Mologen AG

Initiation of coverage

Edison investment research

Innately adaptive

Pharma & biotech

Mologen develops anti-cancer immune maintenance therapies aiming to give long-lasting responses. The investment case rests on a possible 2013 deal on the lead project, MGN1703, based on high-quality interim Phase II data. These indicated a 50% reduction in the hazard risk of disease progression when MGN1703 was dosed every three days. Mologen aims to partner MGN1703 to fund internal development of MGN1601, a cell-based vaccine for metastatic renal cancer. MGN1601 could be an orphan drug with no generic version possible; Mologen intends to sell direct.

Year end	Revenue (€m)	PBT* (€m)	EPS* (c)	DPS (c)	P/E (x)	Yield (%)
12/11	0.14	(6.8)	(55.3)	0.0	N/A	N/A
12/12e	0.20	(7.2)	(51.6)	0.0	N/A	N/A
12/13e	0.10	(9.9)	(64.5)	0.0	N/A	N/A
12/14e	0.10	(14.5)	(94.4)	0.0	N/A	N/A

Note: *PBT and EPS are normalised, excluding intangible amortisation and exceptional items.

MGN1703 – a clear colorectal cancer maintenance effect

MGN1703 is a stable, dumbbell-shaped DNA molecule (dSLIM) that activates innate immunity. Interim data in metastatic colorectal cancer (mCRC) showed that the hazard ratio for disease progression was reduced by 50% compared to a matched placebo group on an intent-to-treat (ITT) basis. Statistical significance was seen when a group of nine ineligible and high-risk patients were excluded. Mologen aims to partner MGN1703 in 2013, but will progress into Phase IIb/III independently of a deal.

MGN1601 – cell-based renal cancer vaccine plus dSLIM

This allogenic renal cancer cell vaccine plus dSLIM has reported data for a 19-patient Phase I metastatic renal cancer safety study, ASET. Immune effects were detected in some patients and one partial response was seen with some stable disease cases. There are good data for a small, initial study. Mologen is developing a Phase II design in metastatic renal cancer patients. If MGN1601 is approved, Mologen plans to sell direct in the EU and US. Generic competition will not be possible as this is a unique, proprietary cell-line, so MGN1601 could yield valuable long-term profits.

Valuation: MGN1703 deal value of €18.20, un-partnered €16.50

The indicative value of Mologen depends on whether a deal on MGN1703 occurs either in 2013 or after Phase III data in 2016. A deal in 2013 would fund Phase II development of MGN1601. However, if a good deal is not feasible, Mologen can progress both studies, but would need a further €25m with a better deal possible in 2016, depending on Phase III data. MGN1703 may face generic competition in the EU in 2025 and in the US in 2023. A major value assumption is that MGN1601 is free from direct generic competition, as it uses a proprietary cancer cell line. It is also assumed that Mologen can sell this orphan product direct to maximise long-term profits. Edison has valued Mologen with a 2013 MGN1703 deal at €18.40 per share, assuming 45% MGN1703 and 25% MGN1601 probabilities. A regulatory-stage 2016 deal indicates about €16.50 per share value.

Mologen AG is a research client of Edison Investment Research Limited

	25 February 2013
Price	€14.0
Market cap	€216m

Shares in issue	15.4m
Free float	40%
Code	MDG
Primary exchange	Frankfurt Prime Standard
Other exchanges	N/A

Share price performance

%	1m	3m	12m
Abs	19.4	16.9	82.4
Rel (local)	19.9	10.5	62.9

52-week high/low	€14.4	€7.5

Business description

Mologen has two lead products: MGN1703 for metastatic colorectal cancer maintenance therapy, entering Phase IIb/III by 2013 and MGN1601, an allogeneic cancer cell vaccine for renal carcinoma. These use dSLIM, a stable DNA construct that stimulates the immune system.

Next events

FY12 report	21 March
Partnering of MGN170	2013
Lung cancer Ph II	H213

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Investment summary: Innately adaptive

Mologen was founded in 1998 based on research work by Professor Burghardt Wittig, the founding CEO. The current CEO and R&D director, Dr Matthias Schroff, was part of the original research team and a leading researcher in the new business, becoming CEO in 2008. Mologen was funded by an IPO on foundation, so has always relied on the public markets, raising €86m to date, including €25m in 2012; it has never had venture funding. Mologen follows a cautious and focused development strategy, with two products with Phase II data: MGN1703 and MGN1601. Both are anti-cancer therapies designed to activate the immune system to either hold the disease in check as maintenance therapy or, in the best case, achieve a therapeutic response. Mologen plans to partner MGN1703 as a single agent and progress the trials of MGN1601, aiming to market direct. Mologen had cash on 30 Sept of €25.2m. The company is based in a high-level floating building on the Free University campus in Berlin. Mologen has 52 employees.

Sensitivities

There are two crucial investor sensitivities. Firstly, whether MGN1703 IMPACT will be partnered with a substantial upfront fee in 2013. If not, Mologen needs funds to complete the Phase IIb/ III. The second, later sensitivity is whether dSLIM, an innate immune stimulant, can generate a sustained maintenance response[i] against tumour cells; Phase III will take until 2015-16 to prove or disprove this. dSLIM certainly activates the innate anti-infective system, but adaptive immunity, if necessary, requires the immune cells to recognise and destroy tumour cells and for cancer tolerance to be overcome. A key part of development will be the use of biomarkers to identify patients who might respond, on immune-related response criteria, over the initial three months of immune therapy. Separately, the MGN1601 sensitivity relates to its showing efficacy in Phase II. This will not be known until at least 2015.

Valuation

The indicative value of Mologen depends on whether a deal on MGN1703 occurs either in 2013 or after Phase III data in 2016. A deal in 2013 would fund both Phase II development of MGN1601 and operations. However, if a good deal is not feasible, Mologen can progress both studies, but may need a further €25m with a better royalty deal possible in 2016, depending on Phase III data. MGN1703 may face generic competition in the EU in 2025 and in the US in 2023. A major value assumption is that MGN1601 is free from direct generic competition as it uses a proprietary cancer cell line. It is also assumed that Mologen can sell this orphan product direct to maximise long-term profits. Edison has valued Mologen with a 2013 MGN1703 deal at €18.40 a share, assuming 45% MGN1703 and 25% MGN1601 probabilities. A regulatory-stage 2016 deal indicates about €16.50 per share value.

Financials

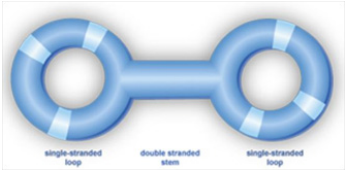
Mologen's ytd statement to 30 September 2012 showed cash of €25.2m after a €22m equity placement in July. Ytd loss was €5.7m after €0.3m of income and grants. Cash expenditure may rise to between €9m and €10m in 2013 as the MGN1703 Phase IIb/IIII study gets underway and the Phase II MGN1601 study is initiated. The MGN1703 study is expected to cost c €15m in external fees, with c €6m for MGN1601. MGN1703 partnering in 2013 would add to cash reserves and cut costs.

[i] This could be an adaptive or innate immune response (Exhibit 2). Clinically, so long as patients do not progress, the therapy will be useful. An adaptive response may be more powerful and would be long lasting.

Outlook: Two immune-therapy products

The core invention underpinning Mologen is the dSLIM DNA construct (see Exhibit 1). This is a stable, dumbbell-shaped DNA structured as a continuous strand. dSLIM triggers the innate immune system. Innate immunity has evolved (see Exhibit 2) to react immediately to infections. Over several months of cancer immune therapy, it can lead to a long-term control of the disease, perhaps though an adaptive response. This is where a patient's immune system recognises tumour-specific antigens. To help tumour recognition, the MIDGE system has been used to transfect a renal cancer cell line to produce four immune stimulatory proteins. These transfected, allogenic cells are administered, with dSLIM, to renal cancer patients to generate an adaptive immune response. The MIDGE system can also be used to generate an immune response against parasites and viruses.

Exhibit 1: Mologen portfolio

Project	Technology	Clinical status	Notes
MGN1703 Metastatic colorectal cancer (mCRC)	dSLIM (double-stem loop immunomodulator) is a 116-base DNA construct with a central 28-base pair double-stranded section and two single-stranded 30-base loops at either end.  Each loop bears three unmethylated CG motifs, which act as ligands. Unmethylated CG motifs are rare in human DNA, so are recognised by Toll-Like receptor 9 (TLR9) in dendritic cells as a signal of infection triggering the innate immune system. This can lead to a long-term adaptive immune response.	IMPACT safety and efficacy Phase II/III study with 59 metastatic colorectal cancer (mCRC) patients recruited; interim analysis on 55. The dose used was dSLIM 60mg twice-weekly until disease progression. Doses are given subcutaneously at two sites (2ml/30mg each) in the upper chest, abdomen or upper thighs. Recruitment ended with initial results released in May 2012. Patient follow-up for overall survival is continuing with final data due perhaps in H213.	Mologen has had a pre-IND meeting with the FDA and discussions with the EMA. A US IND will be filed once the design has been finalised with opinion leaders. The likely next stage is a 300-patient Phase IIb/III study in mCRC. Partnering discussions have been initiated with a deal possible in 2013, but Mologen has cash to start the Phase II/III in 2014. A regulatory filing is possible in 2016-17.
MGN1703 Lung cancer		Phase II trial application made in March. Possible start H113.	Competitor trials are large scale and prolonged.
MGN1601 Clear cell renal carcinoma	Injection of genetically-modified tumour cells transfected with four MIDGE vectors: GM-CSF, IL-7, CD80 and CD154 (CD40L). Repeat injections of transfected cells, together with dSLIM, are given over a 12-week period, with a potential extension to 120 weeks.	In the ASET open-label renal cancer Phase II study, 19 patients were recruited and 10 completed the 12-week course, two of whom had extended therapy. There was one PR (-55%) and three SD cases. Five patients may have been sensitised to other therapies.	Pivotal trial being discussed with the EMA and FDA. Mologen has sufficient cash to conduct a Phase IIb/III.
MGN1331 Leishmaniasis	Uses a MIDGE Th-1 vector to stimulate cellular immunity against the parasite.	Completed preclinical. Phase I in 2014 if externally funded. May be licensed.	Estimated 50,000 cases of potentially fatal visceral disease in the developing world.
MGN1333 hepatitis B	Uses a MIDGE Th-1 vector to stimulate cellular immunity against infected cells.	In preclinical.	Needs to show excellent viral clearance.

Source: Edison Investment Research

Immune therapy clinical trials: Crucial differences

Standard criteria used in cancer therapy clinical trials are based on traditional chemotherapeutic agents. These assume the agent has an immediate therapeutic response. The statistics used to analyse the studies are based on hazard ratios assumed to apply from day one and detect an immediate separation of the Kaplan Meier curves. Exhibit 3 looks at the differences between standard response criteria (RC) and newer immune response criteria, irRC developed from clinical experience, Exhibit 2. This is illustrated with patient examples from the MGN1601 ASET trial.

Exhibit 2: Innate immunity fact file

Innate immunity	This is the first line of defence against infection. It comprises a set of receptors that recognise standard foreign and bacterial molecules. This system reacts immediately, because it is non-specific and it can be repeatedly stimulated. It produces cytokines and other inflammatory mediators. These stimulate natural killer cells.[1]
Is an innate immune response enough?	Innate immunity has no memory and a short-term action. There is a suspicion that regular stimulation of the innate immune response may help to control cancer without an adaptive response, but there is no clear proof that this occurs. MGN1703 is designed to be given every three days as a chronic maintenance therapy and is safe.
Link to the adaptive response	Proteins from destroyed bacteria are processed by the immune system to generate a longer-term and highly specific adaptive response consisting of T-cells and macrophages (which destroy foreign cells and bacteria) and antibodies (which will bind to specific foreign proteins and mark the cells carrying them for destruction). Innate immunity leads naturally to adaptive immunity and adaptive immunity cannot occur without an initial innate response.[2] The adaptive response is long term, although it may require re-stimulation after several years.
Cancer immunotherapy	The goal of cancer immunotherapy and vaccines is to persuade a patient's immune system to recognise its own tumour cells and to mount an adaptive immune response. This is hard to do because tumour cells are aberrant normal tissue, so are naturally tolerated by the immune system.
Differences in clinical design	The clinical trials of these products have shown that immune therapies need to be approached differently to standard chemotherapy in terms of trial design and statistical analysis, because immune therapies can take some months to become effective. If they do become effective, patients can experience long periods of stable disease with no additional therapy and partial and complete responses are also seen.
dSLIM mimics bacterial DNA	A clear signal of bacterial DNA is the presence of unmethylated CpG motifs.[ii] Plasmacytoid Dendritic Cells (pDCs) take bacterial DNA fragments into the endoplasmic reticulum compartment where they are detected by Toll-like receptor -9 (TLR9)[3]. Once activated, TLR-9 triggers a complex wave of immune reactions linking through to the adaptive response. dSLIM mimics bacterial DNA by being taken into pDCs and triggering TLR9. Many immune therapies in development use a similar tactic of some form of bacterial innate system activator.
Action of dSLIM	Exhibit A, available online only, provides a graphical overview of how dSLIM triggers an innate immune response that may lead to an adaptive response. It is not certain if an innate response only is adequate to control cancer.
Regulators limit anti-tumour responses	A major signal preventing immune attack is MHC1. Immune cells will not attack cells bearing the right "self" MHC1. Cancer cells express much less MHC1, so it is clinically possible to generate long-lasting immune tumour responses. The immune system destroys T-cells that recognise "self" proteins to prevent auto-immune disease. The T-cell destruction system uses several regulatory proteins: CTLA-4, PD-1 and PD-L1. Yervoy (ipilimumab, BMS)) targets CTLA-4 and deregulates the immune response in some patients to give significant anti- melanoma responses. [4, 5] BMS has a new antibody against PD-1 in Phase III and PD-L1 is being targeted by several companies. One theory is that cancer vaccines need to be combined with deregulatory effectors and maybe a vaccine (peptide, allogeneic cells or autologous cells) to get a better response. A short-acting targeted chemo/radio therapeutic (no immune side effects) might be given initially to give the immune response time to develop.

Source: Edison Investment Research

Competition in cancer immunotherapy

A database search identifies over 100 vaccine and immune therapy products and candidates, mostly in the early development stages. Only two of these are mainstream marketed products. The best-selling product (probably over $600m) in 2012 is Yervoy (ipilimumab, BMS) to treat metastatic melanoma. It is given intravenously over 90 minutes every three weeks for a total of four doses. This showed a hazard ratio on overall survival of 0.66, providing a benchmark for other immune therapies.

Provenge from Dendreon is a more complex, and expensive to produce, autologous cell product. It is administered three times over one month. Dendreon has been struggling to reach investor expectations, although Provenge should achieve over $300m in 2012.

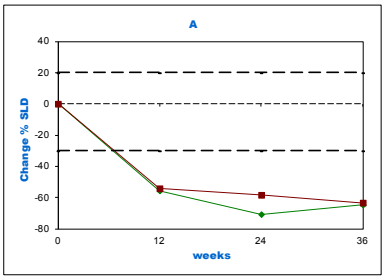
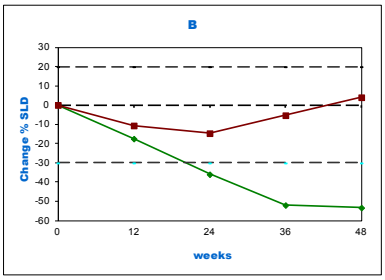
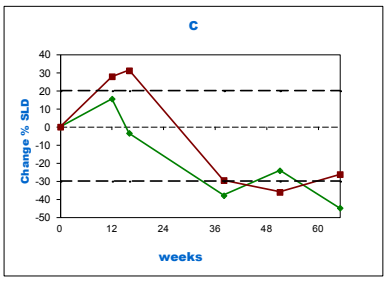
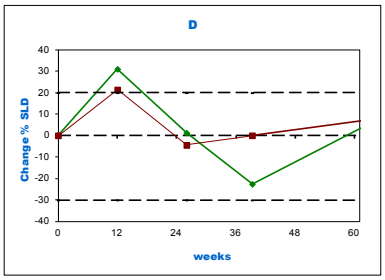
Exhibit 4 shows pivotal trial-stage projects in non-small cell lung cancer, colorectal and renal cancer as being relevant to Mologen. Other areas are melanoma and pancreatic cancer. Pivotal studies in non-small cell lung cancer tended to be big and this is a crowded area that will produce data, and possibly products, well before any pivotal MGN1703 results.

There appears to be considerable interest among pharma companies in products in the immune therapy area, after Yervoy showed that there is a serious market to develop (see Regulators section in

[ii] Cytosine (C) and Guanine (G) are two of the bases in DNA that form the code to produce proteins. In human DNA, about 70-80% of the cytosine in these CpG pairs is chemically modified by enzymes by addition of a methyl group. As bacteria cannot methylate DNA, unmethylated CG pairs are markers of bacterial infection.

Exhibit 2). This implies that Mologen should find a lot of interest in partnering MGN1703. Companies like MedImmune (AZ), Roche, Daiichi Sankyo, GSK and Vical are all active in the area.

Exhibit 3: Standard and immune response criteria in clinical development with ASET examples

Response	RC	irRC	ASET example	MGN1601 example
Complete and partial response Existing lesions shrink, showing a partial response (PR) or complete response (CR), and no new lesions are detected. This response is classed the same under RC and irRC.	Yes	Yes	This was the only patient to experience a PR, although a full CR was not achieved. The response was the same (other than a small 24 wk difference for both RC and irRC criteria.	
Stable disease (SD) no new lesions These are patients where tumour diameters either increase slightly or regress by up to 50%. The definition is the same in RC and irRC.	Yes	Yes	In the MGN1601 example, the tumour burden would be classed as SD on RC, but PR on irRC by 36 weeks.	
Stable disease response with new lesions Under RC, no new lesions are allowed, but irRC allows new lesions in SD as long as the overall burden does not increase by more than 25%. Tumour increase may be due to immune cell infiltration, so small lesions may suddenly be visible. If so, the tumour burden may subsequently decrease to PR, with CR seen in some patients.	No	Yes	This shows a delayed response where initial PD is seen on RC, but not irRC followed by a response on both, although this did not reach PR.	
Progressive disease (PD) Under RC new lesion, or if existing tumour sizes increase by 25%, the patient has PD. In irRC, the overall tumour burden is taken into account. If the burden including new lesion rises by over 25%, a second observation is made after four weeks. If both show an increase over 25%, PD is confirmed. The extra time tests if an immune response is developing. An irRC PD can become SD or PR given time.	Yes	Yes	In the example, there is an initial irRC PD. On RC, this is SD and although there is some response, it is just a trend back to baseline, although no progression.	

Source: Edison Investment Research, based on Wolchok, J. D. et al.[4] Note: Clinical data from Mologen; RC + brown lines irRC = green.

MGN1703

MGN1703 consists of dSLIM injections given twice-weekly. Injection, 2ml per site, is done subcutaneously since antigen-presenting cells in the skin and blood detect bacterial infection. The dose is 60mg based on the maximum injectable viscosity of dSLIM. Two injection sites are used per dose.[iii] This probably needs a nurse, but if feasible, a self-injection kit would help market adoption.

[iii] These are the upper arms, the upper thigh of each leg and right and left side of the abdomen just below the rib cage. There is only transitory injection site reaction at the sites with no tissues necrosis, so the sites are reused once per three-injection cycle, ie every nine days. Other DNA innate stimulation products have shown dose-limiting

Exhibit 4: Selected immune therapy products

Company	Product	Indication	Stage	Description	Status[iv]
Dendreon	Provenge (sipuleucel-T):	Prostate	Marketed	Autologous dendritic cells with antigenic fusion protein-cytokine.	Sales ytd $238m. Price $93k. Three injections, one month.
Bristol Myers Squibb	Yervoy (ipilimumab)	Metastatic melanoma	Marketed	Human mAb against CTLA-4 receptor, an immune regulator.	Sales 2012 ytd $495m. List price of $120k.
	BMS-936558	NSCLC	Phase III	Human mAb against PD-1, an immune regulator.	Randomised open label vs docetaxel 574 pts, data November 2014.
		ccRCC	Phase III		Randomised open label vs Everolimus 822 pts, data February 2016.
Argos Therapeutics	AGS-003	mCRC	Phase III	Autologous cell vaccine used in earlier-stage patients with Sutent.	FDA has agreed an SPA; may start late-2012. OS relative to Sutent alone.
Vaccinogen	OncoVax	CRC	Phase III	Autologous tumour cells with BCG. Marketed in Switzerland.	SPA agreed with FDA for Phase IIIb interim data, perhaps H115.
Transgene	TG4010	NSCLC	Phase II/III	Recombinant virus encoding the mucin-1 antigen and IL-2.	RBP Phase IIb/III, 1,000 pts interim H113, full 2015.
GlaxoSmithKline	GSK1572932 A	NSCLC	Phase III	MAGE-A3 cancer antigen vaccine.	RPB 2,200 pts, data 2022.
NovaR.	Lucanix (belagenpumatecel-L)	NSCLC	Phase III	Allogeneic vaccine with four cancer cell lines with antisense against TGF beta.	RPB 506-pt Phase III data, maybe H212.
Oncothyreon (Merck KGaA; Ono)	Stimuvax	NSCLC	Phase III	Liposomal vaccine containing a mucin-1 peptide.	RPB 1,514-pt Phase III data H113.
Kael-Gemvax	GV1001	NSCLC	Phase III	Injectable telomerase peptide vaccine	1,000 pt Phase III planned, data 2016.
immatics biotechnologies	IMA901	Renal	Phase III	Vaccine using tumour-peptides combined with Sutent and GM-CSF.	Phase III data H114, 330 pts open-label randomised.

Source: Edison Investment Research, BioCentury, Clinical Trials.gov

Trial data

The current, placebo-controlled, double-blind Phase II study, IMPACT, enrolled 59 mCRC patients. The data presented are of an interim analysis on 55 patients, 40 active and 15 placebo. As an unknown therapy from a small company, with the risk of an inactive placebo, patient recruitment was slow. However, by running a rigorous study, the data can be used to support a single regulatory submission. A key observation is that patient quality was very variable. Eight of the 40 analysed patients in the MGN1703 group (20%), but only one in the placebo group (7%), were in the high-risk category. These nine are made of four who were ineligible for the study but were enrolled (they had secondary chemotherapy or tumours, one in the placebo arm, three in the active arm) and five who had high levels of biomarkers indicating a strong risk of progression, all of whom were in the active arm.[v] Excluding these gives a "good risk" subgroup. All patients had confirmed metastatic cancer and had received a standard chemotherapy regimen.[vi] Patients were started on MGN1703 typically within 14 days of ending chemotherapy. Interim data are shown in Exhibit 5, with the Kaplan Meier curves in Exhibits 6 and 7. The end point is progression-free survival (PFS). RC rather than irRC criteria were used, so any patient, any apparent progression was classed as an event. Since the first CT scan evaluation was three months into the study, it led to a large number of events apparently occurring abruptly around that time point.[vii] In fact, it is a data collection artefact. If irRC criteria had been used, the treated group may have shown a better response.

tissue toxicity at injection sites due to the use of artificial DNA. Artificial DNA constructs are more stable, but are known to be toxic. The advantage of the dSLIM looped structure is that it is stable using normal, non-toxic DNA.

[iv] RPB = randomised placebo-controlled study, a standard Phase III design.

[v] The biomarkers are CEA, a typical mCRC antigen at 30x normal levels, gamma-glutamyl-transpeptidase and alkaline phosphastase, both at 2x normal. All these are well established in the literature. CEA indicates a significant tumour burden. Gamma GT and AP indicate liver damage and potential liver metastasis.

[vi] Either FOLFOX/FOLFIRI/XELOX ± Avastin (bevacizumab) with treatment duration between 4.5 and six months (only four did not receive bevacizumab) or oxaliplatin/irinotecan: for at least three months..

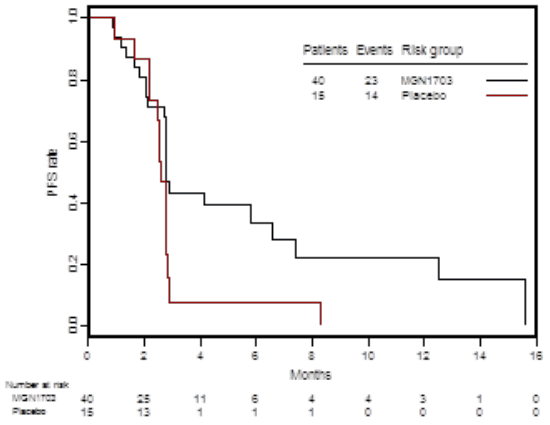
[vii] Physicians tried a different therapy if they saw RC progression, given the unknown performance of MGN1703.

Exhibit 5: Impact PFS data based on RC events assessed at three months

Group	Patient number/events		PFS RC		HR	P (log rank)
	MGN1703	Placebo	MGN1703	Placebo		
ITT	40*/23	15/14	2.8	2.6	0.53	0.067
Good risk	32/16	14/13	5.8	2.7	0.39	0.0133

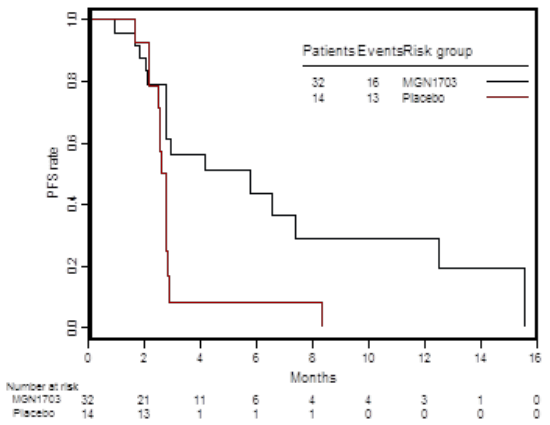
Source: Edison Investment Research, based on Mologen data. Note: *Four patients were enrolled after the cut-off point so are not in this data set.

Exhibit 6: ITT MGN1703 interim data



Source: Mologen

Exhibit 7: "Good risk" MGN1703 interim data



Source: Mologen

The data show that on a standard ITT assessment, there was no improvement in median PFS, but this is probably an artefact of the nature of the therapy and the clinical schedule. As immune therapies need at least three months to work, many patients would progress in the first three months and did, especially the placebo group, where 13 of 15 had progressed with one withdrawal. As they were not examined until about three months, this is when most progression was detected.

The interesting area of the curve is after the three-month point. There was a different hazard ratio, with treated patients having a 50% lower chance of progression. Although the difference in the curves was not statistically significant, there was a strong trend, p=0.067. As noted above, since immune therapies take three to four months to work, the initial Kaplan Meier curves will often be very similar, with differences only appearing after three months. The standard statistical approach assumes an immune therapy will, like chemotherapy, be fully effective from day one. Mologen, in talks with possible partners, has observed that this post-three month response is regarded as being highly indicative.

Looking at the "good risk" subgroup identified by Mologen, the impact is more striking (Exhibits 5 and 7). By the three-month scan, 87% of the placebo group had progressed,[viii] but only 10 (25%) of the treated group had done so, with 16 patients being censored (either no data on the date the interim data are recorded or, in two cases, withdrawn with no progression noted. The curves were statistically different, with the chance of progression only 39% relative to the untreated group. Median PFS increased from 2.6 months to 5.8 months.

Phase III and beyond

Mologen is now designing a 300-patient Phase III study. This might amount to c €15m in external trial costs. A PFS study using irRC definitions should be enough for approval. A survival study would be

[viii] Based on one censored placebo patient and one event at about 8.5 months.

stronger, but depends on patients having no recourse to other therapies when progression is seen; it would also take longer to run. An FDA SPA[ix] may be desirable, but can be restricting.

Assessment of risk is subjective. The interim IMPACT data are very robust but not a clear guide to a Phase III. If Mologen can tighten the enrolment criteria and limit entry to patients with a favourable biomarker profile, the probability of success should increase. A partner may also run two Phase III studies, possibly also with overall survival end points, as this avoids debate over the response criteria. A 45% probability has been assigned as a result. A possible lung cancer indication is expected to run a small Phase II with a 17.5% probability of overall success used for value purposes.

MGN1703 market

The US market for mCRC comprises about 143,460 patients per year. Of these, SEER data show that about 40% have localised disease, so proving a benefit and justifying the treatment economically is difficult. About 36% have regional disease that has spread to the lymph nodes. Some of these will develop progressive disease, but as yet no trials are planned to justify MGN1703 use, although some physicians might use MGN1703 for a period if funding allows.

There are two major uncertainties: the level of adoption and the length of therapy. The IMPACT study used twice-weekly dosing until disease progression and at the time of analysis, only 23 of 40 treated ITT patients had progressed. This leads to uncertainly about the price of the average therapy: either $50k for three months ($200k per year) or $50k for a year, in which case the average actual price may be $15-20k – far too low in the current cancer market. The valuation assumption is that 35% of metastatic patients are treated per year in the US at $50k each.

The core MGN1703 market is 18.6% of patients with distant disease on diagnosis (6% of patients are not staged). The US market is 26,684 metastatic patients annually. Biological and enhanced chemo therapies typically cost c $50,000 per course. This gives a potential US market of $1.33bn, with sales possible in the $600-700m region. Some off-label use and use in some node-positive but non-metastatic tumours might be expected. The proposed lung cancer indication is modelled as similar to mCRC but with a two-year delay implying global peak sales of $800-900m.

The EU market is highly fragmented and very price sensitive, with governments often demanding rebates if an expensive therapy does not work in individual patients. In the UK, NICE will require strong pharmacoeconomic analysis. The simplest assumption is that the EU is 50% of US sales (lower price and lower penetration, but bigger market) with a similar royalty rate. Asia is usually about 35% of the US, with longer Japanese approval times; a separate Asian deal might be struck.

Edison does not forecast deal values in cash flow projections, but an estimate of potential deal values is included in our valuation. Edison expects Mologen to get a $15-25m signing fee with milestones at around $125m and about a 20% royalty. Given that MGN1703 has rigorous Phase II data, a stronger deal might be possible. A 2016 deal scenario on Phase II data has a $30m signing fee with 30% royalty; this is conservative, but depends on Phase III data quality and strength.

Patent and generic competition

The priority date for the PCT patent application is 24 February 2000. In the EU, the patent expires in 2020 but a five-year supplementary protection certificate is normally granted allowing extension to 24 February 2025. In the US, Mologen has received an additional 197 days of patent life because of the

[ix] Special Protocol Agreement. The FDA agrees a protocol for the trial and end points. This is inflexible as any change to the protocol breaks the agreement, but in this case, with probable use of irRC and a single pivotal design, it might be advisable.

review process of the application. The patent term will be until 7 September 2020. In the US, an extension is based on the length of US trials and regulatory review. Assuming a three-year Phase III and one-year review, the extension would be 30 months. This implies an expiry around March 2023.[x] As dSLIM is simple to make, it is assumed that generic competition cuts prices by 75% and reduces Mologen's market share by 75%.

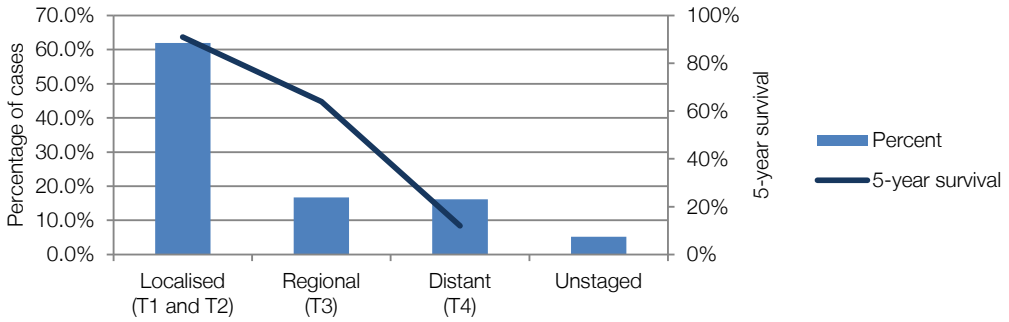
Manufacturing – scalable offering

dSLIM is made by chemically synthesising a single oligomeric DNA strand. Two strands are annealed in house to yield a continuous strand sealed (ligated) using a recombinant enzyme. This makes the molecule very stable and resistant to degradation after injection. Mologen has a clean room manufacturing suite to prepare material for Phase III with external GMP DNA synthesis and separate packing. Commercial production will be contracted out or handled by the partner. The process is very scalable, with an attractive cost of goods.

MGN1601

This product is specific to renal carcinoma (RCC). The US National Cancer Institute estimated there would be 64,770 cases of RCC in the US in 2012. About 10-15% of patients who exhibit a renal cell mass have a benign condition like oncocytoma; Clear cell RCC (ccRCC) accounts for about 80% of the true cancers. Consequently, in the diagnosed population, about 75% will have ccRCC. Renal cancer is staged by tumour size (T1<7cm, T2>7cm) and according to whether it is local, regional (spread to lymph nodes, T3), or metastatic (T4).[6] Exhibit 8 shows survival and cases. This is a generalisation, as large T3 tumours may not have spread, as in the Wilex ARISER study. In that case, five-year survival of node-negative T3 patients was over 50%, much higher than expected.

Exhibit 8: Renal cancer patent staging and five-year survival on diagnosis



Source: Edison Investment Research, based on SEER data

As MGN1601 is targeted to metastatic tumours, it would aim to capture most T4 and a high proportion of T3 cases; Edison assumes half, with a quarter of un-staged cases as these are intermediate in survival (34% five-year survival) but hard to classify. This gives a broad estimate of 15,000 potential cases per year. In theory, all cases and certainly all regional and metastatic local disease should be treated, but trials in earlier-stage patients would be very long and expensive.

[x] Patent-term extensions are half the time from the IND filing date to the date of the NDA filing plus the regulatory review period, with a maximum of five years. Mologen is waiting for a definitive trial design to be agreed by opinion leaders before filing an IND. If the trial period is three years and the review period one year, a 2.5-year extension may be available. An EU Supplementary Protection Certificate is the time from patent filing to EU authorisation less five years, subject to a maximum of five years. Hence, Molgen can claim a five-year SPC.

A swarm of MIDGE[xi]

MGN1601 originated as an autologous cell therapy.[xii] However, RCC cells isolated from individual patients often proved difficult to culture. Fortunately, one cell line was easy to culture and displayed a broad range of tumour antigens. Mologen therefore developed this cell type as an allogenic therapy.[xiii] To produce a vaccine, the cells are transfected with four vectors.[xiv] After expressing the encoded proteins, cells are irradiated so they are live but unviable on administration. Cells are stored and shipped frozen, so there are no major supply and logistics issues. A 10% cost of goods is assumed.

ASET design and data

MGN1601 has been evaluated in a small, 19-patient, open-label clinical Phase I study, ASET. One of the three sites, Berlin, also carried out immune system assays on fresh patient blood samples. This enabled Mologen to derive some clues about the type of immune response seen.

The dose used was an empirical 10 million cells.[xv] Dose frequency is every week for four weeks, then bi-weekly to 12 weeks. Alternative schedules have not been clinically tested. The ASET protocol allowed extended use starting at week 24 and two patients enrolled on this, with five doses given up to 120 weeks. dSLIM is also administered with each cell dose. This gives an innate stimulus with the presence of immunogenic cancer cells. An innate response is thought to be essential for generation of a long-lasting adaptive response, see above.

ASET results

RCC patients (clear cell type) accounted for 16 (84%) of those enrolled, with three (16%) having unknown pathology.[xvi] All patients had failed previous therapies and had no other treatment options. As with the MGN1703 study, RC criteria were used. Nine patients died during the study and did not complete the course of therapy. The 10 remaining patients completed the TPP. One of these 10 had a partial response, with a 55% decrease in tumour volume, and three patients had stable disease. The other six patients had progressive disease on RC, although one of them would have been classed as stable on irRC.

One method of scoring disease severity is the three-level Memorial Sloan Kettering score (MSKCC).[7] It is notable that of the 10 patients who were TPP-treated, four had the lowest MSKCC score and six had the mid-score. Most patients who died were all mid-score (four patients) or high (five patients). The TPP data is therefore biased toward low MSKCC score patients. A high proportion of liver metastasis patients died, whereas almost all patients with lymph-node metastasis stayed in the study.

Exhibit 9 shows the overall survival. Patients that did not complete the protocol all died, with median survival of three months. Patients who were able to complete the 12-week course have seen much better overall survival. Exhibit 10 shows the typical survival curve for metastatic renal cancer. The median time between diagnosis and entering ASET was 24 months. By 24 months, at least 60% of

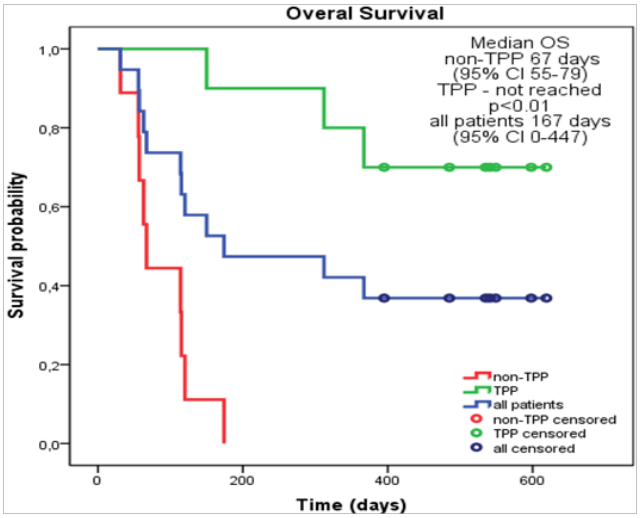
[xi] Minimalistic immunogenically defined gene expression.
[xii] The concept was to culture cancer cells from individual patients, transfer them and re-administer to that patient.
[xiii] Allogenic therapy is the administering of cells from a different individual. Usually, these are highly characterised and cultured. These are a standardised product that can be stored frozen so easier to develop and manufacture.
[xiv] There are:

- CD80 – a protein that simulates a T-cell to recognise a particular cell as foreign or infected;
- CD154 – enables other T-cells to recognise the same antigen to generate a widespread response;
- IL-7 – interleukin 7 is a cytokine that stimulates immune system cells; and
- GM-CSF – causes white cells to proliferate, increasing the level of a potential immune response.

MIDGE vectors are delivered by electroporation. The cells and MIDGE are mixed and an electric field applied. This causes uptake of the MIDGE-enabling expression of the four encoded proteins by each cell.
[xv] A half dose is known from experience of other cell lines to be ineffective and a 10-fold higher dose, as normal on a dose-response curve, is not feasible by intradermal injection.
[xvi] The outcome of specific patients has not been disclosed.

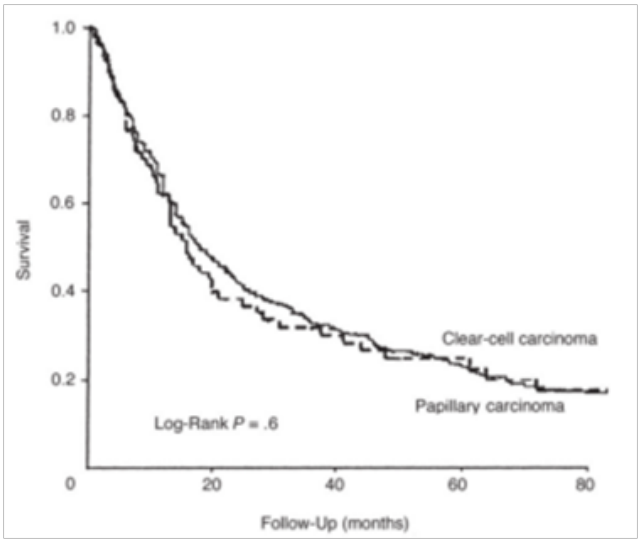
patients in a typical patient cohort would be dead and the survivors would have about a 50% chance of dying in the next five years. It may be this survivor effect that is being detected in the study.

Exhibit 9: ASET Phase II OS data



Source: Mologen

Exhibit 10: Standard survival for metastatic renal cancer



Source: Hollingsworth, J. M., et al. 2007.[6]

Immune effects

The immune assay data for various posters are summarised in Exhibit 11. The data set is very limited and immune system assays can have high error ranges.

Exhibit 11: Selected ASET patient immune response data

Patient identifier	Response*	Survival recorded	MGN1601 challenge (fold)	Recognition antigens (fold)	Ab against MGN1601 cells (fold)	m MDSC response (fold)	T reg response (fold)	T-cell Percentage	
								Visit 1	Visit 9
01	SD	Day 500	2x	NC	34x	0.25x	0.75x	45%	60%
08	SD	Day 450	4x	3x	12x	0.6x	1.1x	36%	40%
17	SD	Day 290	15x	2x	16x	0.75x	0.85x	25%	45%
03	PD	Day500	NC	8x	8x	3.5x	0.95x	39%	31%
04 (died)	PD	Day 350	NC	5x	5x	2x	0.9x	58%	50%

Source: Mologen, collated by Edison Investment Research. Note: *SD = stable disease; PD = progressive disease.

The three stable disease patients all showed that their T-cells were activated by MGN1601's immunogenic cells, with between two- and 15-fold increases. If this response is also against patient tumour cells, it might be recognising and controlling the cancer. The two patients with progressive disease did not show any T-cell recognition of MGN1601. They did show a response against the antigens carried by the MGN1601 cells. Responding patients generated strong antibody responses against the highly immunogenic MGN1601, but so did the two progressive disease patients. The regulatory responses are interesting. Myeloid-derived suppressor cells (MDSC) are believed to prevent the immune system from attacking tumours. In patients with stable disease, general MDSC levels fell but rose in those showing progressive disease, possibly indicating an increase in cancer tolerance. There was no change in the number of regulatory T-cells, but patients with stable disease showed an increase in the percentage of T-cells in the immune fraction, showing a generalised immune system activation, whereas those showing progressive disease saw T-cell numbers fall slightly.

One could interpret the Phase II data either as indicating that some patients developed a positive immune response against the tumour (supported by the cases shown in Exhibit 3 above) or that data indicate a survivor bias, with responses not necessarily related to MGN1601.

A small Phase II will be run to confirm the efficacy profile. Combination approaches may also be tested as a number of kinase inhibitors, like sorafenib (Nexavar), sunitinib (Sutent) pazopanib (Votrient) are commonly used in renal cancer. Interferon and bevacizumab Avastin may also be used. In second line therapies, these are the mTOR inhibitors temsirolimus (Torisel) and Everolimus (Afinitor).

Market value and development risk

At this stage of development, MGN1601 is still a high-risk project. The data justify a controlled Phase II study in early-stage patients. At this stage, Edison gives this project a 25% probability of success, given the limited data set and lack of evidence of clear efficacy.

With 15,000 possible patients in the US, if Provenge-type prices could be obtained of $100,000 per course, the market could be $1.3bn. Globally, prices would have to be lower, but the world market potential of about $2bn seems possible. However, as Dendreon has found, it is not easy to create such a market without superb response data. Assuming a 35% use rate, Mologen could have US sales of about $500m, with a further $200-300m each in the EU and Asia; Asia is expected to be managed through a partnering deal at a 25% royalty.

The technology is protected by granted patents with a priority date of 30 December 2003. Orphan drug protection gives at least five years' exclusivity in the US and 10 years in the EU. Edison regards this as academic, since MGN1601 uses a unique cell line that is not available to competitors. It might be possible to develop a bio-similar product, but clinical trials will be needed to establish its efficacy, so in effect, any competitor will be a new product.

Renal cancer is now treated with several modern targeted therapies: sunitinib, sorafenib, pazopanib, bevacizumab, temsirolimus and everolimus. These tend to deliver good short-term responses, but the tumour becomes resistant so overall survival may not change much even if PFS is extended. MGN1601 needs to work alongside these therapies; see Figlin R et al 2012 for a review.

Earlier-stage projects: Parasites and viruses

By adding a small peptide onto the MIDGE vectors, an immune response targeted towards parasites or viruses can be generated. Mologen has run projects with academic partners funded under EU framework programmes against leishmaniasis (MGN1331) and hepatitis B (MGN1333). MGN1331 is the furthest advanced and ready for a Phase I clinical trial. Mologen is seeking further EU funding and a funding partner before MGN1331 trial initiation; this indicates a 2014 start. Leishmaniasis is a parasitic disease transmitted by sandflies. It is present in the tropical developing world. Visceral infection can be fatal and has estimated world incidence of 500,000 and mortality of 60,000. Affected countries are India, Bangladesh, Nepal, Sudan, and Brazil. Edison has not ascribed value to these projects. MGN1333 could be a useful add-on to existing hepatitis vaccines for non-responders.

Sensitivities

There are two crucial investor sensitivities. Firstly, whether MGN1703 IMPACT will be partnered with a substantial upfront fee in 2013. If not, Mologen need funds to complete the Phase III. The second, later sensitivity is whether dSLIM, an innate immune stimulant, can generate a sustained maintenance

response against tumour cells; Phase III will take until 2015-16 to prove or disprove this. dSLIM certainly activates the innate anti-infective system, but adaptive immunity, if necessary, requires the immune cells to recognise and destroy tumour cells and for cancer tolerance to be overcome. A key part of development will be the use of biomarkers to identify prospective patients who might respond, on immune-related response criteria, over the initial three months of immune therapy. Separately, the MGN1601 sensitivity relates to its showing efficacy in Phase II. This will not be known until at least 2015.

Valuation: A tale of two scenarios

The value scenario for Mologen varies depending on whether a 2013 MGN1703 deal is concluded or if a marketing deal post-Phase III is done. Both are estimated using a 45% probability of reaching the market. The first scenario is a 2013 deal with a 20% royalty, which is a high rate for a Phase II deal, but reflects the robust data from a controlled trial plus the potentially extensive market and high margins. As Mologen will not then need to fund Phase III, the milestones generate a possible €12m to invest in other projects. The indicative value is €18.20, Exhibit 12 shows the valuation parameters. A deal may bring extra benefits, for example a partner might invest in two Phase III studies and could have a bigger distribution impact. A partner may develop indications, like lung, much faster.

Exhibit 12: Valuation assumptions and indicative value on a 2013 MGN1703 deal basis

Product, market and indication	In-market sales(m)		Milestones m	Expected launch window	Patent expiry	Probability of reaching market	Partnering probability in 2013	Expected average royalty	Gross margin rNPV (m)
	Peak	Expiry	2012-30						
MGN1703 US mCRC	$642	$38		2017	03/2023	45%	100%	20%	€150
MGN1703 mCRC EU	$353	$19		2017-18	02/2025				
MGN1703 mCRC Asia	$225	$13		2019	2025				
MGN1703 NSCLC	$865	$70		2019-20	2025	17.5%			€33
MGN1703 partnering			$140	2013					€37
MGN1601 US (Direct)	$529		N/A	2017	2028	25%	N/A	N/A	€229
MGN1601 EU (direct)	$264			2017-18					
MGN1601 Asia (royalty)	$175			2019				25%	
				Total risk-adjusted NPV (12.5%) of net revenues					€450
				NPV cash flow (inc risk-adjusted milestones)					€179
				Continuing value post-2030 (10-fold multiple)					€109
				Cash surplus (funding required) assuming partnering					€12
				Indicative total value					**€299**
				Shares in issue (15.4m) plus granted options (1m)					16.4
				Indicative value per share					**€18.20**

Source: Edison investment Research

The second scenario is a 2016 regulatory-stage deal after Mologen has funded Phase III. This is clearly riskier as Phase IIIs are uncertain and Mologen can only afford one trial. An additional €25m investment would be needed. A $30m, risk-adjusted 2016 signing fee is assumed. To be cautious, a 30% royalty is assumed but this could be much higher. This generates an indicative value of €16.50 (Exhibit 13). There is little difference in the two scenarios, but the value ultimately depends on the deal terms.

It is assumed that MGN1601 is funded, developed and sold internally. Mologen has a lean operation and after the costs of direct marketing for MGN1601, assumed to be 15% of sales in the US and 20% in the more fragmented EU markets, the company should be very profitable, even after the MGN1703 patent expiry. MGN1601 is inherently protected from generic competition.

Exhibit 13: Valuation assumptions and indicative value with a 2016 regulatory-stage MGN1703 deal

Product, market and indication	In-market sales m		Milestones m	Expected launch window	Patent expiry	Probability of reaching market	Partnering probability in 2013	Expected average royalty	Gross margin rNPV (€m)
	Peak	Expiry	2012-30						
MGN1703 US mCRC	$642	$38		2017	03/2023	45%	100%	30%	€225
MGN1703 mCRC EU	$353	$19		2017-18	02/2025				
MGN1703 mCRC Asia	$225	$13		2019	2025				
MGN1703 NSCLC	$865	$70		2019-20	2025	17.5%			€50
MGN1703 partnering			$30	2013					€6
MGN1601 US (Direct)	$529		N/A	2017	2028	25%	N/A	N/A	€229
MGN1601 EU (direct)	$264			2017-18					
MGN1601 Asia (royalty)	$175			2019				25%	
				Total risk-adjusted NPV (12.5%) of net revenues					€510
				NPV cash flow (inc risk-adjusted milestones)					€184
				Continuing value post-2030 (10-fold multiple)					€112
				Cash surplus (funding required) assuming partnering					-€25
				Indicative total value					**€272**
				Shares in issue (15.4m) plus granted options (1m)					16.4
				Indicative value per share					**€16.50**

Source: Edison Investment Research

Mologen retains very close links to the Free University, so has access to research ideas. As a result, a post-tax multiple of 12 seems reasonable as more development projects are likely, which could give post-2025 growth, and Edison assumes at least 15% of sales invested into R&D. Berlin levies a local company tax of about 14.4%, which is deducted before corporate tax, at 15%, is levied. This gives an overall corporate tax rate of about 27%.

Financials

Mologen's ytd statement to 30 September 2012 showed cash of €25.2m after an equity placement of €22m in July. Ytd loss was €5.7m after €0.3m of income and grants. Cash expenditure might rise to between €9m and €10m in 2013 as the MGN1703 Phase IIb/IIII study gets underway and the Phase II MGN1601 study is initiated. The MGN1703 study is expected to cost about €15m in external fees with about €6m for MGN1601. MGN1703 partnering in 2013 would add to cash reserves and cut costs. Financial projections are shown in Exhibit 14. Note that the cash flows in Exhibit 14 exclude any deal payments and assume that MGN1703 costs are incurred; this uses the 2016 deal scenario in Exhibit 13 as the base case.

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Exhibit 14: Financial summary

€000's	2010	2011	2012e	2013e	2014e
Year end 31 December	IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS					
Revenue	89	137	200	100	100
Cost of Sales	0	0	0	0	0
Gross Profit	89	137	200	100	100
EBITDA	(5,189)	(6,619)	(6,954)	(9,711)	(14,477)
Operating Profit (before amort. and except.)	(5,561)	(6,911)	(7,254)	(10,011)	(14,777)
Intangible Amortisation	0	0	0	0	1
Exceptionals	0	0	0	0	0
Other	(141)	(683)	(700)	(700)	(700)
Operating Profit	(5,702)	(7,594)	(7,954)	(10,711)	(15,476)
Net Interest	51	109	73	73	247
Profit Before Tax (norm)	(5,510)	(6,802)	(7,181)	(9,938)	(14,530)
Profit Before Tax (FRS 3)	(5,651)	(7,485)	(7,881)	(10,638)	(15,229)
Tax	0	0	0	0	0
Profit After Tax (norm)	(5,510)	(6,802)	(7,181)	(9,938)	(14,529)
Profit After Tax (FRS 3)	(5,651)	(7,485)	(7,881)	(10,638)	(15,229)
Average Number of Shares Outstanding (m)	10.9	12.3	13.9	15.4	15.4
EPS - normalised (c)	(50.6)	(55.3)	(51.6)	(64.5)	(94.4)
EPS - normalised and fully diluted (c)	(47.4)	(51.0)	(48.0)	(60.4)	(88.4)
EPS - (IFRS) (c)	(51.9)	(60.9)	(56.6)	(69.1)	(98.9)
Dividend per share (c)	0.0	0.0	0	0	0
Gross Margin (%)	100.0	100.0	100.0	100.0	100.0
EBITDA Margin (%)	N/A	N/A	N/A	N/A	N/A
Operating Margin (before GW and except.) (%)	N/A	N/A	N/A	N/A	N/A
BALANCE SHEET					
Fixed Assets	1,548	1,523	127	117	107
Intangible Assets	1,371	1,385	0	0	0
Tangible Assets	177	138	127	117	107
Investments	0	0	0	0	0
Current Assets	5,536	8,308	25,836	15,970	1,765
Stocks	24	33	27	30	30
Debtors	0	6	878	900	1,000
Cash	4,722	7,476	24,931	15,040	735
Other	790	793	0	0	0
Current Liabilities	(802)	(1,109)	(980)	(1,002)	(1,276)
Creditors	(796)	(1,106)	(980)	(1,002)	(1,276)
Short term borrowings	(6)	(3)	0	0	0
Long Term Liabilities	(80)	(11)	0	0	0
Long term borrowings	0	0	0	0	0
Other long term liabilities	(80)	(11)	0	0	0
Net Assets	6,202	8,711	24,983	15,085	596
CASH FLOW					
Operating Cash Flow	(5,586)	(6,405)	(7,091)	(9,641)	(14,055)
Net Interest	51	109	73	73	247
Tax	0	0	0	0	0
Capex	(49)	(268)	(50)	(50)	(50)
Acquisitions/disposals	0	0	0	0	0
Financing	4,132	9,317	24,696	0	0
Dividends	0	0	0	0	0
Net Cash Flow	(1,452)	2,753	17,628	(9,618)	(13,858)
Opening net debt/(cash)	(6,168)	(4,716)	(7,473)	(24,931)	(15,040)
HP finance leases initiated	0	0	0	0	0
Other	0	4	(170)	(272)	(447)
Closing net debt/(cash)	(4,716)	(7,473)	(24,931)	(15,040)	(735)

Source: Edison Investment research

Edison investment research

Contact details	Revenue by geography
Mologen AG Fabeckstr. 30, 14195 Berlin, Germany +49 (0)30 84 17 88 0 www.mologen.com/en	N/A

CAGR metrics		Profitability metrics		Balance sheet metrics		Sensitivities evaluation	
EPS 2010-14e	N/A	ROCE 13e	N/A	Gearing 13e	N/A	Litigation/regulatory	●
EPS 2012-14e	N/A	Avg ROCE 2010-14e	N/A	Interest cover 13e	N/A	Pensions	○
EBITDA 2010-14e	N/A	ROE 13e	N/A	CA/CL 13e	N/A	Currency	○
EBITDA 2012-14e	N/A	Gross margin 13e	N/A	Stock turn 13e	N/A	Stock overhang	◖
Sales 2010-14e	N/A	Operating margin 13e	N/A	Debtor days 13e	N/A	Interest rates	○
Sales 2012-14e	N/A	Gr mgn / Op mgn 13e	N/A	Creditor days 13e	N/A	Oil/commodity prices	○

Management team

CEO and R&D: Dr Matthias Schroff	CFO: Jörg Petraß
Dr Schroff was Mologen's leading scientist at foundation. He joined the board in 2005 and was appointed CEO in 2008. He holds a PhD in biochemistry from the Free University, Berlin.	Mr Petraß joined Mologen in 2001. Following the conferring of procuration in 2005, he was appointed CFO in 2007.

Chairman, Supervisory Board : Dr Mathias P Schlichting	Chairman Scientific Board: Professor Dr Burghardt Wittig
Dr. Schlichting is a co-founder of Mologen. He is a state-registered attorney and a certified supervisory board member for the SMEs.	Professor Dr Wittig co-founded Mologen and was CEO until 2008. He is Professor of Molecular Biology at the Free University, Berlin.

Principal shareholders	(%)
Global Derivative Trading GmbH	27%
Deutscher Ring Krankenversicherungsverein a.G.	9%
Salvator Vermoegensverwaltungs GmbH	8%
Deutscher Ring Lebensversicherungs-AG	6%
BUCHRI Verwaltungs GmbH (Prof Wittig)	4%
Baden-Wuerttembergische Versorgungsanstalt fuer Aerzte	3%
Deutscher Ring Sachversicherungs-AG	3%

Companies named in this report

Pfizer, Wilex, MedImmune , AstraZeneca, Roche, Daiichi Sankyo, GSK , Vical, Dedreon, Vaccinogen, Bristol-Myers Squibb, immatics biotechnologies, Transgene, Argos Therapeutics, Oncothyreon, Merck KGaA, Ono, Kael-Gemvax

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