hundreds of millions of people.

Whilst East Asia may host the largest market size when measured by potential patient population, the most lucrative market financially is undoubtedly the US. This is generally consistent across healthcare markets, however several distinct market dynamics make the US especially attractive for the Osteoporosis Care Market, and even more so for companies offering screening solutions there. Once again, the demographics are rather favorable with a growing relative geriatric population, and with incidence far higher in females, a stable gender balance like that in the US is very important. Dissimilarly and far less favorably, China has a unique gender imbalance in favor of males. Having said that, the US market profile is less attractive than East Asia regarding causative trends such as; substance abuse, vitamin deficiency and insufficient calcium levels. These are still prevalent across the US and assuming this continues, the at-risk population may number 61 million, and the patient population 14 million by 2020.⁵⁵

Health Insurance Coverage

The estimated annual direct medical costs of osteoporotic fractures are predominantly covered by Medicare and will increase significantly by 2025. In parallel, Medicare's national average payment for DXA testing in physician offices has decreased from \$139.46 to \$61.70, with costs to the provider standing at around \$70. These policies have been reinstated by the Affordable Healthcare Act, and therefore the market is ripe for solutions such as BeamMed's to screen patients on mass, and only refer those with higher risk scores for DXA scans.⁵⁶

Medicare links healthcare providers' payments and financial bonuses to their HEDIS quality rating. HEDIS (Healthcare Effectiveness Data and Information Set) is a widely used set of quality performance measures in the US healthcare industry for comparing health plans and for tracking year-over-year performance. Improved HEDIS scoring increases the payments a healthcare provider is eligible to receive from Medicare. Specifically with regard to osteoporosis screening, Medicare recommends a bone density test every 23 months for women over the age of 67. Moreover, the higher the risk score of a patient the higher the reimbursement received by the physician.⁵⁷ Private insurers reference a different rating system, MACRA, and offer greater coverage for procedures with higher MACRA scores. BeamMed's favourable ratings under HEDIS, and potentially under MACRA incentivize end-users to purchase their machines.

With reimbursement in non-facility settings declining and many primary-care physicians doing away with their hefty DXA machines, BeamMed can take advantage of favourable point-of-care circumstances. End-users are looking for new innovative, compact, and most of all, profitable replacements and BeamMed's products seemingly 'tick all the boxes'.⁵⁸

⁵³ http://www.grandviewresearch.com/industry-analysis/osteoporosis-drug-market.

⁵⁴ BeamMed. BeamMed. Corporate Presentation. (2017).

⁵⁵ https://www.iofbonehealth.org/facts-statistics#category-19

⁵⁶ Singer, A. Osteoporosis International. (2014).

⁵⁷ BeamMed. Corporate Presentation. 2017.

⁵⁸ Hardy, Radiology Today V.14 No.10. (2013).

Company's Products

BeamMed's mission is to provide an alternative method of care in assessing one's risk of developing osteoporosis. Their product offers an affordable, convenient and radiation-free bone density test by means of quantitative ultrasound. The screening results provide insights into the skeletal fragility, which assists physicians in diagnosing or predicting the chances of developing osteoporosis.

BeamMed's Sunlight Omnisense product is a bone densitometer that can carry out measurements at multiple skeletal sites, allowing for a greater chance of identifying individual cases of osteoporosis. This flexibility is very important, especially for patients who cannot be tested at a particular skeletal site.

BeamMed's Omnisense line of products are compact, lightweight, portable and standalone, do not require any external infrastructure except for electric power, and are therefore ideal for use in any clinic or physicians' office. The measurement database is segmented by gender, age, and ethnicity making it suitable for assessing bone density in patients aged 0-99 years, even in neonates.

The technology, which refers to the probe design and the Omnipath axial ultrasound signal transmission, is largely patented until 2021. The aforementioned database additionally includes a unique application and reference database for optimal screening of Chinese children. Moreover, the company has developed a proprietary algorithm that determines bones' Speed of Sound (SOS). Both assets are not patented, but are exclusively used by the company.

BeamMed's Product Line:

- **Omnisense 7000**, the flagship product in the Sunlight family of Omnipath-based solutions. The system has been marketed since 2000 and has been installed in thousands of locations worldwide,
- **Omnisense 8000** is a portable version of the Omnisense 7000, offering examinations in territories where access to DXA is not possible.
- **Omnisense 9000** offers the same extensive functionality as the Omnisense 8000, however additionally features a cable-free touch-screen and a user-friendly interface, ideal for use in clinics, pharmacy or any other point of care with a heavy workload. Omnisense 9000 is based on a panel PC computer with advanced hardware and software.
- MiniOmni is a smaller and more advanced version of the Sunlight Omnipath quantitative ultrasound proprietary technology, offering increased portability at a lower cost. Unlike the other systems in the series, which are bundled with a computer, MiniOmni includes an electronic card, probe and software with USB connectivity into any Windows™ 7/8-based laptop or desktop computer.
- **Tetrax**, a medical device originally developed by Tetrax Ltd, for diagnosing posture issues and imbalance. As of December 2012, distribution is limited to China, Korea, Singapore and Malaysia

BeamMed offers the following products for the pediatric population:

- Sunlight BonAge is an innovative Pediatric Configuration ultrasound device for accurate bone age evaluation of pediatric skeletal development and growth, based on the proven Sunlight Omnisense technology. BonAge has not yet been approved by the FDA.
- Sunlight Pediatric Software allows an accurate bone density assessment of children aged 0-18 years. It functions with any of the Sunlight range of bone densitometers: Omnisense 7000, Omnisense 8000, and MiniOmni. Sunlight Pediatric was developed in response to the growing need to measure and monitor children during their critical growth years.
- Sunlight PREMIER Software enables safe and accurate bone density assessment in premature babies. The widespread prevalence of osteopenia of prematurity (OOP) among pre-term infants makes Sunlight PREMIER an essential and unique tool in hospitals' neonatal units. Currently, the company does not promote this product due to strategic and logistic considerations.

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BeamMed. BeamMed Corporate Presentation. (2017)

Omnipath based devices are installed in the thousands worldwide, though mainly in mainland China. Omnisense multi-site ultrasound devices, allow for first-line early assessment, diagnosis and monitoring of osteoporosis. Countries with distribution channels include: China, India, Hong Kong, Taiwan, and Philippines. BeamMed's largest markets are in China and the US.

Omnisense systems have class III Pre Market Approval (PMA) from the FDA for marketing in the US since 2000 (this was first granted to Sunlight, which was acquired by BeamMed in 2006). Due to hardware changes in the more advanced series' devices, Ominsense systems were reclassified as class II under the 510K regulatory pathway in 2008. In October 2011, BeamMed received 510K market approval for the MiniOmni, its latest product in the Omnisense series. Additionally, MiniOmni and Sunlight Omnisense 9000 hold CE market approval in Europe. Moreover, BeamMed devices have market approval in China, Canada and Israel.

US Healthcare professionals performing examinations using BeamMed's Omisense and MiniOmni devices are reimbursed by both private insurance companies and Medicare. The company's products have been proven effective by dozens of healthcare providers, helping them gain Medicare stars, which are dependent upon HEDIS data collection protocol. In Asian countries where BeamMed operates, the medical system is mainly private, and therefore reimbursement issues do not limit BeamMed's sales. In China, BeamMed's devices are also acquired by public sector institutions such as hospitals.

Competitive analysis

In 2006, BeamMed began providing Osteoporosis patients with an alternative care diagnosis method using an affordable, convenient and radiation-free bone density test by means of quantitative ultrasound. BeamMed's Sunlight Ominsense devices were the first devices that enabled ultrasound-based, multi-site measurement for early assessment of Osteoporosis with a pioneering axial technology along the bone. The company operates in the Bone Densitometers industry, where several traditional diagnostic methods indirectly compete with the quantitative ultrasound technology, on which BeamMed's devices are based.

DXA bone density tests are perceived as the gold standard, however, usually these systems are room-sized and are expensive to purchase and operate. Bone density tests performed with central DXA technology are usually taken on the lower spine and hips, and expose patients to radiation. In recent years however, smaller roentgen machines with lower radiation have been developed that measure bone density above the wrists, hand and

fingers by companies such as Lunar-GE (IDXA, Prodigy), Hologic (Discovery, Explorer) and Osteometer Meditech (DXA-200, DexaCare).

BeamMed and its direct competitors are considered as providing peripheral screening tests, which are based on ultrasound and other technologies, such as pDXA (peripheral dual energy x-ray absorptiometry) and pQCT (peripheral quantitative computed tomography).

Direct competitors for the Omnisense systems are ultrasound based devices such as Hologic (Sahara), Lunar-GE (Achilles), Furuno (CM-200) and OsteoSys (Sonost 3000), as well as other smaller, less familiar players. The competitors mentioned all offer devices with ultrasound-based measurements taken at the heel. These devices are heavy, require water or oil circulation, are considered less accurate, and less convenient as patients need to remove their shoes to be tested. The Chinese market has witnessed limited competition from local players with devices similar to the Omnisese 7000. In conclusion, we believe that the company will face limited competitive hurdles in this market.

BeamMed's Sunlight product line overcomes the cost and radiation exposure challenges of Dual X-ray Absorption technology (DXA). Whereas DXA technology is used for bone density tests by measuring the amount of minerals in the bones, BeamMed's omnipath technology correlates with bone strength by multiple bone properties, such as microstructure, elasticity, cortical thickness and bone density, all accounted in the result. The price in the US for a bone density test ranges between \$70 - \$100, and \$9-\$10 after reimbursement by Medicare. The end user price for BeamMed's system is approximately \$9,000 in the US, wheras the price for competiting systems is in the range of \$10,000-\$12,000.

Additional advantages of BeamMed's devices include: high accuracy, light-weight, ease-of-use, user friendliness, and multi-site examination (lower arm, finger, tybia or metatarsal). The product can easily and safely be used at multiple points-of-care: doctors offices, clinics, HMOs, and retail venues such as pharmacies and check-up centers. Moreover, the company's line of devices are equipped with a unique built-in database which is segmented demographically. Having said that, BeamMed has a few relative disadvantages over competitors, primarily their products' measurement time, and their more limited scientific basis compared to GE devices.

BeamMed's unique sales strategy versus traditional technologies is in marketing its products to primary care clinics and parties that are interested in screening tests for larger populations rather than hospitals and X-ray centers. The device can be used by any trained operator, and in any physician's office. The relatively low price of the MiniOmni as well as its plug-in features to the physician's computer, considerably increases BeamMed's market share potential.

Financial Valuation and Projections

Financial Analysis

Entera Bio

Entera was incorporated on June 1, 2010. The Company is a clinical-stage biopharmaceutical company, focused on the development and commercialization of orally-delivered large molecule therapeutics. Currently, the company is focused on the development of oral capsules for the treatment of hypoparathyroidism and osteoporosis. Since Entera is engaged in research and development activities, it has not yet derived income from its activity and has incurred, through June 30, 2017, accumulated losses in the amount of \$34.4M

The company also has negative working capital and cash outflows from operating activities. Research and development expenses for H1 2017 were \$1.3M compared with \$0.9M for H1 2016. The increase is mainly due to

clinical trials conducted for the Entera's leading indications. As of June 30, 2017, the company holds \$2.4M in cash, and its deficit equity of \$26.7M (see Appendix A for P&L statement).

BeamMed

BeamMed is a private company, incorporated in Israel in April 2004. The company sells its systems worldwide, primarily in East Asia. In 2016, the company's revenues were \$3.1M (out of which, \$2.5M in Asia), compared with \$2.5M (\$2.1M in Asia) in 2015, and \$2.9M (\$2.3M in Asia) in 2014. According to BeamMed's management, the price for an end-user system is \$9K in the US and \$30-60K in Asia (primarily China).

Transfer prices for the company's retail operations are \$5-7K (primarily in the US and Asia). Gross profit was steady at 54% of revenues during 2015 and 2016. Marketing and sales expenses were \$630K in 2016, similar to that in 2015. General and administrative expenses were \$820K in 2016, similar to those in 2015. As of June 30, 2017, the company had \$2.1M in cash and a \$400K owner's loan. Equity as of June 30, 2017, stands at \$3.2M.

Valuation

<u>Entera Bio</u>

Clinical development: The company is set to begin phase 2b/3 clinical trials of its product for Hypoparathyroidism, and phase 2a of its second product for Osteoporosis by the end of 2017. An additional indication in the second product's pipeline addresses non-union fractures, an indication which currently has no proven treatment solution. Phase 2a initiation is expected at the beginning of 2018. Additional programs based on their platform are currently under development.

Distribution agreement: The company has two leading indications: EB 612 (Hypoparathyroidism) and the EB 613 (Osteoporosis). Below are our assumptions:

- Hypoparathyroidism We adopt the company's decision to take the drug into the market without a strategic partner. Thus, managerial focus will also be on sales and in establishing a sales force. We also expect higher profit margin as the company will form a sales force. We assume, based on the company's timeline, that they will introduce this drug to market in 2021.
- Osteoporosis the company plans on partnering with a large pharmaceutical company, whereby the partner will conduct a phase 2b/3 pivotal trial, regulatory approvals registrations and commercialization. The potential agreement with the partner would include milestone payments and annual royalty payments from sales of the drug (expected in 2025). We based our forecast on these recent deals and assume future deals will generate \$50M with 10% royalties from sales:

| Investor (Country) | Investee (Country) | Amount | Product | Date | | | |
|-----------------------------------|--|----------------|--|---------------|--|--|--|
| Johnson & Johnson | Protagonist | ¢EON4 | Inflammatory Bowel Disease | luno 2017 | | | |
| (US) | Therapeutics (US) | 2201vi | injectables in pill form | June 2017 | | | |
| Hefei (Sinopharm) (CN) | Oramed (IL) | \$50M | Orally ingestible Insulin | Nov. 2015 | | | |
| Google Ventures, | | | General platform, including; TNF-alpha | | | | |
| Novartis, AstraZeneca | Rani Therapeutics (US) | \$70M | inhibitors, interleukin antibodies, | Feb. 2016 | | | |
| and many others (US) | | | insulin and GLP-1 | | | | |
| 25 major financial | | \$26.4M (as of | Developing and commercializing oral | Via Nacdag in | | | |
| institutions (US) | Chiasma (US) | August 30, | therapies - Phase III clinical trial for the | 2017 | | | |
| | | 2017) | treatment of acromegaly | 2017 | | | |
| Sources: (1) (Business Insider Au | Sources: (1) (Business Insider Australia, 2017): (2) (Bouters, 2015): (3) (BioSnace, 2016): (4) (NASDAO, 2017) | | | | | | |

Success rates – the company engages in a high-risk therapeutic area in promoting its EB 612 indication. Success rate data indicate higher success rates for Endocrinology (40%) in comparison with the total average of all indications (31%) from phase II to phase III. However, phase III success rate is lower (65%) than the success rate for all indications (58%). We address these clinical risks in our rNPV valuation for each indication.

Osteoporosis as a relatively small therapeutic area is categorized under "others" by drug development/financial research as presented below:

Source: Clinical Development Success Rates, 2006-2015. Biomedtracker 2016.

Capitalization rate: We calculate our discount rate at 19.6%, based on our CAPM model (see Appendix B).

Main valuation parameters for EB 612 and EB 613

| Indications | Current development stage | Success Rate Phase II | Success Rate Phase III | Regulatory approval success rate | Launch | Patent period |
|--------------------|-------------------------------|--------------------------|---------------------------|--|--------|------------------|
| Hypoparathyroidism | 2b/3 (to commence in 2018) | 40% | Pivotal study | 65% | 2021 | 2029 |
| Osteoporosis | 2 | 40% | 70% | 86% | 2025 | 2029 |

| Parameters/Indications | | Hypoparathyroidism | Osteoporosis | |
|--|--|----------------------------|--------------|--|
| Total market per product (000K) | | 1,000,000 | 12,300,000 | |
| Market Growth (CAGR) | | 10% | 3.3% | |
| Company share from Market (Peak Sales) | | 25% | 20% | |
| Royalties to the Company/ gross profit | | 90% (10% cost of revenues) | 8% | |
| Royalties to original developer (Oramed) | | 3% | 3% | |

Based on the aforementioned parameters, we evaluate EB 612 based on rNPV of \$96.4M; we evaluate EB 613 based on rNPV of \$21.7M.

Technological Platform Valuation

Entera's product pipeline is supported by the company's broad business and technological base. Valuation of Entera's "technological basis" is in fact a valuation of the company's "residual value". This valuation was conducted using the Feed Rate methodology that is common in the field of life sciences, rather than using the conventional terminal value, normally used by non-life science companies, for the following reasons:

- The terminal value reflects a type of steady state in company sales with a certain fixed growth rate (g) based upon past data. This is not the case for life science companies, where the terminal value is derived from projects in development.
- The terminal value for a given company usually constitutes between 70-80% of its worth. In contrast, the main share of the value of a life science company is attributed to income generated during several years following product launch (for the most part, approximately 6-10 years), after which a certain decline occurs (for example, expiration of a patent, and the emergence of competing products).

The technological platform valuation is based on the average number of new projects that a company can yield annually. Estimating the capitalization value of future projects is based on pre-clinical and clinical development aspects, assessment of unallocated costs, and a higher capitalization rate than the one used during the forecast years, due to the uncertainty of the company's future projects.⁵⁹

Our valuation includes early clinical stage indications such as EB 613 PTH 1-34 non-union fractures and early stage trials. We view Entera's technological platform as basis for its management to carry out additional worthy technology acquisitions, and incorporate them into the company's product pipeline in advanced clinical phases.

Main technology platform valuation points:

- We assume one new project every four years with an average value of \$59.1M (equal to the average value of the current pipeline programs)
- Unallocated costs are mainly G&A and sales costs, with a similar share from the project's value as in the current pipeline programs
- We estimate unexpected costs to be 10% of the average value
- Statutory tax rate of 15% is assumed, which is lower than a federal tax of 35%

⁵⁹ Bogdan & Villiger, "Valuation in Life Science - Practical Guide", 2008, Second Edition.

- The capitalization rate is higher than the one used in the pipeline valuation, reflecting increased uncertainty
- It is assumed that the "platform" generates projects for n years: in our valuation, and based on the average patent period, n=13 years. We therefore subtract all projects generated after n years from the technological platform value .

The following formula reflects the value of the technology:

$$V(\text{tech}) = \frac{(fVproject - (1+r)costs)}{r} * 1 - \frac{1}{(1+r)^n}$$

Main valuation parameters of the technological platform:

| Average # of New Projects per Year | 0.25 |
|------------------------------------|---------|
| Project Value (\$K) | 59,070 |
| Unallocated Costs (\$K) | -40,820 |
| Unexpected Costs (\$K) | -5,907 |
| Тах | 15% |
| Capitalization | 24.6% |
| | |
| Terminal Technology Value (\$K) | 10,645 |
| Technology Value - 2017-2029 (\$K) | 608 |
| Technology Value (\$K) | 10,037 |

Equity Value

Non-operational assets/liabilities and unallocated costs

As of 30, June 2017, Entera has non-operational assets (cash) of approximately \$2.4M with an estimated annual burn rate of \$3.7M (\$300K per month based on their H1 2017 financial report). The company has Convertible Loans in the amount of \$4.5M. We subtract a bi-monthly burn rate of \$600K.

The equity valuation elements are presented in the table below:

Equity value:

| Pipeline Analysis | | <u>rNPV (\$K)</u> |
|---|------------------------------------|------------------------------------|
| EB 612 EB 613 Total rNPV Pipeline | Hypoparathyroidism Osteoporosis | 96,411 21,728 118,139 |
| Unallocated Costs | | -40,820 |
| Terminal Technology Value | | 10,037 |
| Enterprise Value | | 87,357 |
| Non-operational assets/liabilities | | -2,783 |
| Equity Value | | 84,574 |

Sensitivity Analysis

The table below presents Entera's equity value in relation to the capitalization rate. We set a range of 0.5% change from our CAPM model (see Appendix B).

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Sensitivity Analysis - Capitalization Rate vs. Equity Value

| <u>Cap. rate</u> | <u>Equity Value (\$K)</u> |
|------------------|---------------------------|
| 20.6% | 74,135 |
| 20.1% | 79,216 |
| 19.6% | 84,574 |
| 19.1% | 90,225 |
| 18.6% | 96,188 |

We estimate Entera's equity value to be in the range of \$79.2M - \$90.2M; a mean of \$84.6M.

BeamMed

Forecast

According to the company's management, as of 2017 the company has signed with three leading US distributors: McKesson, Henry Schein and Medline. Thus, we believe sales will increase in the US and Asia in the coming years. We set our valuation for the next 5 years, until 2022. Below is our revenue forecast:

| Revenues by Market | | | | | | | | | |
|---------------------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|
| Sales (\$K) | | | | | | | | | |
| <u>Year</u> | <u>2014A</u> | <u>2015A</u> | <u>2016A</u> | <u>2017E</u> | <u>2018E</u> | <u>2019E</u> | <u>2020E</u> | <u>2021E</u> | <u>2022E</u> |
| Asia | 2,334 | 2,052 | 2,467 | 2,660 | 2,800 | 3,150 | 3,150 | 3,500 | 3,850 |
| % of rev. | 82% | 81% | 78% | 70% | 58% | 53% | 45% | 47% | 46% |
| ROW | 265 | 194 | 254 | 300 | 300 | 300 | 300 | 400 | 400 |
| % of rev. | 9% | 8% | 8% | 8% | 6% | 5% | 4% | 5% | 5% |
| America | 255 | 302 | 428 | 840 | 1,750 | 2,450 | 3,500 | 3,500 | 4,200 |
| % of rev. | 9% | 12% | 14% | 22% | 36% | 42% | 50% | 47% | 50% |
| Total | 2,855 | 2,548 | 3,149 | 3,800 | 4,850 | 5,900 | 6,950 | 7,400 | 8,450 |

We then assume a minor improvement in cost of sales. As the company's sales increase, fixed costs will decrease (by 4% in our forecast). The company will retain a similar profit margin with steady growth in marketing and sales (we assume a CAGR of 5%). For general and administration expenses, we assume a 2% CAGR.

Below is our P&L forecast:

| Year | <u>2015А</u> <u>(\$К)</u> | <u>2016А</u> <u>(\$К)</u> | <u>2017Е</u> <u>(\$К)</u> | <u>2018Е</u> <u>(\$К)</u> | <u>2019Е</u> <u>(\$К)</u> | <u>2020Е</u> <u>(\$К)</u> | <u>2021Е</u> <u>(\$К)</u> | <u>2022E</u> <u>(\$K)</u> |
|-------------------------------------|------------------------------|------------------------------|------------------------------|------------------------------|------------------------------|------------------------------|------------------------------|------------------------------|
| Total revenues | 2,548 | 3,149 | 3,800 | 4,850 | 5,900 | 6,950 | 7,400 | 8,450 |
| YoY % | | 24% | 21% | 28% | 22% | 18% | 6% | 14% |
| | | | | | | | | |
| COGS | 1,163 | 1,463 | 2,052 | 2,522 | 2,950 | 3,475 | 3,700 | 4,225 |
| Net Earnings | 1,385 | 1,686 | 1,748 | 2,328 | 2,950 | 3,475 | 3,700 | 4,225 |
| | 54% | 54% | 54% | 52% | 50% | 50% | 50% | 50% |
| | | | | | | | | |
| Marketing and Sales Expenses | 663 | 629 | 660 | 693 | 728 | 765 | 803 | 843 |
| % of rev. | 26% | 20% | 17% | 14% | 12% | 11% | 11% | 10% |
| General and Administrative Expenses | 767 | 821 | 821 | 837 | 854 | 871 | 889 | 906 |
| % of rev. | 30% | 26% | 22% | 17% | 14% | 13% | 12% | 11% |
| | | | | | | | | |
| Operating profit (loss) | - 45 | 236 | 267 | 797 | 1,368 | 1,839 | 2,009 | 2,476 |
| % of rev. | -2% | 7% | 7% | 16% | 23% | 26% | 27% | 29% |

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Valuation - Key points:

- As of June 30, 2017, the company holds \$2.1M in cash and an owner's loan of \$400K.
- Depreciation and CapEx will remain constant until the terminal year where we set a similar pattern.
- Changes in working capital are high due to the company's business model.
- Statutory tax is 23%.
- The discount rate of 18.7% is based on our CAPM model (see Appendix B).

| Enterprise Value (EV) | \$K |
|--|-------|
| EV - 2017-2022 | 3,403 |
| EV - Terminal value | 3,599 |
| EV - Company | 7,002 |
| Non-operational assets/liabilities | |
| Cash | 2,151 |
| Loans | -394 |
| Total Non-operational assets/liabilities | 1,757 |
| Equity Value | 8,759 |

Sensitivity Analysis

The table below presents BeamMed's equity value in relation to the capitalization rate. We set a range of 0.5% change from our CAPM model (see Appendix B).

Sensitivity Analysis - Capitalization Rate vs. Equity Value

| Cap. rate | Target Price (\$K) |
|-----------|--------------------|
| 19.7% | 8,330 |
| 19.2% | 8,538 |
| 18.7% | 8,759 |
| 18.2% | 8,994 |
| 17.7% | 9,243 |

We estimate the equity value to be in the range of \$8.5M - \$9.0M, with a mean of \$8.8M.

D.N.A Biomedical solutions

DNA is a holding company, which holds, based on the company financial reports, 35% in Entera and 40% in BeamMed (fully diluted).

In a recent capital raising dated 8, October 2017, Entera completed fund raising of \$10.2M (based on a \$97M equity value, fully diluted). This represents DNA share (35%) in \$34M.

It is worth mentioning that Entera's capital structure is currently undergoing changes prior to their IPO (Initial Public Offering), which is expected in the next coming months.

Thus, we calculate DNA's equity value as follow:

| \$K | 100% | DNA share | DNA share |
|---|---------|-----------|-----------|
| Entera rNPV | 84,574 | 35% | 29,601 |
| BeamMed – rNPV | 8,759 | 40% | 3,504 |
| | | | |
| DNA - Pipeline Value | 33,105 | | |
| | | | |
| DNA General and Administrative Expenses | (2,498) | | |
| Non operational assests/liabilities | | | |
| Cash | 287 | | |
| Total non operational assests | 287 | | |
| Equity Value | 30,894 | | |

Based on the above, we evaluate DNA's equity value at \$30.9M/NIS 110.0M; a stock target price of NIS 0.83.

Investment Thesis and Price Forecast Risks

Biotech companies, particularly those in the research and development stage, are relatively high-risk companies. Key risks that may affect DNA include:

Delay/postponement of marketing regulatory approval decisions

In order for DNA to market or out-license its products, it is necessary for them to receive marketing approval from regulatory agencies, such as the FDA (US) and EMA (EU). Our estimates regarding time to market are based on the assumption that these products will successfully complete Phase II- and III clinical trials without significant delays. Failure to fulfill the clinical endpoints of these experiments will force the company to conduct additional clinical trials or abandon the development of certain projects. We consider this to be the main risk factor for the company's activity at this stage.

Risks involved in obtaining sources of financing, and stock trading

As a biotech holding company in the research and development stage, with minimal revenue from sales, DNA will be required to conduct fundraising prior to becoming profitable, unless early licensing deals are made. Failure to raise funds, or fundraising under conditions that are not beneficial to the company, may affect its worth. In addition, the low level of tradability may deter some investors from buying DNA stock.

General risks related to similar companies

The value of small companies in the biotech field could, to a relatively high degree, be affected by publications not related directly to their activities. Such publications may refer, for example, to competitors, macro trends in the healthcare sector, and political events.

Contact Details & Management

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Ze'ev Bronfeld is the Chairman of the DNA Biomedical Solutions Ltd. Directorate. In this capacity he also serves as a Director of Entera Bio and DNA. Mr. Bronfeld has served as a director of Protalix Ltd. since 1996, and brings vast experience in management and in growing biotechnology companies. He has served as its Chief Executive Officer since 1986.. He holds a B.A. in Economics from the Hebrew University of Jerusalem.

Yonatan Malcha is the General Manager and Director of DNA Biomedical Solutions Ltd. Mr Malcha was previously co-CEO of Ethos Capital Ltd. He is acting Chairman of CardioArt Technologies Ltd, a manufacturer and marketer of measurement equipment for treating Congesative Heart Failure (CHF). Mr Malcha holds a BA in Economics and Statistics and an MA in Economics and Finance – both from Bar Ilan University.

Tony Klein is the deputy CEO (Finances) of DNA Biomedical Solutions Ltd. Mr Klein was previously a Senior Manager at Kesslman & Kesslman (PwC, Israel) and Financial Manager at Biomedix, a leading Health Technology Incubator. Mr Klein has a BA in Economics and Accounting from the Ruppin Academic Centre and is a certified accountant.

Extracted from: DNA Biomedical Solutions, Annual Report for 2016. (2017). pp.2,13,16.

BeamMed Ltd.

| Beam | eamMed Inc. BeamMed Ltd. | | /led Ltd. |
|------|-----------------------------|--------|--------------------------|
| U.S. | 950 South Pine Island Drive | Israel | 8 HaLapid St. |
| | Plantation, FL 33324 | | Petah Tikva 4925822 |
| | P: +1 (800) 769-6808 | | P: +972-3-9236869 |

Tal Marom is the CEO of BeamMed. Prior to joining BeamMed in 2007, he founded and served as CEO of Mennen Medical Ventures, a private investment company that was spun off from international medical devices company Mennen Medical, where he had been VP Sales and Marketing. Previously, Mr Marom was VP Sales at Top Image Systems and prior to that Director of Government Projects at the company. Earlier, he was an Investment Manager at Koor Technologies and worked as a lawyer at the Tel Aviv law firm of I. Gornitzki & Co. Mr Marom holds a BA in Accountancy and a LLB (Law), both from Tel Aviv University.

Gilad Zamir is the VP Sales and Marketing of BeamMed. He joined BeamMed in 2007 from Mennen Medical where he served as a Regional Sales Manager for Europe and Asia-Pacific and as Product Manager of the company's monitors product line. Prior to that, he held similar positions at Flowmedic, which focuses on medical devices for treating circulatory disorders. Previously, he was Marketing Manager at MB Innovative Medical Technology, and a Product Manager at Dover Medical and Scientific Equipment. A qualified lawyer, Mr Zamir worked at leading Tel Aviv law firm Shachal & Co. He graduated as a Practical Bio-Med Engineer with expertise in Respiratory Therapy and Biomedicine Pumps from the Tel Aviv Biotechnology Institute and he holds a BA in Law from the Ramat Gan Academic College for Law.

Tsafrir Rubin is the CFO at BeamMed. Mr Rubin joined BeamMed in 2008 from the Carlton Tel Aviv Hotel where he was CFO and accountant. In this role, he oversaw the hotel's finances, inventories and expenditures and was responsible for its information technology systems. Earlier, he worked as an accountant for Rozanski Halifi Meiri &

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Co., where he performed audits on private and public companies and internal audits for publicly-listed corporations. Mr Rubin is a Certified Public Accountant with a BA in Business Administration and Finance from the College of Academic Management Studies, Israel.

Extracted from: BeamMed Official Website

Entera Bio Ltd.

Entera Bio Ltd.

Kiryat Hadassah Minrav Building, 5th Floor PO BOX 12117 **E:** info@enterabio.com Jerusalem 91220 ISRAEL

Luke Beshar is the Executive Chair and Director of *Entera Bio*. Mr Beshar is the Former CFO of NPS Pharmaceuticals, the company that developed Natpara. He has over 35 years of executive and financial leadership and was instrumental in repositioning NPS as a global leader in rare diseases and the \$5.2 billion buyout of NPS by Shire.

Dr Phillip Schwartz is the Chief Executive Officer of *Entera Bio*. Dr. Schwartz has over 25 years of direct experience in research and drug development, with more than 15 years at Dana Farber Cancer Institute, Harvard Medical School, and Rockefeller University. For 10 years he held leading roles in Clinical Affairs and Business Development with both Serono and Endo Pharmaceuticals.

Dr Roger Garceau is the Chief Development Advisor and Director of *Entera Bio*. Dr Garceau is the Former CMO of NPS Pharmaceuticals and an expert in GlobalClinical Development and Regulatory Affairs for orphan drugs. He has more than 30 years of industry expertise, most recently having led the Natpara clinical development and regulatory approval process.

Mira Rosenwig is the Chief Financial Officer of *Entera Bio*. Ms. Rosenzweig has over 15 years of experience in financial and executive management. Prior to Entera Bio, she was VP and CFO at Camtek Ltd. (NASDQ: CAMT) and Director of Finance at Elron Electronics (NASDQ-TASE: ELRN).

Dr Hillel Galitzer is the Chief Operating Officer of *Entera Bio*. Dr. Galitzer has over 15 years of biotech and research experience, most recently leading early-stage biotech companies and previously conducting medical research in various therapeutic areas. Dr. Galitzer has a PhD in Medical Research -Molecular Biology from the Hebrew University Jerusalem, focusing on PTH and calcium regulation.

Extracted from: Entera Bio Investor Presentation. p.39.

Appendicies

Appendix A - Financial Reports

DNA Biomedical Solutions Ltd.

| Balance Sheet (ILS 000s) | 2015 | 2016 | Q2-2017 |
|---|---------|---------|---------|
| Current Assets | 11,440 | 21,928 | 1,149 |
| Cash and Cash Equivilents | 8,709 | 16,942 | 1,021 |
| Deposits withheld | - | 4,132 | - |
| Receivables and Accounts receivable | 2,731 | 854 | 128 |
| Non-Current Assets | 16,309 | 16,246 | 100,027 |
| Fixed Assets | 752 | 766 | - |
| Non recognized Assets | 9,336 | 9,201 | 94,629 |
| Investment in shared transactions | 6,221 | 6,279 | 5,398 |
| Total Assets | 27,749 | 38,174 | 101,176 |
| Current Liabilities | 4,560 | 40,879 | 927 |
| Payables and Accounts Payable | 3,729 | 2,872 | 927 |
| Loans exchanged for shares | - | 38,007 | - |
| Bonds convertible into shares | 831 | - | - |
| Non-current Liabilities | 107,813 | 80,708 | 0 |
| Loans exchanged for shares | 31,423 | 18,591 | - |
| Shares of subsidiary company | 50,968 | 42,414 | - |
| Options of subsidiary company | 16,903 | 18,456 | - |
| Liabilities for sale of shares and stock options for subsidiary company | 8,405 | 1,050 | - |
| Net liabilities from employee-employer terimination | 114 | 197 | - |
| Total Liabilities | 112,373 | 121,587 | 927 |
| Equity | 84,624 | 83,413 | 100,249 |
| Total Liabilities + Equity | 27,749 | 38,174 | 101,176 |

| Profit and Loss Statement (NIS 000s) | 2014 | 2015 | 2016 | Q2-2016 | Q2-2017 |
|--|--------|-----------------|--------|---------|---------|
| Part in Companies' Losses | - | - | - | - | 12,437 |
| R&D Expenses | 7,360 | 8,215 | 10,171 | - | - |
| G&A Expenses | 5,234 | 8,253 | 12,326 | 970 | 902 |
| Profits on investments in financial assets at fair value through profit/loss | 218 | - | - | - | - |
| Portion of profits (losses) - Shared transaction | 230 | 328 | 148 | 137 | 118 |
| Operating Loss | 12,146 | 16,796 | 22,349 | 1,107 | 13,221 |
| Decrease/Increase in financial liabilities measured in fair value through | 67,934 | 1,736 | 16,558 | - | - |
| profit/loss | | | | | |
| Finacial expenses | 228 | 559 | 572 | 15 | - |
| Losses before tax on revenues | 80,308 | 19,091 | 6,363 | 1,122 | 13,221 |
| Tax rebates | 550 | - | - | 5,394 | 202,840 |
| Total Yearly Loss | 79,758 | 19, 0 91 | 6,363 | 4,272 | 189,619 |
| Fund for conversion differences | 5,351 | 334 | 1,275 | 90 | 10,648 |
| Subtraction of differences between reports of subsidiaries which were | - | - | - | - | 4,529 |
| released alongside | | | | | |
| Fund for conversion differences | - | - | - | 1,299 | - |
| Total Net Annual Loss | 85,109 | 19,425 | 7,638 | 5,481 | 183,500 |
| Loss to owners of the company | 72,275 | 17,535 | 5,932 | 3,767 | 189,619 |
| Loss to those without controlling stakes | 7,483 | 1,556 | 431 | 505 | - |
| Sub Total | 79,758 | 19, 0 91 | 6,363 | 4,272 | 189,619 |
| Net loss to owners of the company | 77,061 | 17,835 | 4,784 | 4,855 | 183,500 |
| Net loss to those without controlling stakes | 8,048 | 1,590 | 304 | 626 | - |
| Sub Net Total | 85,109 | 19,425 | 5,088 | 5,481 | 183,500 |
| Loss based on shares attributed to owners of the company (ILS) | 0.70 | 0.16 | 0.05 | 0.03 | 1.62 |
| Diluted loss per share attributed to owners of the company (ILS) | 0.70 | 0.16 | 0.16 | 0.05 | 1.02 |

BeamMed Ltd.

| Balance Sheet (NIS 000s) | 2015 | 2016 | Q2-2017 |
|---|--------|--------|---------|
| Current Assets | 11,997 | 12,265 | 3,541 |
| Cash and Cash Equivalents | 5,870 | 5,728 | 2,029 |
| Restricted Deposits | 640 | 635 | 122 |
| Accts Receivables (Customers) | 152 | 373 | 69 |
| Other Receivables | 951 | 1,589 | 215 |
| Inventory | 4,384 | 3,940 | 1,106 |
| Non-current Assets | 3,858 | 3,090 | 806 |
| Intangible Assets | 3,712 | 2,979 | 707 |
| Deffered Income Taxes | - | - | 72 |
| Fixed Assets | 146 | 111 | 27 |
| Total Assets | 15,855 | 15,355 | 4,347 |
| Current Liabilities | 3,488 | 2,182 | 974 |
| Accts Payable (Suppliers) | 1,238 | 185 | 170 |
| Other Payables | 796 | 510 | 375 |
| Loans from shareholders | 1,454 | 1,487 | 394 |
| Tax Payable | - | - | 35 |
| Non-current Liabilities | 106 | 414 | 176 |
| Deffered Income Taxes | 0 | 395 | 127 |
| Royalties owed to Government of Israel | - | - | 49 |
| Net Liabilities from employee termination | 106 | 19 | - |
| Total Liabilities | 3,594 | 2,596 | 1,150 |
| Total Equity | 12,261 | 12,759 | 3,197 |
| Share-based equity | 9 | 10 | 3 |
| Premium on shares | 16,120 | 16,123 | 4,253 |
| Shares in Financing | 720 | 720 | - |
| Equity fund for payments by shares | 481 | 478 | 140 |
| Cost of company shares held in self-retention | - | - | 170 |
| Minority Interest | - | - | 36 |
| Total Losses | 3,629 | 3,132 | 993 |
| Total Liabilities + Equity | 15,855 | 15,355 | 4,347 |

| Statement of Profit and Loss (\$000s) | 2015 | 2016 | Q2-2016 | Q2-2017 |
|---------------------------------------|-------|-------|---------|---------|
| Sales | 2,548 | 3,149 | 1,208 | 1,736 |
| COGS | 1,163 | 1,463 | 611 | 771 |
| Net Earnings | 1,385 | 1,686 | 597 | 965 |
| Marketing and Sales Expenses | 663 | 629 | 263 | 369 |
| General and Administrative Expenses | 767 | 821 | 365 | 446 |
| Revenue (Loss) from operations | 45 | 236 | 31 | 150 |
| Financing Expenses | 27 | 27 | 14 | 14 |
| Financing Income | 12 | 34 | 28 | 31 |
| Net Financing Expenses/Income | 15 | 7 | 14 | 17 |
| Profit/Loss before income tax | 60 | 243 | 17 | 167 |
| Income tax | 0 | 30 | - | 60 |
| Total Net Annual Profit/Loss | 60 | 213 | 17 | 107 |
| Loss to controlling stakeholders | 57 | 225 | 16 | 110 |
| Loss to other stakeholders | 3 | 12 | 1 | 3 |

Entera Bio Ltd.

| Balance Sheet (US\$000s) | 2015 | 2016 | Q2-2017 |
|--|--------|--------|---------|
| Current Assets | 1900 | 5433 | 2,777 |
| Cash and Cash Equivalents | 1,205 | 4,163 | 2,340 |
| Restricted Deposits | 0 | 1,075 | 23 |
| Other Current Assets | 695 | 195 | 414 |
| Non-current Assets | 847 | 853 | 881 |
| Property and equipment | 193 | 199 | 227 |
| Intangible assets | 654 | 654 | 654 |
| Total Assets | 2,747 | 6,286 | 3,658 |
| Total Current Liabilities | 804 | 10,542 | 11,345 |
| Accounts Payable (Trade) | 351 | 53 | 255 |
| Accounts Payable (Other) | 453 | 604 | 772 |
| Convertible Loans | 0 | 9,885 | 10,318 |
| Total non-current Liabilities | 27,630 | 20,990 | 19,078 |
| Convertible Loans | 8,053 | 4,835 | 4,530 |
| Preferred shares | 13,062 | 11,031 | 9,649 |
| Warrants to purchase preferred shares and shares | 4,332 | 4,800 | 4,629 |
| Issuing of preferred shares and warrants | 2,154 | 273 | 214 |
| Net severance pay obligations | 29 | 51 | 56 |
| Total Liabilities | 28,434 | 31,532 | 30,423 |
| Total Equity | 25,687 | 25,246 | 26,765 |
| Other comprehensive income | 41 | 41 | 41 |
| Other reserves | 1,354 | 2,844 | 5,091 |
| Additional paid in capital | 2,335 | 2,485 | 2,485 |
| Accumulated deficit | 29,417 | 30,616 | 34,382 |
| Total Liabilities + Equity | 2,747 | 6,286 | 3,658 |

| Statement of Profit and Loss (US\$000s) | 2015 | 2016 | Q2-2016 | Q2-2017 |
|---|-------|-------|---------|---------|
| Research and Deveopment Expenses | 2,115 | 2,648 | 924 | 1,280 |
| General and Administrative Expenses | 1,586 | 2,719 | 1,789 | 2,894 |
| Operating Loss | 3,701 | 5,367 | 2,713 | 4,174 |
| Net Financial Expenses (Income) | 581 | 4,168 | 4,109 | 408 |
| Net Comprehensive Loss | 4,282 | 1,199 | 1,396 | 3,766 |

Appendix B - Capitalization Rate

DNA's two holding companies *Entera and BeamMed, respectively* operate in two different fields; biotechnologyand medical devices.

Entera

Cost of equity capital (ke) represents the return required by investors. The capitalization rate is calculated using the CAPM (Capital Asset Pricing Model). It is based on a long-term 20-year T-bond with a market risk premium, and based on Professor Aswath Damodaran's (NY University) commonly used sample (www.damodaran.com). As of December 31, 2016, the US market risk is estimated at 5.69%. A three-year market regression Beta is 1.25, according to a sample of 426 companies representing the US biotechnology sector. We used an unleveraged beta of this sample, which is higher than a leveraged beta, due to high rate of cash versus debt. The implied CAPM is 7.8%.

CAPM model (ke) is estimated as follows: $ke = rf + \beta(rm-rf) + P$

Entera is a small cap company, in which marketability and size premiums need to be considered. Duff and Phelps data research in the years 1963-2016 indicates that a 11.79% premium needs to be added to the CAPM for small cap companies. We therefore estimate the company's CAPM to be 19.64%.

| CAPM Model | | Value | Source |
|-----------------------------|------------|--------|---|
| Long-term (20 years) T-bond | R(f) | 0.76% | US Department of the Treasury (20Y) |
| Market risk premium | R(m)- R(f) | 5.69% | based on Professor Damodaran's sample (1/17) |
| Beta unleveraged | β | 1.25 | Beta sample of 426 Drugs (Biotechnology) firms (1/17) |
| Cost of Capital | ke | 7.8% | |
| Size Premium | | 11.79% | Duff and Phelps data, 10dz. |
| САРМ | CAPM | 19.64% | |

BeamMed

Cost of equity capital (ke) represents the return required by investors. The capitalization rate is calculated using the CAPM (Capital Asset Pricing Model). It is based on a long-term 20-year T-bond with a market risk premium, and based on Professor Aswath Damodaran's (NY University) commonly used sample (www.damodaran.com). As of December 31, 2016, the Israeli market risk is estimated at 6.69%.

A three-year market regression Beta is 0.92, according to a sample of 254 companies representing the US healthcare products sector. We used an unleveraged beta of this sample, which is higher than a leveraged beta, due to high rate of cash versus debt. The implied CAPM is 6.9%.

BeamMed is also a small cap company, in which marketability and size premiums need to be considered. Duff and Phelps data research in the years 1963-2016 indicates that a 11.79% premium needs to be added to the CAPM for small cap companies. We therefore estimate the company's CAPM to be 18.72%.

| CAPM Model | | Value | Source |
|-----------------------------|------------|--------|--|
| Long-term (20 years) T-bond | R(f) | 0.76% | US Department of the Treasury (20Y) |
| Market risk premium | R(m)- R(f) | 6.69% | Professor Damodaran's sample (1/17) |
| Beta unleveraged | β | 0.92 | Beta sample of 254 healthcare products firms (1/17) |
| Cost of Capital | ke | 6.9% | |
| Size Premium | | 11.79% | Duff and Phelps data, 10dz. |
| САРМ | CAPM | 18.72% | |

Appendix C – Key Team Bios

Kobi Hazan is the Lead Analyst at Frost & Sullivan Research & Consulting Ltd., a subsidiary of Frost & Sullivan in Israel. He has over 14 years of experience in capital markets, including; research, analysis, investment advisory, and management. Mr. Hazan served as a Fund Manager for provident and mutual funds at Analyst Ltd. and, since 2012, he owns and manages the Amida Israel Fund, a hedge fund specializing in Israeli equities. Kobi holds an Economics and Management degree from The College of Management Academic Studies. He is licensed as an Investment Advisor in Israel.

Dr. Anna Cirmirakis joined the Frost & Sullivan Transformational Healthcare team as a Healthcare consultant in February 2015. She works primarily with biotech,pharma and diagnostics companies on a wide range of strategic projects including product evaluation, market analysis as well as competitive intelligence. Prior to her role as a consultant she studied Human Genetics; she holds a PhD in biotechnology from University College London. Anna is a specialist in the field of monoclonal antibody production with a keen interest in regenerative medicine, immunotherapies and biologics.

Dr. Tiran Rothman is an Analyst and Consultant at Frost & Sullivan Research & Consulting Ltd., a subsidiary of Frost & Sullivan in Israel. He has over 10 years of experience in research and economic analysis of capital and private markets, obtained through positions at a boutique office for economic valuations, as chief economist at the AMPAL group, and as co-founder and analyst at Bioassociate Biotech Consulting. Dr. Rothman also serves as the Economics & Management School Head at Wizo Academic College (Haifa). Tiran holds a PhD (Economics), MBA (Finance), and was a visiting scholar at Stern Business School, NYU.

Dr. Moria Kwiat is a specialist in the field of biotechnology. Moria holds a Ph.D. in Chemistry and nanotechnology, M. Sc. and B. Sc. in Biotechnology from Tel Aviv University. Moria has a broad scientific background in interdisciplinary fields and over 12 years of conducting original research, with expertise at the interface between biology and materials worlds. She has a strong track record of developing biosensors for diagnostics utilizing electrical devices. Moria is the co-author of multiple scientific papers with vast experience in scientific writing.

Disclaimers, disclosures and insights for more responsible investment decisions

Entera Bio has not disclosed any other scientific information regarding the content of its platform carrier, pipeline results or any other relevant details, aside from the aforementioned. BeamMed was awarded Frost & Sullivan's 2015 Best Practice award

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