EDISON

Clal Biotechnology Industries

Financial update

A strategic approach to MediWound

Pharma & biotech

Clal Biotechnology Industries' (CBI's) portfolio of investments continues to progress on multiple fronts. Most importantly, MediWound (CBI owns a 35% stake) announced in March that it had been approached by a third party to consummate a strategic transaction. The exact nature of the proposed transaction is unclear and could range from a product out-licensing to the acquisition of all of MediWound. The companies are in advanced discussions and conducting mutual due diligence.

Year end	Revenue (NISm)	PBT* (NISm)	EPS* (NIS)	DPS (NIS)	P/E (x)	Yield (%)
12/15	55.8	(209.4)	(1.44)	0.0	N/A	N/A
12/16	30.5	(454.1)	(2.89)	0.0	N/A	N/A
12/17	73.6	(54.2)	(0.15)	0.0	N/A	N/A

Note: *PBT and EPS are normalised, excluding amortisation of acquired intangibles, exceptional items and share-based payments.

Continued growth at MediWound

MediWound recently announced its full year 2017 results. Revenues, which are based on NexoBrid sales in the EU, were up 60% in 2017 compared to the previous year. The company also updated timelines with top-line results from the US NexoBrid Phase III expected by the end of the year and protocol submission for the EscharEx Phase III to the FDA now expected in H218 (previously both were expected in H118).

Clinical progress at Gamida Cell

Gamida Cell (18%-owned by CBI) recently presented Phase I/II data on CordIn in patients with severe sickle-cell disease. All 13 patients had rapid engraftment at a median of seven days and in the nine patients with long-term follow up, transfusion independence with a normal haemoglobin profile was achieved. However, two patient deaths were reported, one due to secondary graft failure and the other due to severe graft versus host disease (a common complication from BMT).

BioCanCell getting closer to additional funding

In January, BioCanCell (44% owned by CBI) announced it had executed a non-term sheet for a $25m private equity investment in the company. The funding has not closed yet but if it does, BioCanCell will have the funding to initiate two registrational studies for its lead program, BC-819 in non-muscle invasive bladder cancer (NMIBC). The company also recently updated data for BC-819 in combination with BCG, where 54% were recurrence free after 24 months.

Valuation: NIS1,011m or NIS6.46 per share

We are increasing our valuation from NIS918m or NIS5.87 per share to NIS1,011m or NIS6.46 per share. This was mainly due to rolling forward our NPV and increasing the value of two of its portfolio companies (Neon and Cadet) due to funding and business development milestones. This was mitigated partly by a more conservative view of the trajectory NexoBrid launch in the EU and delaying the US launch to 2020 due to delayed clinical timelines.

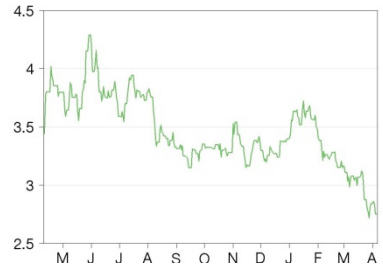
10 April 2018

Price*	**NIS2.75**
Market cap	**NIS430m**

*Priced at 6 April 2018

	NIS3.48/US$
Net cash ($m, unconsolidated) at 31 December 2017	8.1
Shares in issue	156.5m
Free float	35.3%
Code	CBI
Primary exchange	TASE
Secondary exchange	N/A

Share price performance



%	1m	3m	12m
Abs	(10.3)	(24.2)	(17.0)
Rel (local)	(6.5)	(18.0)	(18.8)
52-week high/low	NIS4.3	NIS2.7	

Business description

Clal Biotechnology Industries is a healthcare investment company focused on investing in a variety of therapeutic, diagnostic and medical device companies covering a full range of development phases from preclinical to post-market. The company holds 10 direct investments with interests ranging between 5% and 70%. It also has five indirect investments through its 50% stake in the Anatomy Fund, which it manages.

Next events

Gamida Cell IPO	H218
MediWound NexoBrid Phase III results	YE18
MediWound EscharEx Phase III trial initiation	YE18

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Edison profile page

Portfolio progress

In March, MediWound announced it had been approached by a third party interested in a strategic transaction. The exact nature of the proposed transaction was not disclosed but could include anything from a product out-licensing to the acquisition of all of MediWound. If it does involve licensing the rights to a MediWound product, we believe it would likely be for EscharEx, which has a larger addressable market than NexoBrid. It is important to note that we currently do not include any upfront or milestone payments in our EscharEx model so a licensing agreement could provide upside to our valuation for the product. Also, a takeout price above our current NPV/share for MediWound ($7.65 with current MediWound shares outstanding) would also provide upside to our valuation. The parties are in advanced discussions and conducting mutual due diligence so we should receive further updates in the coming weeks and months. We will update our model once an agreement, if any, is finalised.

In terms of the underlying business, MediWound recently announced its full-year 2017 results. Revenues, which are based on NexoBrid sales in the EU, were up 60% (to $2.5m) in 2017 compared to the previous year.

The company also updated timelines for its clinical programs for NexoBrid and EscharEx. In terms of the 175-patient US NexoBrid Phase III, top-line results are now expected around the end of the year (compared to our previous expectation of H118). The reason for the delay is that there is a lot of fluctuation in the monthly enrolment numbers as they are highly dependent upon how many patients burn themselves in any given month and meet the enrolment criteria. Also, MediWound's regulatory consultants recommended that it not lock the database until three months follow up was completed on all patients.

With regards to EscharEx, the company now expects to submit the Phase III protocol to the FDA in H218 (versus previous expectations of H118) with the actual initiation of the study likely sometime around the end of 2018 or the beginning of 2019. Also, the company announced that after speaking with regulatory experts, it believes the Phase III programme might only need 500 patients across two studies (250 each study), 200 fewer than the previous expectations of 700 (350 each study). If agreed to by the FDA, this could lead to significant R&D cost savings for the EscharEx programme.

Gamida Cell clinical progress

Gamida Cell recently presented the results from its 13-patient trial of CordIn in 13 patients with sickle-cell disease (SCD) who were in need of allogeneic bone marrow transplant (BMT) at the 2018 BMT Tandem Meetings (21-25 February, Salt Lake City). Engraftment was observed after a median of seven days post-treatment in all 13 patients. And in the nine patients with long-term follow up, transfusion independence with a normal haemoglobin profile was achieved. However, two patient deaths were reported, one due to secondary graft failure and the other due to severe graft versus host disease (a common complication from BMT). The company plans to continue development although we do not yet include this programme in our valuation as it is still relatively early and timelines are unclear.

As a reminder, enrolment is underway for Gamida Cell's 120-patient Phase III study of NiCord in patients with haematological malignancies, which will take place worldwide in 12 sites. This trial is investigating the ability of NiCord to provide an umbilical cord blood (UCB) graft with an ample amount of cells that have fast and vigorous in vivo neutrophil and platelet producing potential to improve transplantation outcomes (as low cell dose is associated with delayed engraftment and poor outcomes). The primary endpoint for the trial is time to neutrophil engraftment following transplantation (on or before the 42nd day post-transplant) compared to a non-manipulated cord

blood unit. The company intends to use the funds from its recent $40m fund-raising to progress its Phase III trial, which is expected to read out in H219.

BioCanCell potential funding and clinical data

In January, BioCanCell (44% owned by CBI) announced it had executed a non-term sheet for a $25m private equity investment. The lead investor expects to contribute $7m to the offering and has the right to allocate $8m from other equity investors. Existing investors would provide another $5m and additional new investors would provide an additional $5m. As this is a non-binding term sheet, the exact amount of investment is unknown and it is possible that the financing does not close at all. If and when it does close, BioCanCell will have the funding to initiate two registrational studies for its lead program, BC-819 in non-muscle invasive bladder cancer (NMIBC). However, it is likely that CBI's percentage ownership of BioCanCell will fall from current 44% due to dilution from the placement.

BioCanCell is preparing to initiate two pivotal clinical trials in 2018. BC-204 will be an open label Phase II single-arm trial in 140 patients who are unresponsive to BCG therapy and the primary end point is durable response rate (either partial or complete) at 12 months. It is expected to begin in H118. BC-301 will be an open-label Phase III trial in approximately 495 patients of BC-819 in combination with BCG in versus BCG alone and is expected to begin in H218. The BC-301 trial has been granted a special protocol assessment (SPA) by the FDA and the primary end point is median time to recurrence. The BC-301 trial will be the first comparative study and we expect the results to elucidate the clinical value of BC-819 for NMIBC.

BioCanCell also recently presented updated data for BC-819 at the ASCO Genitourinary Cancers Symposium (8-10 February, San Francisco). In a Phase II trial of 38 patients with NMIBC, a combination of BC-819 and BCG (the current standard of care) achieved a 24-month recurrence-free rate of 54% an improvement over prior data at the 24-month mark for BC-819 alone. In an open label 18-patient Phase I/II single-arm trial, intravesical infusion of BC-819 into the bladder showed a 24-month recurrence-free rate of 29%. In another open-label 39-patient Phase II single-arm trial, the intravesical infusion of BC-819 into the bladder demonstrated a 24-month recurrence-free rate of 33%.

Agreement to sell CureTech

In late March, CBI announced an agreement to sell CureTech (53% owned by CBI) to InSight Innovations. This is not a surprise following the termination of the CureTech agreement with Pfizer for CureTech's pidilizumab in October 2017 and the announcement by CBI that CureTech would no longer be considered a material portfolio company.

As part of the agreement with InSight Innovations, CureTech's shareholders will receive up to $550m in milestone payments, additional royalties and CBI will receive $3m upfront. Also, if CureTech's pidilizumab is approved and InSight Innovations receives a priority review voucher (PRV), CureTech's shareholders would receive 20% of any monies received if that voucher is then sold. There were several sales of PRVs in 2017, with prices ranging from $125m to $150m (hence CureTech's shareholders could receive $25m to $30m). As a reminder, PRVs can currently be granted to companies that receive approvals for drugs treating a variety of indications, including rare pediatric diseases such as diffuse intrinsic pontine glioma (DIPG), currently the lead indication for CureTech's pidilizumab. We continue to not include CureTech in our valuation for CBI as timelines for future development and hence the payment schedule of the milestones are unclear. We will revisit this if we gain additional clarity.

Update on rest of portfolio

Biokine's (27% owned by CBI) partner BioLineRx announced partial results from the monotherapy portion of its 30-patient single-arm Phase II trial to evaluate BKT-140/BL-8040 in combination with KEYTRUDA (pembrolizumab), the anti-PD-1 therapy, in patients with metastatic pancreatic adenocarcinoma. The results showed that BL-8040 induced an increase in the number of total immune cells in the peripheral blood while reducing the frequency of peripheral blood regulatory cells that may impede the anti-tumour immune response. Top-line clinical results from this trial are on track for H218. We do not currently include pancreatic cancer in our model so any positive data from the trial could provide upside to our valuation for Biokine.

Also, Cadent announced that it has initiated a Phase I for its lead program CD-1883, a positive allosteric modulator. CD-1883 is being developed to treat spinocerebellar ataxia, an orphan genetic disorder characterised by cerebellum dysfunction or degeneration that causes difficulty co-ordinating movements, and essential tremor (ET), a neurological disorder characterised by involuntary and rhythmic shaking, most commonly of the hands and forearms. CD-1883 increases the sensitivity of calcium-sensitive potassium (SK) channels that play an essential role in regular neuronal firing with the intent to restore regularity and improve motor function.

Exhibit 1: CBI's key investments

Investment	Technology	% held	Founded	Status	Advantages	Targets
MediWound*	Enzyme technology for severe burns and chronic wound	35%	2001	NexoBrid: Launched in Europe; In Phase III development in the US. EscharEx: Phase II complete.	Reduces time to successful eschar removal, reduces need for surgery and need for grafting.	NexoBrid Phase III study readout YE18; EscharEx Phase III trial initiation in end of 2018 or beginning of 2019.
Gamida Cell*	Cord stem cell transplant for hematologic diseases	18%	1998	NiCord: Enrolling Phase III; CordIn: Two ongoing Phase I/II trials; Natural killer cells: Initiated Phase I.	UCB for transplantation only requires partial matching and nicotinamide technology increases the limited population and quality of stem and progenitor cells. NiCord received FDA breakthrough therapy designation.	Enrolment is underway for a Phase III study of NiCord; NASDAQ listing targeted for H218.
BioCanCell	BC-819 is a DNA plasmid for non-muscle invasive bladder cancer	44%	2004	Ongoing Phase II BC-819 and BCG combination trial	BC-819 is a 4.5 kb recombinant DNA plasmid containing H19 regulatory sequences that drives expression of the potent diphtheria toxin A and inhibits protein translation in malignant bladder cells. Monotherapy clinical studies demonstrated promising efficacy rates.	Initiate two (monotherapy and combination therapy) pivotal clinical trials in 2018. NASDAQ listing targeted for H218.
Biokine	Cyclic peptide inhibitor of CXCR4 for AML and other malignancies	27%	2000	Phase III in stem cell mobilisation. Phase II in relapsed/ refractory AML with BioLineRx; Phase Ib/II: collaboration with Genentech, combination BKT-140/BL-8040 and Tecentriq (atezolizumab) for multiple oncology indications.	Phase I/II trials showed vigorous mobilisation of CD34+ stem and progenitor cells from the bone marrow, inducing cell death and sensitising the malignant cells to anti-cancer therapies.	Phase II mobilisation results for BL-8040 in H118. Phase II pancreatic results in H218.

Source: Clal Biotechnology Industries. Notes: *Material assets according to CBI. All key investments included in our rNPV.

Exhibit 2: CBI direct holdings

Investment	Technology	% held	Founded	Status	Advantages	Targets
eXIthera	Factor XIa inhibition to prevent thrombosis and stroke	54%	2012	Phase I: Safety, tolerability, PK, PD of parenteral EP-7041	Positive Phase I dose escalation readout showed EP-7041 was safe and well tolerated in healthy volunteers and also demonstrated positive PK and PD data.	Potential licensing deal for EP-7041 in H118. Phase II initiation in H218. Selection of oral candidate expected in coming months.
Vedantra	Cancer and infectious disease immunotherapy	66%	2011	Preclinical	Engineering a molecular vaccine that possesses both hydrophilic and hydrophobic properties (amph-vaccine) to exploit albumin to transport small payloads to the lymph node to initiate effective T- and B-cell responses.	Amphiphile technology-based HPV vaccine for the treatment of HPV-related head and neck malignancies expected in the clinic in H118.
Neon	Personalised neoantigen therapeutics for cancer	5%	2015	Phase I: NEO-PV-01 and OPDIVO combination therapy	Initial results published in Nature. Several collaborations in the pipeline with large pharma, academic institutions, and other clinical stage biopharmaceutical companies. Recently completed a $106m crossover Series B financing.	Initial NEO-PV-01 and OPDIVO combination results expected in H118; Potential NASDAQ listing in H218.
Cadent	Treatment of CNS disorders by targeting calcium-sensitive potassium (SK) channels	24%	2010	Phase I	CD-1883 increases the sensitivity of SK channels that play an essential role in regular neuronal firing with the intent to restore regularity and improve motor function.	Potential NASDAQ listing in H218.

Source: Clal Biotechnology Industries. Notes: DIPG = diffuse intrinsic pontine glioma, CXCR4 = CXC- chemokine receptor-4 pathway, AML = acute myeloid leukaemia, NMDAR = N-methyl-D-aspartate receptor.

Exhibit 3: CBI indirect holdings through 50% stake in Anatomy

Investment	Technology	Anatomy investments at fair value to CBI ($m)	Founded	Status	Advantages	Targets
FDNA	Genetic disease diagnostics with facial recognition	1.1	2011	Market	Combines computer vision, machine learning and artificial intelligence to analyse facial features, genomic data, and patient symptoms	Innovation needs to be linked to clinical outcomes
Sight Diagnostics	Computer vision point-of-care blood diagnostics system	1.0	2011	Parasight: Market; OLO: Pivotal trial	Point-of-care full complete blood count system	OLO: Clinical validation and commercial test development. FDA approval
Colospan	Developing bypass device (CG-100) for colorectal surgery	1.6	2010	CE approved in Europe.	Prevents life threatening leakage and makes it possible to cut down the use of stomas. Positive initial clinical results	CG-100: Soft launch in Europe in 2018 for market feasibility. Recruiting approximately 137 patients to participate in the safety and efficacy trial through H219 and expects to file for FDA marketing approval following trial results.
MinInvasive	Device for arthroscopic rotator cuff repair	1.6	2011	Market	Needle-based shoulder tendon repair device that eliminates the need for suture anchors	MicroPort granted exclusive rights to distribute device in China. FDA cleared and anticipating US launch.
Pi-Cardia*	Non-implant based technology for aortic valve stenosis	1.6	2009	Clinical	Developed a low profile catheter to treat aortic stenosis without replacing the valve	Clinical validation.
Total, including $1.5m in additional investments		**8.5****				

Source: Clal Biotechnology Industries. Note: *as of year-end 2017 **Pi-Cardia is also held directly (21% stake includes direct costs of CBI and 50% stake in Anatomy).

Valuation

We are increasing our valuation from NIS918m or NIS5.87 per share to NIS1,011m or NIS6.46 per share. This was mainly due to rolling forward our NPV and increasing the value of two of its portfolio companies. We have increased the value of the Neon investment (5% owned by CBI) to

$12.4m from $5m based on the valuation of the most recent funding round completed in December 2017. We have also increased the value of its Cadent stake (it owns 24%) from $7.1m to $18m, due to company disclosures that the implied value of Cadent following the Novartis milestone is $75m. This was partly mitigated by a more conservative view of the trajectory NexoBrid launch in the EU and delaying the US launch to 2020 due to delayed clinical timelines (although we have kept peak sales the same). We expect to update our valuation of MediWound further once we get more information about the advanced discussions with the potential strategic partner. We also note that our valuation may change as a result of BioCanCell's ongoing funding round.

Exhibit 4: Clal Biotechnology Industries valuation table

Product	Setting	Status	Launch	Peak sales ($m)	Probability of success	Royalty rate	rNPV ($m)	% owned by Clal B	Clal B rNPV ($m)
MediWound	Burns	Market and Phase III ready	Nexobrid: Market, EscharEx: Phase III	375	Nexobrid US 80%, Europe 100%, EscharEx 50%	Nexobrid: 100% EscharEx: 20%	207	35%	72.4
Gamida Cell	Leukemia (AML, ALL, CML, CLL)	Phase III	2020	437	50%	100%	423	18%	76.1
Biokine	AML	Phase II	2023	1,286	30%	40% of what BioLineRx receives from a sublicense (assume 20%)	43	27%	11.6
BioCanCell	Bladder cancer	Phase II and Phase III ready	2022	530	30%	100%	142	44%	62.4
Neon								5%	12.4
Vedantra								66%	9.1
ExlThera								54%	10.3
Cadent								24%	18.0
Anatomy portfolio									8.5
Portfolio total ($m)									281
Cash, unconsolidated (As of 31 December 2017) ($m)									8
Overall valuation									289
Shekel/Dollar Conversion rate									3.5
Overall valuation in Shekels (NISm)									1,011
Shares outstanding (m)									156.5
Per share (NIS)									6.46

Source: Edison Investment Research, Clal Biotechnology Industries reports

Financials

As a reminder, due to significant ownership stakes, CBI consolidates the financials of several of its investments (MediWound, Vedantra, CureTech and the Anatomy fund) and on this basis, it had NIS165.1m ($47.4m) in cash, cash equivalents and bank deposits as of Q417. CBI's cash position at the corporate level (excluding consolidation) was NIS28.4m ($8.1m) at the end of 2017.

Total consolidated revenues of NIS43.5m ($12.5m) were generated through the sales of MediWound's NexoBrid in Europe, Israel and Argentina, licensing agreements and rent in addition to a gain of NIS11.0m ($3.2m) from the decrease of equity interest in associates and a NIS19.1m ($5.5m) gain from the disposal of subsidiaries or loss of control in 2017.

Significant investment was made into the development of underlying technologies and products of CBI's material assets as indicated by R&D spend of NIS32.6m ($9.4m) in 2017 although this is down from NIS42.0m ($12.1m) in FY16. For the year, general and admin costs, which include payroll and related expenses, management fees, and marketing and advertising expenses on a consolidated basis, were NIS61.7m ($17.7m), down from NIS81.1m ($23.3m) in the prior year.

We outline historical financials in Exhibit 5; however, we are not providing forecasts at this time.

Exhibit 5: Financial summary

NIS'000s	2015	2016	2017
Year end 31 December	IFRS	IFRS	IFRS
PROFIT & LOSS			
Revenue	55,759	30,484	73,635
Cost of Sales	(42,549)	(46,967)	(32,433)
Gross Profit	13,210	(16,483)	41,202
R&D expenses	(54,094)	(42,011)	(32,644)
SG&A expenses	(82,747)	(81,107)	(61,679)
EBITDA	(175,382)	(434,812)	(103,330)
Operating Profit (before amort. and except.)	(179,999)	(451,764)	(103,633)
Intangible Amortisation	0	0	0
Exceptionals	0	0	0
Operating Profit	(179,999)	(451,764)	(103,633)
Other	(35,553)	(11,850)	(31,078)
Net Interest	6,197	9,510	80,478
Profit Before Tax (norm)	(209,355)	(454,104)	(54,233)
Profit Before Tax (FRS 3)	(209,355)	(454,104)	(54,233)
Tax	14,023	60,104	31,795
Profit After Tax (norm)	(195,332)	(394,000)	(22,438)
Profit After Tax (FRS 3)	(195,332)	(394,000)	(22,438)
Average Number of Shares Outstanding (m)	135.8	136.2	149.4
EPS - normalised (NIS)	(1.44)	(2.89)	(0.15)
EPS - FRS 3 (NIS)	(1.44)	(2.89)	(0.15)
Dividend per share (NIS)	0.0	0.0	0.0
BALANCE SHEET			
Fixed Assets	1,225,127	927,359	849,112
Intangible Assets	1,035,753	741,543	626,342
Tangible Assets	17,077	16,536	14,854
Other	172,297	169,280	207,916
Current Assets	307,645	191,351	185,228
Stocks	6,691	3,248	6,539
Debtors	18,784	16,415	13,612
Cash	256,105	171,022	165,077
Other	26,065	666	0
Current Liabilities	(66,785)	(68,277)	(31,182)
Creditors	(14,782)	(8,507)	(7,975)
Short term borrowings	0	0	0
Short term leases	0	0	0
Other	(52,003)	(59,770)	(23,207)
Long Term Liabilities	(373,520)	(297,938)	(194,962)
Long term borrowings	0	0	0
Long term leases	0	0	0
Other long term liabilities	(373,520)	(297,938)	(194,962)
Net Assets	1,092,467	752,495	808,196
CASH FLOW			
Operating Cash Flow	(156,274)	(52,529)	(59,400)
Net Interest	23,298	0	0
Tax	(14,023)	(60,104)	(32,005)
Capex	0	0	0
Acquisitions/disposals	27,971	(395)	(3,876)
Financing	22,499	23,123	80,611
Dividends	0	0	0
Other	146,116	5,447	72,644
Net Cash Flow	49,587	(84,458)	57,974
Opening net debt/(cash)	(207,517)	(256,105)	(171,022)
HP finance leases initiated	0	0	0
Other	(999)	(625)	0
Closing net debt/(cash)	(256,105)	(171,022)	(228,996)

Source: Edison Investment Research, Clal Biotechnology Industries reports

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