

Annual 2017, Q1-2018 and 12 mos. Since Initiation Updates

30 May, 2018

CELLECT

On track with its strategic plans; successfully completed proof of concept for ApoTainer™; sufficient cash to support clinical and preclinical trials; price target unchanged

Primary Exchange: NASDAQ

Ticker: APOP

Sector: Biotechnology

Industry: Stem cells

Data as at 28 May, 2018

(Source: Yahoo Finance)

Closing price: \$6.91

Market cap: \$45.0M

of shares: 6.51M

Stock performance (Y.T.D.): -25%

Daily-trading-vol. (3 mos.): \$21.5K

Stock target price: \$16.90

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Company Overview

Cellect Biotechnology Ltd. (hereinafter: "Cellect" or "the company") is developing a technological platform, the "ApoGraft", which functionally selects stem cells from a mixed population of cells based on their sensitivity to apoptosis. The first product under development is the ApoTainer™ selection kit. The company is currently conducting a proof-of-concept phase I/II trial with blood cancer patients in Israel, which is expected to be completed by the end of Q3-2018. Based on trial results and safety issues, the company plans to integrate its technology into a range of procedures that utilize stem cells, as well as into the manufacturing process of adult stem cell based products.

Highlights & Analysis

Cellect released its Annual and Q1-2018 reports detailing the following:

Cellect is on track with its strategic plans

- Cellect announced on 9 April, 2018 that it has successfully completed the proof of concept testing of its first in type new product prototype, ApoTainer™ using Cellect's FasL-coated magnetic beads for maximizing efficacy and scalability of stem cell based products' manufacturing. The ApoTainer™ is designed to replace highly complex and expensive procedures currently used by laboratories (e.g. Bone marrow transplantations)
- Positive results from a sample of 20 patients under trial at Tel Aviv's Ichilov Medical Center, in which the ApoGraft™ process has shown significantly beneficial effects on stem cells derived from fat tissue. There was 100% acceptance and zero related adverse events
- Cellect has also announced the opening of the second clinical trial site at Hadassah Medical Center

Cellect has Initiated a second program focusing on the selection of mesenchymal stem cells (MSCs) from fat cells, which poses great potential.

- Cellect has initiated a second program focusing on a selection of mesenchymal stem cells (MSCs) from fat cells also called adipose stem cells (ASCs). Those cells have the potential to differentiate and regenerate into cells of mesenchymal lineage such as adipocytes (fat cells), osteoblasts (bone cells), chondrocytes (cartilage cells and other cells) and myocytes (muscle cells).

Sufficient cash to support current clinical early phase and other pre-clinical pipeline development

- As of March 31 2018, Cellect had approximately \$9.9 million in cash and cash equivalents and marketable securities. On January 31, 2018, Cellect sold to institutional investors an aggregate of 484,848 ADSs in a registered direct offering at \$8.25 per ADS resulting in gross proceeds of approximately \$4.0 million

In our view, the company is on track to meet its strategic goals. Should the company see positive results in its ongoing trial (ApoGraft POC final results estimated in late 2018); the financial potential of their stock is projected to increase the company's share price.

We maintain our estimation of the company's equity value at \$101.4M; corresponding to a price target ranging between \$15.40 and \$18.70; a mean of \$16.90.

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Company Activity and Strategy

The company was founded in 2011, with its first indication platform, Apograft™, optimizing the selection of hematopoietic stem cells by selectively neutralizing harmful immune cells that may cause severe side effects such as GvHD (graft versus host disease) once transplanted into a patient. The technology is based on an apoptosis (programmed cell death) signal that selectively destroys some of the mature cells responsible mainly for the GvHD while maintaining the viability and functionality of the stem cell entities in the graft. The Apograft™ is currently undergoing a phase I/II open-label clinical trial in Israel involving matched related donor hematopoietic stem cell transplantations for blood cancers patients (leukemia, lymphoma and high-risk MDS patients).

The company develops a platform technology which enables enrichment of stem cells component in any starting mixed populations of cells. A simple, robust, reproducible, short and easy to use technology provides stem cells with an enriched batch of cells that can be used for any procedure requiring mature stem cells. The technology may be used in all regenerative medicine markets that use adult stem cells upon showing safety and efficiency of selection. It can be applied both as an off-the-shelf product for medical purposes and for laboratory research.

Cellect's first planned commercial product candidate is for bone marrow transplantations within the cancer therapy market. Once proof-of-concept results are obtained and safety issues are resolved, the company plans to integrate its technology in many production procedures of stem cell-based products by partnering with cell therapy companies. Additional indications such as type 1 diabetes and solid organ transplantation have also been tested and may be expanded, as well as other sources of stem cells (fat, cord blood).

In addition to the selection of hematopoietic stem cells, Cellect has initiated a second program focusing on the selection of mesenchymal stem cells (MSCs) from fat cells. In recent years, there has been increased interest in mesenchymal stem cells and their potential utility in tissue engineering and repair. Expansion of cells in culture is necessary prior to transplantation or re-introduction into the patient. Depending on the source and method of isolation, this procedure can be significantly time-consuming and expensive. Cellect's ApoGraft™ Technology, which pending approval, will be offered as an easy to use, off the shelf and scalable device, aims to mass produce those cells with increased speed, effectiveness, and cost efficiency. A rapidly increasing number of clinical trials using MSCs for multiple indications such as bone and cartilage, cardiovascular and autoimmune diseases as well as cancer, will increase demand. The company may provide a safe and cost-effective production platform to meet such market needs.

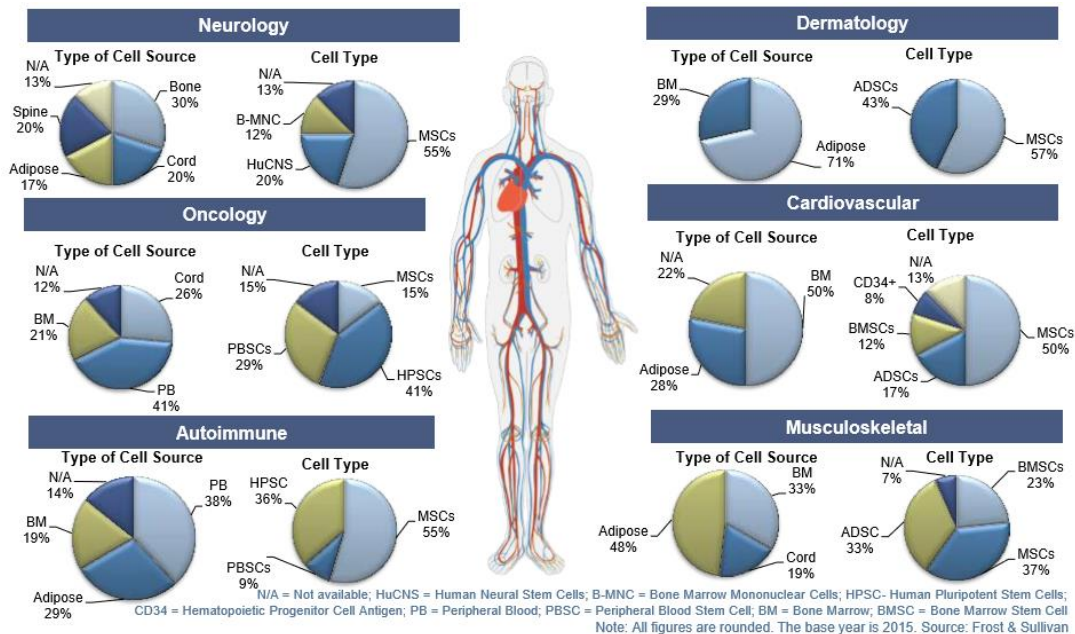


Figure 1. Stem Cell Sources and Stem Cells Used in Pipeline Clinical Trials. MSCs are extensively used in all indications, with bone marrow MSCs being the most studied and commonly used.

Cellect develops a unique enabling technology that provides stem cells as a raw material, and therefore holds great promise to engage in all regenerative medicine markets that use stem cells for numerous indications, a \$7.5 billion market with a rapid growth rate of 20.1% as of 2018. By enabling the use of HSCs not exclusively for malignant indications but as well for severe autoimmune deficiencies and metabolic disorders in an rapidly growing market, the potential that the company holds is high. But before using the ApoGraft™ technology broadly, the safety, efficacy and low cytotoxicity have to be proven in a first indication.

Currently, in line with its developmental stage, the company has positive data from a non-interventional study performed on samples from healthy donors. In addition, successful completion of the ongoing phase I/II proof-of-concept clinical study may provide Cellect multiple opportunities for business IP licensing deals before having a marketing approval for its products. The company has a wide IP protection to support the entire technology platform and a vast number of applications in markets worldwide.

As a relatively new form of therapeutic and mostly still in early development stages, cell therapy has yet to prove its clinical advantages and needs to reduce costs over other forms of therapeutics before widely adopted; therefore this engagement may pose a considerable risk to the company.

Market Overview

The Stem Cells market, which forms part of the wider cell therapy market, has a complex operating environment. It is based on several key players in the cell therapy ecosystem (Figure 2), which are all important to understand when evaluating a company like Collect. Collect is positioned within the industry as a Biotech company, providing technology for the enrichment of stem cells that may support multiple stem cell companies and research initiatives.¹⁶

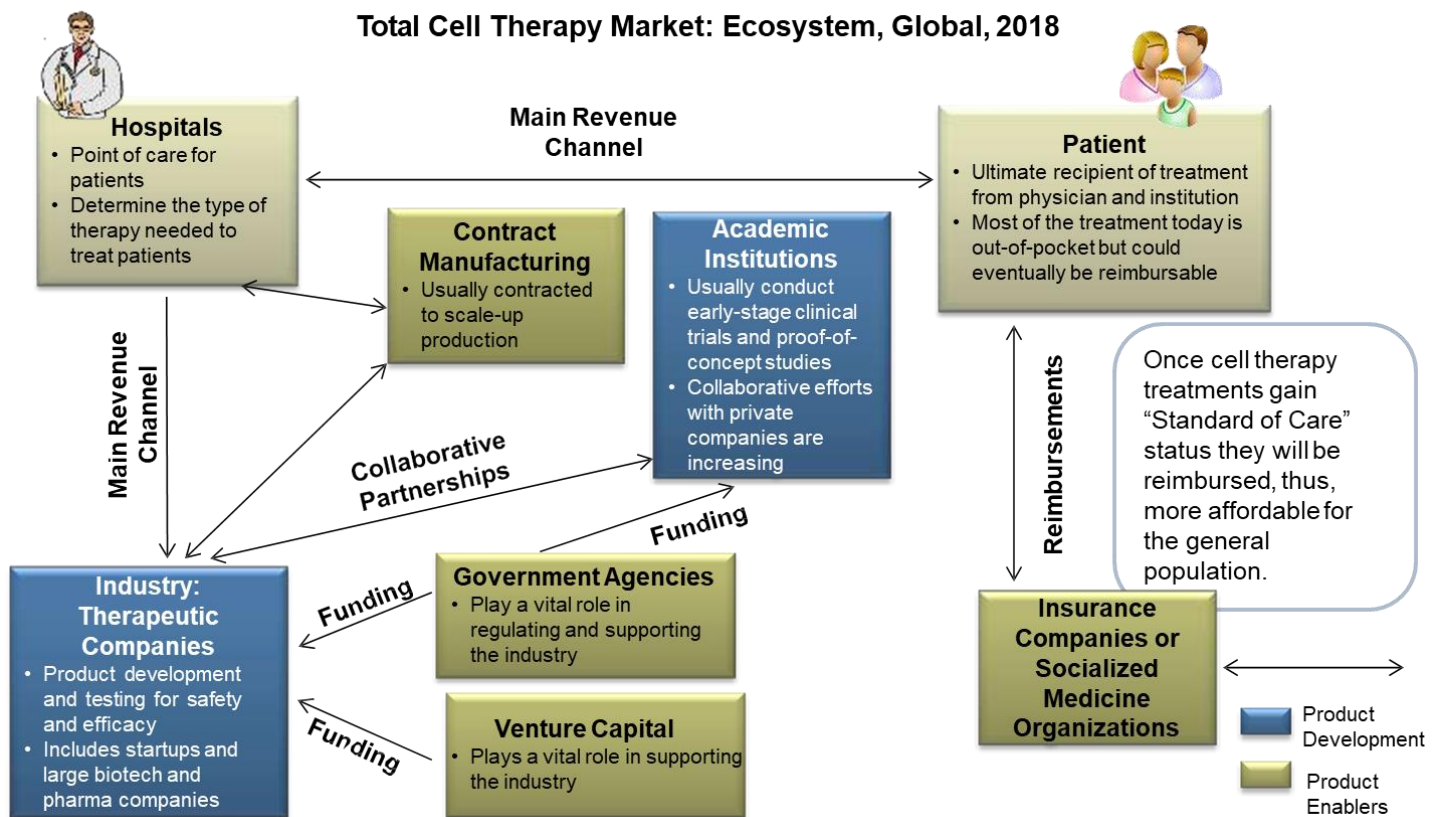


Figure 2. The Ecosystem of the Cell Therapy Market.

Source: Frost & Sullivan, *Future of Cell Therapy in the Regenerative Medicine Market*, May 2016.

Stem cell therapy is the largest segment of regenerative medicine which involves the use of living cells to replace or augment damaged or diseased cells and tissue. It uses adult or embryonic stem cells to regenerate cells as a medical intervention, as well as growing large masses of cells, tissues and organs in the laboratory for transplantation into the human body. It is a new human-health paradigm designed to combat diseases like cancer that have become more common as global ageing is established. Instead of using drugs, chemicals, radiation and surgeries, this therapy replaces the damaged tissue or organ with regenerating stem cells using biological processes similar to those found in nature. By 2030, there will be globally more people over 60 than under the age of 10. Already, there are more adults over the age of 60 than children under the age of 5. Healthcare systems are burdened by costly treatments for an ageing and increasingly ailing population.

Cell therapy holds 60% of the overall regenerative (recovering) medicine market in clinical trial numbers. The cell therapy market can be viewed in four main categories: Cell-based immunotherapy; Stem cell therapy (Collect's market); Cell-gene therapy; and Stem cell-gene therapy. Closely related to this market is the supporting technologies field that includes cell acquisition, cryopreservation, cell production, expansion and sub-culture. Collect's technology relates to cell production and expansion.

An overview of the market:

Established Cell Therapy Companies	Cell therapy is a fast-growing, emerging market. Stem cell therapy, comprising the largest part of the market, has the largest number of clinical trials globally. Furthermore, combination therapies, such as stem cell-gene and cell-gene, are showing great curative potential, which has led to US Food and Drug Administration (FDA) fast-track status.
Small- to Medium-sized Companies	Significant opportunities exist for small- to medium-sized companies in this rapidly expanding market. With growing government and private funds, the global market is ripe for new companies with innovative therapies to come to the forefront.
Pharmaceutical Companies	Large pharmaceutical companies such as Pfizer, Novartis, and Juno Therapeutics are entering the market because there is strong evidence of the safety and efficacy of numerous products in the pipeline. In addition, the curative potential of some of the cell-gene therapies is driving the creation of new partnerships, mergers, and acquisitions.
Support Industry Expansion	As the commercial production of stem cell, cell, and gene therapies increases, the need for fully-enclosed systems, such as bioreactors, and disposable products for Current Good Manufacturing Practice (CGMP) production will also grow.
Manufacturing Facilities	Very few large-scale manufacturing facilities exist. The cost of goods sold is high relative to marketable product output. Vector production capabilities are currently limiting the rate of production for stem cell-gene and cell-gene products.

Figure 3. Market Overview

Source: Frost & Sullivan, *Future of Cell Therapy in the Regenerative Medicine Market*, May 2016.

Cell therapy is already treating millions of patients globally and will probably disrupt the pharmaceutical landscape and revolutionize the way that patients are medicated in the future. There are over 500 companies active globally, with more than 50% located in the United States. The market potential is the largest in the United States but is also growing rapidly in Japan and South Korea due to the implementation of the favorable government policies.

The United States has the largest number of industry-based clinical trials despite stringent regulations, as well as the largest number of private cell therapy companies. Europe is surprisingly lagging behind the United States in cell therapy, with the United Kingdom and Germany at the forefront in this region. Because of Japan's relaxed regulations, it is becoming hotspot for innovation, and foreign partnerships are welcome, while reimbursement standards are being re-evaluated. The Chinese government welcomes foreign investment, collaborations and partnerships, although there are some ethical as well as quality concerns that are being currently addressed by the government.

The total cell therapy market size in 2018 is estimated at nearly \$7.5 billion and is set to grow at a compound annual growth rate (CAGR) of 20.1% until 2020. Although the United States dominates the market, relaxation of government regulations opens new opportunities in Asia, especially in countries like Japan.

Company's Products

Cellect develops safe and cost-effective products for different stem cell treatments. Cellect technology enables the standardized selection process for stem cells resulting in the reproducible mass production of raw material from various sources and for any indication.

Cellect develops a line of products comprised of various containers such as infusion bags, flasks and test tubes designed to address different markets such as medical, research and biopharma companies. Its applications involve stem cell isolation following collection (autologous or allogeneic) and/or co-culture and expansion. It is a simple, low cost and fast procedure that does not require a special laboratory or equipment.

Selected products and their stages of development:

- ApoGraft™ – the proprietary stem cell selection process is currently being tested in an Open -Label Phase I/II clinical study in which 12 blood cancers patients will be given ApoGraft™ treated cells and their response will be compared to historical data.
- ApoTainer™ – an off the shelf device based on the ApoGraft™ technology, for which POC was shown. The first prototype is planned for the end of 2018 and product launch estimated for 2023.

Both the product and the technology are in the proof-of-concept stages and thus, investment at this time would be high risk. Clinical Trial Phase I/II results will provide Cellect clinical proof of concept and facilitate finding licensing partners.

Cellect's intellectual property is validated by proof-of-concept studies and includes 7 global patent applications covering: the concept of using apoptosis-inducing agents for stem cell selection; composition of the ApoTainer™ matter and method of manufacturing; methods of use; mesenchymal stem cell selection; Expiration dates range between 2027 and 2034. Four of those patents have already been granted in the US.

Since June 2015 Cellect has had a strategic joint product development agreement for its medical kit with **Entegris**, a US company that specializes in advanced plastic devices for high-tech industries. Entegris will be responsible for completing the design and production of the polymer product, including the development costs, while Cellect will be responsible for the biological aspect and testing (including human trials). These two companies have been also reviewed by the prestigious binational US/Israeli foundation and have received a \$1M funding.

ApoGraft™ – A Cellect Proprietary Function-Based Cell Selection Technology

What makes Cellect's process unique in principle compared to other methods available today, is that only a small subpopulation of mature cells is eliminated by the death signal. The "graft versus tumor effect", which allows some donor cells to attack any remaining cancer cells is an important role of HSCT is preserved. According to Cellect, these aspects have been tested in animal models, showing eliminated GvHD and full preservation of the anti-cancer effect, results further supported by numerous independent publications.^{1 2 3} Further preclinical data provided by Cellect are included in scientific publications under preparation.

1 Askenasy N, et al. Biol Blood Marrow Transplant. 2013;19:185

2 Mizrahi K, et al. Stem Cells and Development. March 2014, Vol. 23, No. 6: 676

3 Mizrahi K, et al. Bone Marrow Transplant. 2014 May; 49(5):640-8.

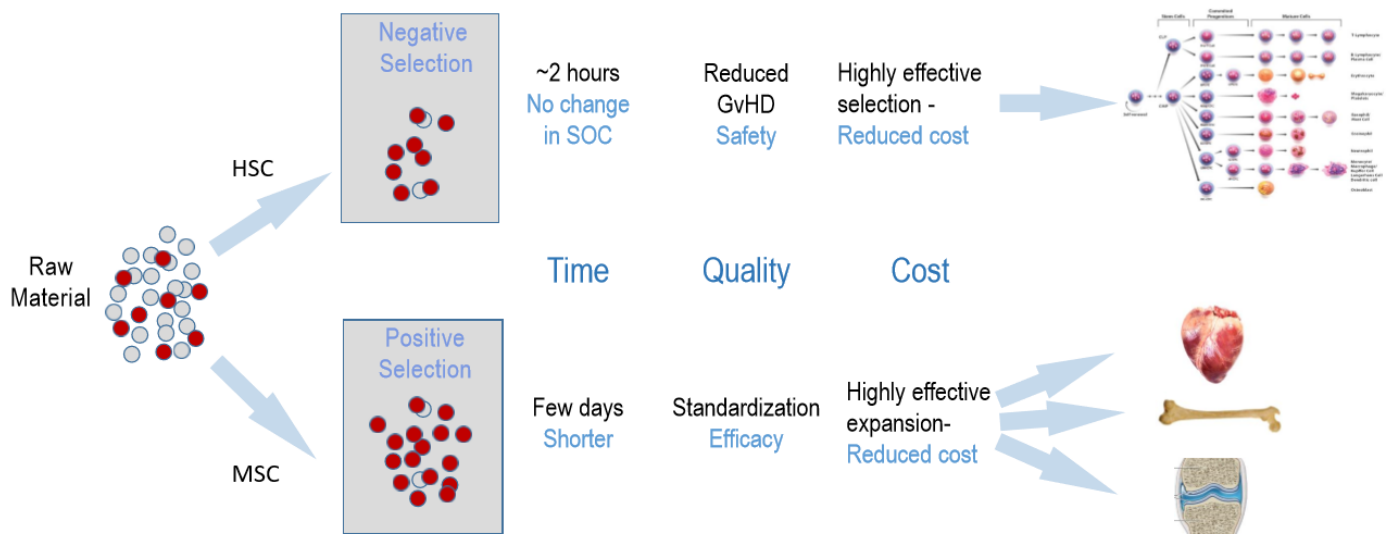


Figure 4. Collect positive and negative cell selection

Source: Collect Biotechnology Ltd.

ApoTainer™ – An Off-the Shelf Device for Hematopoietic Stem Cells for Bone Marrow Transplantations

Collect's first planned commercial product candidate is ApoTainer™, a unique plastic blood container, currently under development for the improved safety of the treatment of cancer by bone marrow transplantation by prevention of Graft versus Host disease. The design of the ApoTainer™ concept makes it scalable giving it the potential to play a crucial role in other applications, for example where large quantities of stem cells are required.

The ApoTainer™ concept is based on Collect's key ApoGraft™ technology, where subsets of adult white blood cells can be induced to undergo programmed cell death (apoptosis) under certain conditions while stem cells proved to be resistant to that biological process hence allowing functional selection of the stem cells.

The ApoTainer™ contains immobilized Fas Ligand (FasL) protein that triggers the death of some mature cells by apoptosis, allowing the remaining stem cells to flourish in their natural microenvironment (Figure 4). In the device currently under development for bone marrow transplantation, this process eliminates harmful immune cells that may trigger an immune rejection as well as GvHD responses, thus potentially reducing medical complications.

Importantly, the cells begin apoptosis and are committed to a suicide path but still stay intact during the process. Therefore, there is no need to discard or physically separate the dead cells or stem cells from the container. Instead, the container can be hooked up intravenously to the patient and the stem cells directly delivered, potentially providing an output immediately usable for any medical or research purpose of enriched hematopoietic stem cells within hours of the procedure.



Figure5. Mechanism of Action of Collect flagship technology

Collect's overall product development strategy

Initially, the focus of the ApoGraft™ will be in hemato-oncology, which is the most popular segment for cell therapy collaborations and deals, comprising 29.2% of all the cell therapy related deals made in 2015. Close to 19% of cell therapy focuses on oncology-related products, making it the second-largest market segment. An increasing number of immunological treatments for graft versus host disease (GvHD) that include the use of Mesenchymal Stem Cells and CAR T-cells are being explored; furthermore, a combination of cell-gene and stem cell-gene with immunotherapy are used by directly transferring genes into cells for the purpose of treating hematopoietic cancers. Clinical trials using cell-gene therapy to treat terminally ill cancer patients have been successful, showing great curative potential, and pushing forward the cell therapy market. Although only 4% of the marketed products are oncology related, a large pipeline indicates that this will be a high-growth segment. Nonetheless, enabling the large-scale production of cell-gene and stem cell-gene therapies will become a vital manufacturing concern to this industry in the upcoming years. Therefore, Collect may position itself as a central player in this market segment, supporting the production procedure of multiple stem-cell companies as potential clients.

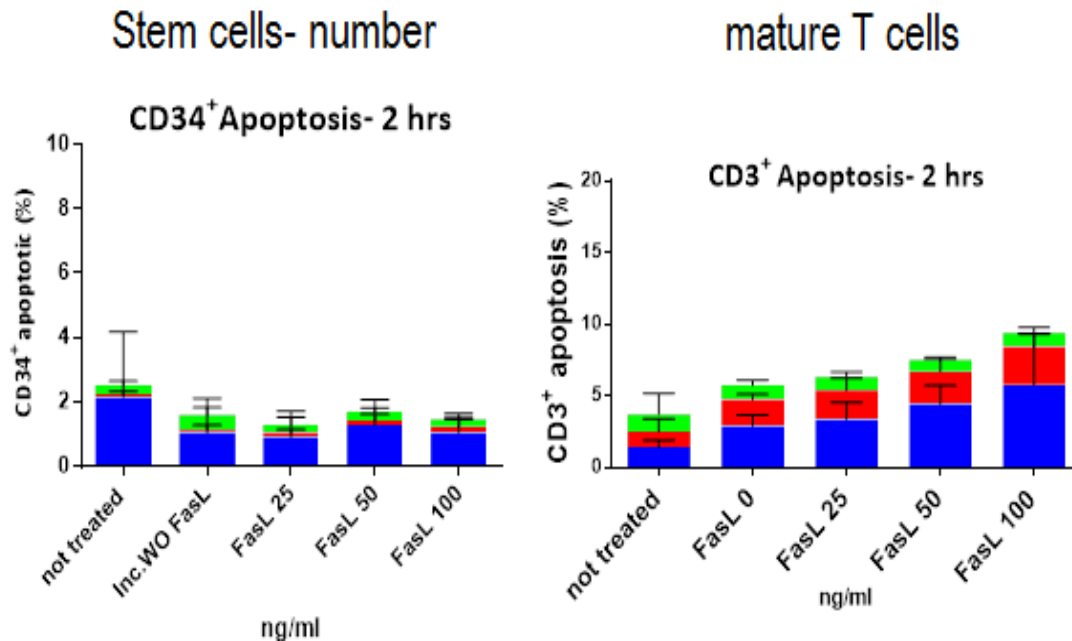
Collect's ongoing study allows the enrollment of leukemia, lymphoma and high-risk Myeloma (MDS) patients. Leukemia constitutes 3.7% of all new US cancer patients with approximately 62,130 estimated new cases in 2017 according to National Cancer Institute. Acute myeloid leukemia (AML) is the second most common type of leukemia with 21,380 estimated new cases of AML in 2017 and a five-year survival rate of approximately 26%.

Pre-Clinical and Clinical data - GvHD in Leukemia Patients

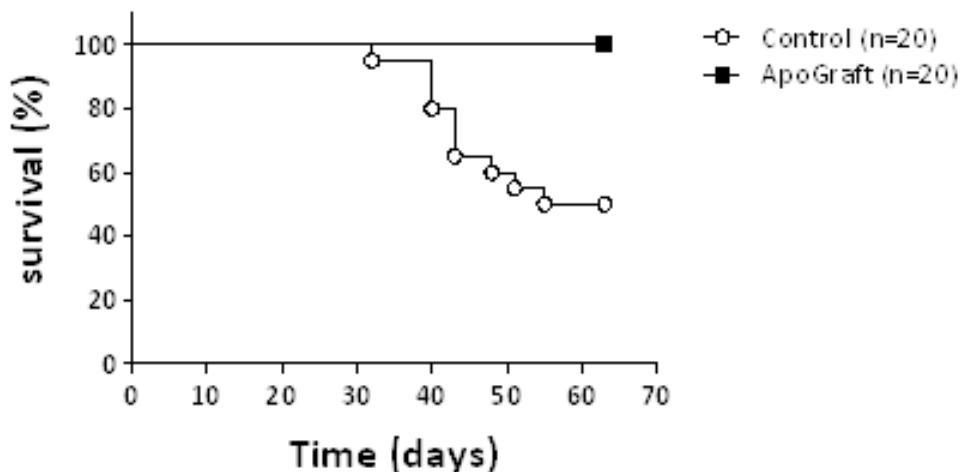
Pre-clinical results:

In vitro studies were performed in order to define the most relevant effector molecules for the apoptosis selection procedure (whereby the Fas Ligand protein from the TNF superfamily signaling proteins was identified), as well as the optimum concentrations and conditions for murine studies. *In vivo* safety and efficacy studies were carried out in murine and human transplant models while using various sources of human hematopoietic cells (mobilized peripheral blood, bone marrow and umbilical cord blood). The technology was tested in a relevant donor type (self, family and unrelated). Efficacy was evaluated by measuring the relevant adverse effects such as GvHD, mortality, lack of engraftment and reduced anti-tumor effects.

Findings included the verification of the resistance of stem cells to apoptosis and their preservation (quantity as well as quality) after the process; the depletion of GvHD effector cells causing morbidity and mortality from 80% to none; the preservation of successful engraftments; the preservation of anti-tumor activity; and verification that apoptosis-insensitive progenitors are privileged for engraftment through competitive advantage over the apoptosis-sensitive differentiated progeny (Figure 6).



Legend: Color index: blue-early apoptosis, red-late apoptosis, green-Necrosis (cells death): Apoptosis is preferentially induced in mature T cells (CD3+), whereas progenitor cells are not affected (CD34+).



Source: Collect Biotechnology Ltd.

Figure 6. Pre-eliminary data showcasing the superiority of Collect flagship technology.

A safety study in mice for survival rate. Kaplan Meier survival curve of NOD.SCID transplanted mice. Statistical analysis performed using Log-rank (Mantel-Cox) test (**P<0.0003)

Clinical studies:

The company is conducting an open-label pilot phase I/II safety and proof-of-concept clinical trial of ApoGraft™ in the prevention of acute GvHD. The main purposes of the trial are to assess the safety and tolerability of the treatment. In this trial, the company is testing allogeneic stem cells transplanted from the mobilized peripheral blood of a matched related donor with the primary objective of assessing the safety of the ApoGraft™ process. The trial group includes 12 patients, and completion of enrollment was expected in

Q1 2018 followed by another 6 month follow-up period after transplantation, with an estimated completion by Q3 2018. As of March 2018, the cohort of three patients has been recruited and followed up for 3 months. The initial results showed a full engraftment and no related side effects. The trial is conducted in the bone marrow transplantation (“BMT”) unit of Rambam Medical Center, Israel, however, due to the delays in the recruitment, Collect has started a collaboration with Hadassah Medical Centre in Jerusalem and continues the patients’ enrollment process⁴ In January 2018, Data and Safety Monitoring Board (DSMB) has approved a dose escalation in the clinical trial.

In addition, the company has completed a safety trial of mobilized peripheral blood samples from healthy donors after ApoGraft™ process, examining their readiness for transplantation in a lab. Data supported the positive preclinical results and the protocol for the clinical trial and were used to optimize the conditions for the Phase I/II trial.

If ApoGraft™ technology will be shown to be efficacious, , the technology could potentially be used to treat numerous diseases in which mature cells presence in the transplanted graft is an issue. These include numerous blood cancers, Parkinson’s disease, vascular diseases, Myocardial Infarction, heart failure, CNS disorders and autoimmune diseases. This technology is expected to alleviate adverse effects seen with other methods of adult stem cell transplantations, especially reduction in cell fractions as well as the elimination of immune responses. The estimated completion of the Phase I/II study is Q2 2019 instead of originally planned Q3 2018.

On September 5, 2017, Collect announced that the FDA had granted Orphan Drug Status to Collect’s ApoGraft™ for both Acute and Chronic GvHD. Orphan drug designation is a regulatory path that includes tax credits related to clinical trial expenses, an exemption from the FDA user fee, FDA assistance in clinical trial design, an accelerated path to market and potential market exclusivity for seven years following approval.

ApoGraft™ process on Mesenchymal Stem Cells (MSCs) Applicable for Broad Range of Stem Cell Therapies

Collect has initiated a second program focusing on a selection of mesenchymal stem cells (MSCs) from fat cells, also called adipose stem cells (ASCs). Those cells have the potential to differentiate and regenerate into cells of mesenchymal lineage such as adipocytes (fat cells), osteoblasts (bone cells), chondrocytes (cartilage cells and other cells) and myocytes (muscle cells). However, the differentiation potential of these cells is considered to be limited.

MSCs have the ability to migrate to inflammatory sites and trigger anti-inflammatory and immuno-suppressive response. There are several studies that have demonstrated a non-tumorigenic nature of the cells and upon their administration, there were no problems with immuno-incompatibility. In addition, the therapeutic properties along with their ease of accessibility make MSCs the most desirable cells for a clinical trial of various disease. Collect’s investment in standardising mass production of those cells is well justified.

There are some key advantages of the ASCs such as:

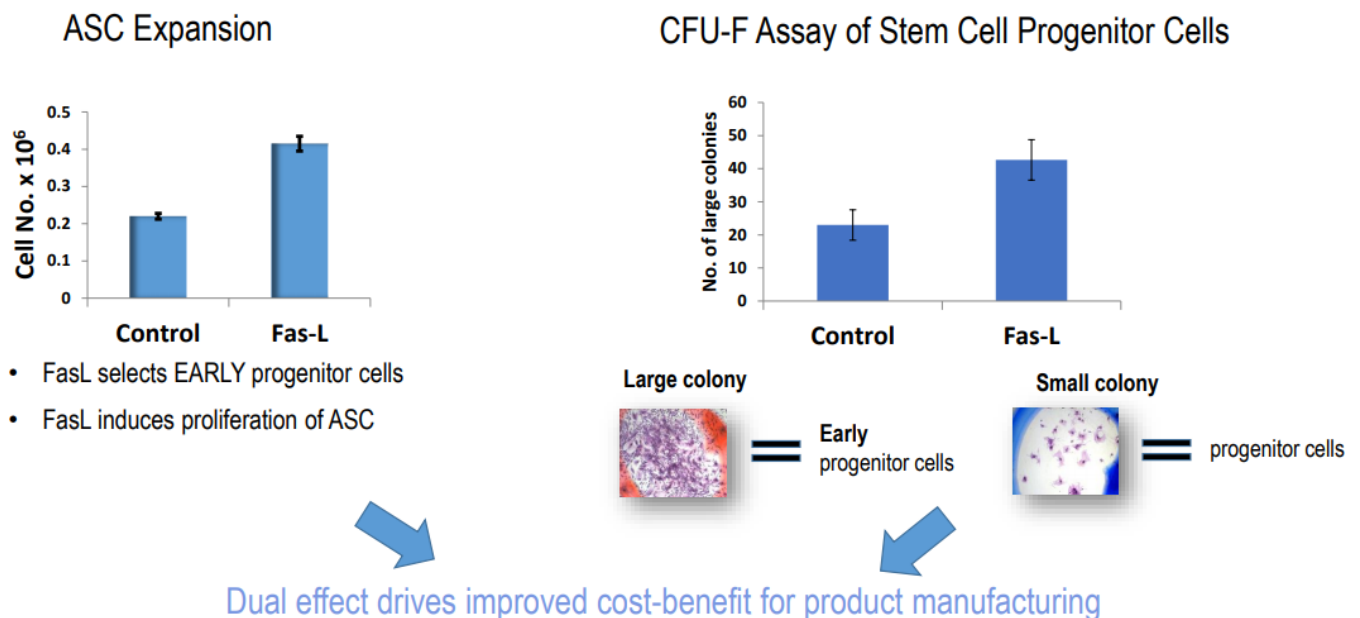
- Easily obtainable from accessible tissue sources, such as bone marrow, blood, and adipose tissue
- MSCs can be either donor-derived or patient-derived for clinical use
- MSCs are immune privileged and have a low risk of rejection

⁴ Company Webpage, Collect Biotechnology, <http://collectbio.com/our-solutions/#ourSolutions>.

- Potential to treat a wide variety of diseases, such as inflammatory diseases, orthopaedic disorders, heart disease, and cancer.

One of the main disadvantages is that those cells require expansion in culture prior to transplantation or re-introduction into the patient. Depending on the source and method of isolation, this procedure can be significantly time-consuming.

Their ApoTainer™ technology can address this unmet need as it has been successfully tested for the expansion of the ASCs as shown in Figure 7. The study was conducted with "Ichilov Medical Center" (Tel Aviv, Israel) and showed positive results for fat-derived stem cells taken from fat tissues via liposuction from more than 20 patient samples. Using ApoTainer™ provided significant beneficial effect both on the number and activity of the adipose-derived stem cells. In addition, differentiation into bone (osteoid) and fat (lipoid) tissues were assessed. Although the extent to which these results can be used to support FDA requirements remains unclear, these results are promising. They indicate that the ApoGraft™ may be used to provide high quality mesenchymal and/or stromal stem cells for subsequent expansion and use for a variety of indications.



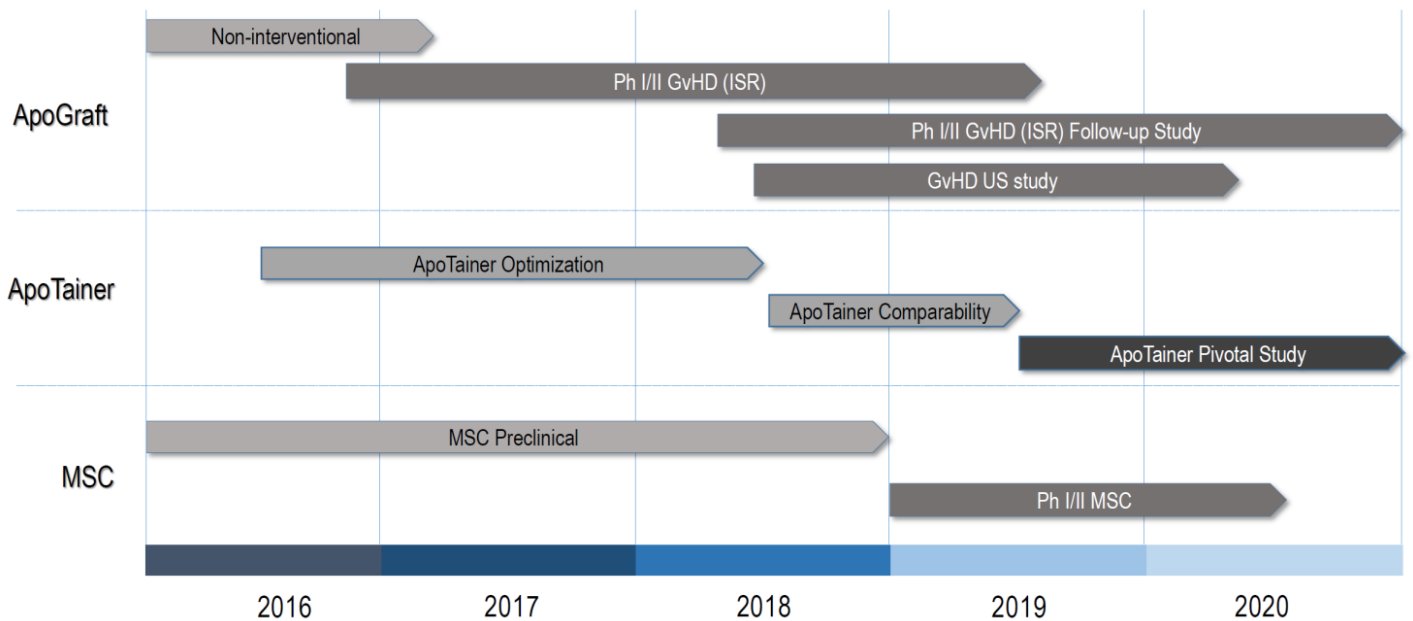
Source: Collect Biotechnology Ltd.

Figure 7. Adipose stem cells expansion with FasL

Collect's ApoGraft™ Technology in the ApoTainer™ aims at the mass production of those cells in a shorter, effective and cost-efficient way. With the rapidly increasing number of clinical trials requiring large volumes of MSCs and their widespread application for multiple indications such as bone and cartilage diseases, cardiovascular and autoimmune diseases as well as cancer, the company may provide a safe and cost-effective production platform to meet market needs.

Market opportunities are extensive but should be carefully considered for adipose tissue-derived stem cells prior to selecting an indication. Non-uniformity and reduced potency of the cell product, which typically characterizes this segment, also needs to be addressed. Collect will need to strategically address these issues in order to prove the superiority of its products and penetrate new market niches and geographies and set target indications for treatment in accordance.

Summary of Clinical Studies



Source: Collect Biotechnology Ltd.

Figure 8. Summary of Collect's Clinical Trials

The clinical development of Collect's technology is expected to be approved by the US FDA as a 'combination therapy, potentially regulated under medical device regulations (PMA and Class III). This regulatory pathway is applicable with typically shorter development timelines (compared to a biopharmaceutical product) and lower expenses due to less and smaller clinical trials. However, this regulatory pathway is yet to be approved by the FDA. Additionally, Collect intends to file for an orphan designation and a breakthrough technology status which are expected to reduce the time and costs of development if approved.

Pipeline Competition

The following late stage firms already have marketed or late-stage pipeline stem-cell based products for GvHD after Hematopoietic transplantation (full list of GvHD pipeline is shown in Appendix II):

- a) Remestemcel-L (Prochymal® and now also called MSC-100-IV) of Mesoblast is the world's first approved allogeneic stem cell therapeutic product that has received both Fast Track and Orphan Drug status by the U.S FDA (the latter also received by European Medicines Agency). In 2012 it received approval in Canada and New Zealand for the treatment of acute GvHD in children and for Crohn's disease. It became the first stem cell product to receive FDA Expanded Access approval, making the product immediately available to patients with life-threatening GvHD. The Japanese Government has approved TEMCELL® HS. Inj., a product based on our proprietary mesenchymal lineage adult stem cell technology licensed to JCR Pharmaceuticals Co. Ltd for the treatment of graft versus host disease. TEMCELL® (Prochymal®) is the first allogeneic cell-based product to receive full regulatory approval in Japan in February 2016. As of March 2018 new version of Prochymal® called MSC-100-IV (an optimized product manufactured in Singapore) is being investigated in Phase 3 clinical trials and is nearing a final read out.
- b) NiCord® of Gamida could be a cost-saving treatment, because only a single unit of cord blood is needed for it, and shorter hospital stays are possible with its use. NiCord® is a new modality in the

treatment of blood cancers. It has been developed as an alternative to bone marrow transplants for patients who cannot find a donor with fully-matched tissues. Those cord-blood derived CD34+ cells are expanded using nicotinamide (pyridine-3-carboxamide) and can be used for haematopoietic transplant and reconstruction for the treatment of haematological and autoimmune disorders and metabolic disorders NiCord® is currently in multiple phase III clinical trials for acute myelogenous leukaemia (AML), chronic myelogenous leukaemia (CML), acute lymphocytic leukaemia (ALL), Myelodysplastic syndrome (several types of leukemia) and also phase II for stem cell engraftment and sickle cell anemia. In March 2017 it was granted an Orphan Drug Status in the EU for the treatment of Haematopoietic stem cell transplantation.

The approval of these candidate therapies will influence the market penetration of upcoming early stage stem-cell companies that may incorporate Collect's technology for this indication. Collect's clinical advantages over the currently used or advanced therapies may be in terms of its low cost and efficient manufacturing, as indicated in Table1:

	Current Procedures	ApoTainer™ **
Risk of GvHD	30% - 50%	Negligible
Chemotherapy	Wide	Reduced
Rate of Infection	High	Low
Procedure and hospitalization	Months	Days
Cell Selection Cost	~ \$70,000	< \$10,000
Total cost of procedure	~ \$300,000	< \$100,000

** Company Estimates

Source: Collect Biotechnology Ltd.

Table1. Collect comparison to currently used therapies

The stem cell selection procedure is an aid product for the stem-cell market. In this ecosystem, there are a few companies that target their product at clinical applications. The major advantage of the Apograft™ technology as compared to current practice is the reduction of GvHD without risking an increase in graft failure and a decrease of the anti-tumor effect.⁵ So far, none of the currently available stem cell selection methods is based on a functional aspect of stem and progenitor cells (sensitivity to apoptosis). Functional selection used by Collect's technology makes it unique with no head-to-head competition.

Nowadays, the most commonly used method for ex-vivo lymphocyte depletion or CD34+ positive selection of stem cells is an immune-magnetic sorting technique that uses monoclonal antibodies. It allows the production of highly purified CD34+ cells or other stem cell compositions, combined with defined numbers of low or very low T-cells, T- and B-cells or lymphocyte subsets.⁶

Other technologies that are also used for stem cell selection involve fluorescent labelling (according to the cell surface markers which are not functional markers), selected by fluorescence-activated cell sorting (FACS). This method involves very costly process and very expensive infrastructure.

⁵ Yair Reisner, David Hagin and Massimo F. Martelli Haploidentical hematopoietic transplantation: current status and future perspectives From bloodjournal.hematologylibrary.org at TEL AVIV UNIV on May 5, 2012

Republished online September 14, 2011; doi:10.1182/blood-2011-07-338822 2011 118: 6006-6017

⁶ http://www.bmtcare.com/index.php?option=com_content&view=article&id=83&Itemid=83&lang=en

“Apheresis” technology that is used with peripheral blood in order to isolate the stem cells from the rest of the blood and return the remaining blood to the patient is already widely available on the market and FDA approved. Collect sees its technology as a way to (1) augment apheresis stem cell selection and further decrease the risk of unwanted contamination and (2) a way to theoretically eliminate the need for markers for donor selection.

Direct competitors would be companies like ‘StemCell Technologies’, and ‘Milteny biotec’, which are being considered the most significant challenge. Milteny biotec develops and manufactures a portfolio of products as well as offering its process for clinical applications. Its technology is based on MicroBeads, columns, and magnetic separators for small or large scale separations. At this stage, their clinical trials range from safety/feasibility (phase I/II) to pivotal stage (phase III) and post-market surveillance trials. Over 35,000 clinical cell treatments are used to date, and over the years, more than 25,000 leukemia patients have been treated with cells manufactured by the CliniMACS System. In 2014, the CliniMACS® CD34 Reagent System was approved by the FDA for GvHD prophylaxis in patients with acute myeloid leukemia (AML) in first complete remission undergoing allogeneic SCT from a matched related donor.⁷

As this technology is already standard in cell separation, it will strongly influence the market penetration of upcoming stem-cell aid companies such as Collect, which will have to show clear benefits over the other existing and already approved methods in terms of efficiency, simplicity and cost.

In addition, Cytori Therapeutics is an example of a later-stage cell therapy company with an innovative technology platform that is based on the use of human adipose tissue as the raw material to develop cellular therapy models. Cytori was the first company to introduce a technology platform that uses cells from adipose tissue. It is focused on the development of autologous cell therapies from adipose tissue to treat a variety of medical conditions. Its product development pipeline covers a broad spectrum of therapeutic areas including orphan and rare diseases, genitourinary disorders, orthopedics, cardiovascular disease, and acute and chronic wound care. Non-significant results in Phase III clinical trials are in part the result of the lack of selection and heterogeneity of the adipose-derived stem cell products.

Collect’s new research into ASCs further enlarge the bandwidth of Collect’s platform, and together with the bone marrow program, covers most of the raw materials for stem cells used in the industry. Thus, it increases potential strategic alliances for commercialization of Collect’s ApoGraft™ platform, specifically in the orthopedic and aesthetic domains, two lucrative industries with substantial demand.

In recent years, the FDA has stated that only “minimal manipulation” of autologous tissues/cells would be allowed. In November 2017, the FDA issued its final guidelines for minimal manipulation and homologous use of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/PS).⁸ It should be noted that “final FDA guidelines” do not establish legal, enforceable responsibilities; however, they most often become FDA rulings within a “reasonable” period of time.

The FDA’s new strict regulations with regards to adipose stem cells state that any isolation of them will be considered more than minimally manipulative. These new FDA regulations will require clinics that make use of autologous treatment to submit an IND (investigational new drug) application. In that term, Collect may need an IND for the adipose cell product, or otherwise, the physician who uses the product will need to settle this requirement instead.

⁷ source: Milteny biotech-<http://www.miltenyibiotec.com>

⁸<https://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/CellularandGeneTherapy/UCM585403.pdf>

In addition, the FDA has homologous requirements. If the cells are used as support such as in cosmetic uses, that would be homologous, but if they are used for orthopaedic conditions, it would be considered non-homologous.⁹ Collect will need to address these issues as well.

Another major issue would be the purity of the fat stem cell suspensions currently used for clinical applications. The fat-derived stem cells are a relatively new, yet fast growing segment in the adult stem cell domain. One of the challenges in this segment is obtaining pure high-quality adipose-derived stem cells from a heterogeneous population. Because separation techniques are often inadequate, there is an issue with non-uniformity of the resulting products used to treat patients. In this sense, Collect offers a well-controlled selection process and a batch release criteria product, specifically addressing this drawback. The functional selection technology and the results achieved in the preliminary studies support a more characterized product with better uniformity and potential for improved potency.

For more in-depth analysis of Collect's clinical pipeline, and the competitive landscape in which it seeks to operate please see our [Initiation of Coverage report, dated 27 April 2017](#) and [updates pursuant to it](#).

⁹<https://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/CellularandGeneTherapy/UCM585403.pdf> (pg. 18-19)

Q1-2018 Financial Results

Research and development (R&D) expenses for the first quarter of 2018 were \$0.81 million, compared to \$0.97 million in the fourth quarter of 2017 and \$0.80 million in the first quarter of 2017. The decrease in the first quarter of 2018 as compared to the fourth quarter of 2017 was primarily due to a decrease in share-based compensation and payroll bonus.

General and administrative (G&A) expenses for the first quarter of 2018 were \$0.98 million, compared to \$0.97 million in the fourth quarter of 2017 and \$0.72 million in the first quarter of 2017. The increase in the first quarter of 2018 as compared to the fourth quarter of 2017 was primarily due to an increase in business development expenses.

Net loss for the first quarter of 2018 was \$1.0 million, or \$0.008 per share and \$0.16 per ADS, compared to \$0.96 million, or \$0.008 per share and \$0.16 per ADS, in the fourth quarter of 2017, and \$3.5 million, or \$0.039 per share and \$0.78 per ADS, in the first quarter of 2017.

Cash and cash equivalents, marketable securities and short-term deposits totaled \$9.8 million as of March 31, 2018, compared to \$7.9 million on December 31, 2017, and \$7.3 million on March 31, 2017. The change in the cash and cash equivalents was primarily due to net proceeds of \$3.7 million (after deducting placement agents' fees) raised through a registered direct offering and concurrent private placement completed in January 2018, offset by cash used in operations during the period.

Shareholders' equity totaled \$7.7 million as of March 31, 2018, compared to \$5.4 million on December 31, 2017, and \$5.0 million on March 31, 2017.

2017 Annual Financial Results

Research and development expenses for 2017 totaled NIS 11.5 million (approximately \$3.3 million), representing an increase of NIS 3.2 million (approximately \$1.2 million), or 39%, compared to NIS 8.3 million (approximately \$2.1 million) for 2016. The increase was primarily attributable to an increase of NIS 1.7 million (approximately \$0.5 million) from share based payment and an increase of salaries and related personnel expenses totaling NIS 1.8 million (approximately \$0.5 million) reflecting the growth in Collect's activities resulting from an increase in the number of employees engaged in research and development related activities from thirteen to eighteen.

General and administrative expenses for 2017 totaled NIS 12.9 million (approximately \$3.7 million), an increase of NIS 4.9 million (approximately \$1.7 million), or 61%, compared to NIS 8.0 million (approximately \$2.0 million) for 2016. The increase resulted primarily from an increase of NIS 2.2 million (approximately \$0.6 million) in share based payment, an increase of NIS 1.2 million (approximately \$0.3 million) in professional services due to increased legal, investor relations, and public relations expenses as the company was listed on the Nasdaq for duration of the reporting period, and an increase of NIS 1.6 million (approximately \$0.5 million) from other expenses which mainly concern business development activities.

Operating loss for 2017 was NIS 24.4 million (approximately \$7.0 million), compared to an operating loss of NIS 15.9 million (approximately \$4.1 million) for 2016, an increase of NIS 8.5 million (approximately \$2.9 million), or 53%.

Cash and cash equivalents and marketable securities as at December 31 2017, totaled NIS 27.7 million (approximately \$8.0 million). During 2017, the company funded its operations principally with NIS 47.3 million (approximately \$12.7 million) from the issuance of ordinary shares and warrants in 2016 and 2017.

- **Net cash used in operating activities** was NIS 17.7 million (approximately \$5.1 million) in 2017, compared with approx. NIS14.4 million (approximately \$3.7 million) in 2016.
- **Net cash provided by financing activities** in the years ending December 31, 2017, 2016 and 2015 consisted of NIS 15.8 million (approximately \$4.6 million), NIS 34.9 million (approximately \$9.1 million) and NIS 6.4 million (approximately \$1.6 million) respectively. These were comprised, primarily of net proceeds, mainly from the issuance of ordinary shares (including ordinary shares represented by ADSs) and warrants.
 - In March 2016, Collect issued an aggregate of 5,783,437 ordinary shares pursuant to a private placement, at a price of NIS 1.39 (approximately \$0.36) per share. In addition, the company issued warrants to purchase up to 1,927,801 ordinary shares, which had an exercise price of NIS 2.1 (approximately \$0.54) per warrant. The warrants expired on March 7, 2018.
 - In August 2016, Collect issued an aggregate of 1,292,308 ADSs and listed warrants to purchase 1,035,121 ADSs in its IPO, at a price of \$6.50 per ADS resulting in gross proceeds of approximately \$8.4 million. On September 11, 2017, Collect sold an aggregate of 531,136 ADSs in a registered direct offering at \$8.10 per ADS resulting in gross proceeds of approximately \$4.3 million. In addition, the company issued to the investors unregistered warrants to purchase 265,568 ADSs in a private placement.
 - On January 31, 2018, Collect sold to certain institutional investors an aggregate of 484,848 ADSs in a registered direct offering at \$8.25 per ADS resulting in gross proceeds of approximately \$4.0 million and issued to the investors unregistered warrants to purchase 266,667 ADSs in a private placement.

Analysis

Collect's approach focuses on the selection of pure, high-quality stem cells that require less time for cell expansion than other processes currently deployed in the industry. This highly specific and personal manufacturing approach may have advantages in terms of efficacy, cost, and time-to-treatment. To some extent, it permits the preparations of the cell therapy product on-site rather than large-scale central manufacturing.

Its platform offers purification and efficient quantification of stem and progenitor cells through an improved and rapid selection process that significantly decreases complications that exist with standard selection techniques. In the case of Hematopoietic stem cells (HSCs), this process potentially eliminates the immune-related toxicity in allogeneic transplantation. In the case of fat-derived stem cells (where most of its uses are autologous), it improves the number, uniformity and potency of the Mesenchymal stem cells (MSCs).

Thus, as reviewed in our recent analysis reports, we find a potential for the ApoGraft™ platform to be employable by a much wider array of companies and medical centers developing stem cell based products and treatments. Specifically, to aesthetic and orthopedic indications where fat-derived stem cells are the main raw material. Market opportunities are extensive, but should be carefully considered for adipose tissue derived stem cells prior to selecting an indication.

In our view, the company is on track to meet its strategic goals. Should the company see positive results in its ongoing trial (ApoGraft POC final results estimated in late 2018), the financial potential of their stock is projected to increase the company's share.

We maintain our estimation of the company's equity value at \$101.4M; corresponding to a target price ranging between \$15.40 and \$18.70; a mean of \$16.90.

For a full breakdown of our valuation methodology please see our [Initiation of Coverage report, dated 27 April 2017.](#)

Appendix – Financial Reports

Balance Sheet	(\$000s)	(\$000s)	(\$000s)
Current Assets:	31.12.2016	31.12.2017	31.3.2018
Cash and cash equivalents	6,279	3,961	7,151
Short term deposits	19,660	-	-
Marketable securities	4,997	4,038	2,703
Accounts receivable	1,461	236	217
Total – Current Assets	32,397	8,235	10,071
Non-Current Assets:			
Restricted cash	140	88	133
Other long term assets	-	50	47
PPE, net	1,373	388	399
Total - Assets	33,910	8,761	10,650
Current Liabilities:			
Trade payables	1,401	491	412
Other accounts payable	2,084	691	503
Total Current Liabilities	3,485	1,182	915
Non-Current Liabilities:			
Warrants exercisable into shares	1,938	2,141	2,003
Total Non-Current Liabilities	5,423	3,323	2,918
Total Liabilities	8,908	4,505	3,833
Total Equity	25,002	933	6,817
Total Liabilities + Equity	33,910	8,761	2,918

Statement of Profit and Loss	(\$000s)	(\$000s)	(\$000s)	(\$000s)
Reporting Period:	2016	2017	31.3.2017	31.3.2018
Research and development expenses	2,147	3,318	784	813
General and administrative expenses	2,072	3,729	708	982
Other Income	(73)	0	0	0
Total Operating expenses	4,146	7,047	1,492	1,795
Operating Loss	4,073	7,047	1,492	1,795
Financial expenses (income) due to warrants	172	1,123	1,881	(633)
Other financial expenses (income), net	9	29	85	(145)
Total loss	4,254	8,141	3,459	1,017

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Some of the companies we cover

