EDISON

Mologen

Strategic review

‘Next Level’ of development

Pharma & biotech

Mologen’s strategic review has focused its efforts on the development and commercialisation of late and early clinical assets, notably lead candidate lefitolimod (oncology and HIV) and EnanDIM, a next-generation TLR9 agonist. Partnering opportunities for lefitolimod are being actively sought; we anticipate Phase III data in 2018. Manufacturing efforts will be out-sourced to achieve suitable scale. MGN1601 (renal cancer vaccine) is on hold. Mologen’s move to a more clinical development-focused company means preclinical R&D assets (MIDGE vector system) will be spun off or divested. We value Mologen at €201m or €8.87/share.

Year end	Revenue (€m)	PBT* (€m)	EPS* (c)	DPS (c)	P/E (x)	Yield (%)
12/14	0.0	(17.0)	(1.01)	0.0	N/A	N/A
12/15	0.0	(20.5)	(0.99)	0.0	N/A	N/A
12/16e	0.0	(24.9)	(1.10)	0.0	N/A	N/A
12/17e	0.0	(25.8)	(1.14)	0.0	N/A	N/A

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

Lefitolimod the near-term focus

Lefitolimod, a TLR9 agonist, is in four clinical trials, notably Phase III (IMPALA) and Phase II (IMPULSE) maintenance therapy trials for mCRC and SCLC respectively. IMPALA is expected to finish enrolment (c 540 patients) by year end (data expected in 2018), while the IMPULSE trial is expected to read out results in early/mid-2017. The expansion arm of the TEACH, Phase I trial for HIV and a separate Phase I combination trial with ipilimumab (Yervoy, BMS) recently enrolled first patients.

‘Next Level’ strategy

Mologen plans to reorganise its structure to outsource significant portions of both R&D and production facilities by end 2016. Costs will remain broadly the same in the mid-term as the costs shift away from early-stage research towards development and commercialisation. Financing is intending to come from existing authorised capital, along with existing authorisation to use conditional capital.

Pipeline readjusted

Development of MGN1601, a Phase II-ready product candidate being tested in renal cancer, has been put on hold. However, it will potentially be reinitiated on out-licensing of lead candidate lefitolimod. The MIDGE technology platform, a DNA vector system, will be divested/spun off while EnanDIM, a next-generation TLR9 agonist currently in preclinical development, will be advanced to Phase I.

Valuation: €201m or €8.87 per share

Our valuation of Mologen has decreased to €201m (vs €337m) or €8.87/share (vs €14.89/share. The lower valuation is mainly due to changes in portfolio composition and reimbursement assumptions, but changes in incidence and product lifetime assumptions are also factored. We assume Lefitolimod will be out-licensed in oncology in 2018 and have valued royalties accordingly; however, we do not model in any potential upfront or milestone payments. Our model suggests a cash runway into early 2017; we forecast additional illustrative financing of €30m in 2016.

21 July 2016

Price	**€1.31**
Market cap	**€30m**

Net cash (€m) at 31 March 2016	20.1
Shares in issue	22.6m
Free float	54%
Code	MGN
Primary exchange	Frankfurt (Prime Standard)
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	(49.8)	(63.9)	(74.5)
Rel (local)	(50.7)	(62.9)	(70.5)

52-week high/low	€5.328	€2.659

Business description

Mologen is a German biotech company developing novel immunotherapies. The lead products are lefitolimod (TLR9 agonist) for metastatic colorectal cancer maintenance, metastatic small cell lung cancer maintenance and HIV; and MGN1601, an allogeneic renal cell vaccine.

Next events

IMPALA recruitment completed	H216
IMPULSE: Start analysis	Q416

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Edison profile page

Investment summary

Company description: Commercialisation the focus

After its recent strategy review, Mologen is now focusing the majority of its resources on lead candidate lefitolimod both in relation to its clinical programmes and market launch. Mologen was founded in 1998 based on research work by Professor Burghardt Wittig, the founding CEO. From 1 November 2015, Dr Mariola Söhngen assumed the role of CEO, taking over from Dr Matthias Schroff. Dr Söhngen is the co-founder of Paion, where she was CMO. Walter Miller was appointed the CFO of Mologen on 1 April 2016; most recently he was the CFO of Nuvisan, an international CRO. Mologen has raised €130m to date, including €28.3 (gross) in April 2015. Lefitolimod is in four clinical trials, a Phase III study (IMPALA) for the maintenance treatment of metastatic colorectal cancer, a Phase II trial (IMPULSE) for small cell lung cancer; a Phase I trial (TEACH) in HIV and a Phase I combination study in advanced malignancies. Development for MGN1601, a therapeutic cancer cell vaccine, which completed a Phase I/II study (ASET) for kidney cancer, has been put on hold and the MIDGE technology platform will be divested/spun off. The company is based in Berlin and currently has c 60 employees, although a short-term reduction in these numbers is expected.

Valuation: rNPV of €201m or €8.87/share

Our valuation of Mologen has decreased to €201m (vs €337m) or €8.87/share. This valuation change is mainly attributable to a change in pricing assumptions and MGN1601 being placed on hold. The valuation is based on a risk-adjusted, sum-of-the-parts DCF model, applying a standard 12.5% discount rate and including estimated end-Q116 net cash of €20.1m. The valuation remains focused on lefitolimod in mCRC and SCLC; in addition, we now value the HIV and combination pipeline. While no longer actively developed, MGN1601 is still valued but at a discounted rate to our previous valuation. We assume that lefitolimod will be out-licensed in oncology indications on successful completion of the IMPALA trial (2018), although this may occur earlier (eg positive IMPULSE results). We assume this would trigger the resumption of MGN1601 development in 2019, while HIV will be out-licensed post Phase II. We have readjusted our product lifetimes, specifically in relation to Lefitolimod, with patent expiries now predicted in 2028 and 2030 in the USA and Europe for both mCRC and SCLC. We do not include upfront fees and/or milestones, which would be expected on securing a partner and successful commercialisation of the product, providing potential upside to our valuation.

Sensitivities: Clinical execution risks

The key sensitivities relate to the clinical performance of lefitolimod and Mologen's ability to secure the additional financing and/or a partner to complete the full clinical programme. Results from the IMPULSE and IMPALA studies will have a major bearing on lefitolimod's chance of regulatory approvals and commercial success. We have made assumptions about the potential market opportunity available to lefitolimod, which do not currently include significant stratification of patient populations. Lefitolimod may be most active in certain subgroups, which could reduce the target patient pool. However, confirmed activity in a patient subset may result in a higher treatment price, greater reimbursement rates and more favourable economic terms from any partnership. It should also be noted that success or failure of Lefitolimod in one indication may not translate across to other indications.

Financials: Cash needed to reach IMPALA readout

Cash at 31 March 2016 was €20.1m. The most recent capital raise was in April 2015 when €28.3m gross (€26.2m net) was raised from the rights issue (one-for-three) of c 5.7m new shares at €5.00/share. Our model suggests that current cash is sufficient to fund operations to early 2017, depending on the progress of the IMPULSE and IMPALA studies for lefitolimod. Importantly, this

provides a cash runway that accommodates some important milestones in 2016, particularly the start of primary analysis of the IMPULSE study data in SCLC and completion of patient recruitment in the IMPALA trial. However, a funding gap remains in respect of the IMPALA study (estimated data readout by end-2018). We estimate this to be in the €25-35m range and include an illustrative €30m financing, nominally attributed to debt, in our FY16 forecasts, to allow completion of the study. Mologen has announced that funding will be covered by existing authorised capital, together with existing authorisation to use conditional capital.

Outlook: Lefitolimod commercialisation is key

The recent strategic review aims to prepare Mologen's lead product candidate lefitolimod for a potential market approval. IMPALA (Phase III mCRC) and IMPULSE (Phase II SCLC) trials continue as planned, with completion of patient recruitment for IMPALA expected by year end (results expected in 2018) and the results of IMPULSE in H117. We assume the launch of lefitolimod in its first indication (the maintenance treatment of metastatic colorectal cancer) to be in 2020 for Europe and 2021 for the US; we model that out-licensing in oncology indications will be achieved in 2018. Outsourcing of manufacturing will enable Mologen to effectively ramp up its production capacity and potentially multi-source its supply line through contract manufacturing, further increasing the licensing appeal of Lefitolimod if IMPALA and/or IMPULSE are positive. Earlier-stage trials include a Phase I TEACH study in HIV, which has started its expansion study (final results due in H1 2017), while a Phase I combination trial with ipilimumab (Yervoy) in advanced malignancies (potential data readout by 2018) could increase the licensing appeal of lefitolimod in oncology if results are positive. Exhibit 1 outlines Mologen's development pipeline.

Exhibit 1: Mologen development pipeline

Product	Technology/Mechanism	Target	Status	Notes
Lefitolimod (MGN1703)	Immune Surveillance Reactivator. TLR9 agonist; dSLIM (double-stem loop immunomodulator) is a dumbbell-shaped, DNA-based construct.	Metastatic colorectal cancer (mCRC); maintenance therapy (post-chemo induction).	Phase III (IMPALA) started Q314; 540 patients; OS primary endpoint. Phase II (IMPACT) complete; 59 patients.	IMPALA is an open-label, randomised (1:1), controlled, two-arm, multi-national study (120 sites across EU); full recruitment expected in H216, initial data in FY18.
		Small-cell lung cancer (SCLC); maintenance therapy (post-chemo induction).	Phase II (IMPULSE) initiated Q214; 100 patients; OS (at 12 months) primary endpoint.	IMPULSE is an open-label, randomised (3:2), controlled, two-arm, multi-national EU study; full recruitment completed; initial data expected in H117.
		Human immunodeficiency virus (HIV).	Phase I (TEACH) initiated Q215; 15 patients; NK cell activation primary endpoint.	TEACH is a non-randomised interventional study. Based on broad immune system activation, study has been extended with the first patient recently enrolled. Final results expected 2017.
		Advanced solid malignancies	Phase I initiated Q316. 60 patients; Maximum tolerated dose primary endpoint.	Lefitolimod will be tested in combination with the CTLA-4 immune checkpoint inhibitor Ipilimumab. First patient to be enrolled shortly with end of recruitment by 2018. Initial data readout expected by 2018.
MGN1601	Cell-based cancer vaccine; genetically modified tumour cells transfected with four vectors: GM-CSF, IL-7, CD80 and CD154 (CD40L), and combined with dSLIM (MGN1703).	Metastatic renal cell carcinoma (mRCC).	Phase I/II (ASET) complete; 19 patients.	Mologen have placed this asset on hold and potentially will reinitiate development upon successful out-licensing of lefitolimod.
EnanDIM	Next-generation TLR9 agonists; linear DNA construct with structural feature to protect against degradation.	Oncology and anti-infectives	Preclinical model experiments that confirm broad immune activation.	Designed to combine the chemically unmodified DNA components of MGN1703 with the ease of production advantages of linear molecules. Potential patent life extension of the franchise.

Source: Mologen; Edison Investment Research. Note: MIDGE = minimalistic immunogenically defined gene expression; proprietary platform, also classified as a DNA vector. EnanDIM = Enantiomeric, DNA-based, ImmunoModulator.

‘Next Level’ strategy

Mologen’s new strategy looks to streamline the company’s organisation focusing on the commercialisation of lefitolimod via out-licensing. The MIDGE vector system may be divested or spun off, including the three products MGN1404 (malignant melanoma), MGN1331 (leishmaniasis) and MGN1333 (hepatitis B). Financial limitations and a focus on lefitolimod mean further development of the MIDGE technology platform is not feasible. MGN1404 is currently being tested in a Phase I trial, while MGN1331 and MGN1333 are preclinical. We do not assign any value in our models to the platform and we await further news that will provide clarity on any divestment/spin off. MGN1601’s development has been put on hold; it is a Phase II-ready, genetically modified human renal cancer cell line that was designed using the MIDGE technology platform alongside low-dose lefitolimod as an adjuvant. It has been granted Orphan Drug Status from the European Medical Agency (EMA). Mologen has placed MGN1601 on hold and will look to reinitiate development on successful out-licensing of lefitolimod. Alongside Mologen’s TRL9 product candidate lefitolimod is the EnanDIM platform. It is a linear single-stranded, DNA-based TLR9 agonist that contains no chemical modifications, but is protected from enzyme degradation by the presence of the stereoisomeric ribose molecules at the end of the DNA backbone. This cannot be recognized by DNA-degrading enzymes, allowing for increased lifetime of the EnanDIM molecule over unmodified DNA. EnanDIM will be advanced to Phase I. Alongside changes to the pipeline, an initial reduction in headcount from the reduced clinical, preclinical and manufacturing commitments will be offset in the mid-term as additional expertise is brought in to commercialise lefitolimod. We expect the new company structure and strategy to be implemented by year end. Mologen recently provided more clarity on funding requirements for its ‘Next Level’ strategy in this year’s AGM invitation.

Outsourcing key to strategy

Mologen has recognised that it does not have the sufficient capabilities in house to ramp up the manufacturing of lefitolimod for a potential market launch. It will close in-house clinical supply manufacturing and look for a contract manufacturer with the capacity and expertise needed to deliver lefitolimod in market quantities. This enables a solid production line to be put in place, while controlling costs that would be incurred if Mologen invested in the expertise and facilities needed to internally scale production. Furthermore, multiple manufacturers could be used to enable protection of lefitolimod supply. Additionally, early-stage, in-house R&D will be outsourced as Mologen directs its attention to clinical assets. All outsourcing activities will be led by Mologen staff, ensuring expertise and knowledge is retained in house.

Building commercialisation expertise

Mologen has indicated that it is proactively searching for licensing partners and has brought in a consultancy firm specialising in biotechnology. The team is expected to aid the executive board in evaluating and assessing strategic options that have arisen from the ‘Next Level’ strategy. A key objective will be refining the business case around lefitolimod and how it is targeting and searching for licensing partners. As commercialisation opportunities near, we assume internal expertise will be brought on board to support this process. While headcount is initially being reduced (in R&D and manufacturing), we expect numbers to remain steady in the mid-term as commercial expertise is brought on board. The successful commercialisation of lefitolimod is key for Mologen’s current strategy and the timing and terms will have a substantial impact on the company’s future, with the results of both IMPALA and IMPULSE key to any future deal.

Lefitolimod: Pivotal data expected in 2018

Using the body's own defences

Lefitolimod is an immune surveillance reactivator (TLR9 agonist) that broadly activates the immune system, enabling it to increase the recognition and combat of abnormal cells. It is being developed as a maintenance treatment for use after effective induction chemotherapy, to reduce tumour burden and help mount an immune response against free circulating tumour-associated antigens.

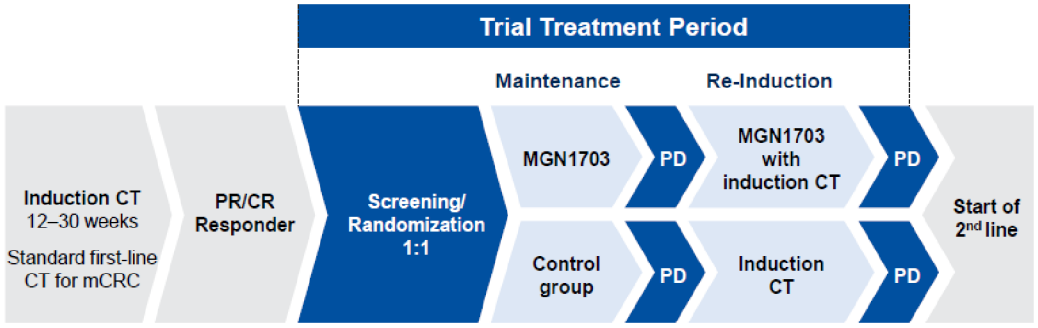
The innate immune system is the first line of defence against infection, comprising a set of receptors that recognise foreign DNA, reacting instantly to produce cytokines and other inflammatory mediators and to stimulate, among others, natural killer (NK) and NK T-cells. The innate immune system ultimately links through to the adaptive immune system; the latter is highly specific to a target antigen and creates immunological memory after the initial response. The majority of immunotherapies (approved and in development) target the adaptive immune system; in primarily targeting the innate system, Mologen's approach could complement these, and combinatorial therapy approaches could prove synergistic.

Immunotherapies are likely to be most effective when the disease burden is low and the immune system less compromised. Although traditionally thought to be immunosuppressive, some chemotherapies promote 'immunogenic cell death', whereby the release of tumour-associated antigens induces an immune response. This concept has led to the rationale that immunotherapies may have the greatest potency when used in adjuvant settings.

IMPALA: Patient recruitment nearing completion

IMPALA, the pivotal Phase III trial of lefitolimod in mCRC as a maintenance treatment after first-line chemotherapeutic treatment, is expected to complete patient enrolment by year end and initial data are expected in 2018. We assume lefitolimod will file in 2019 before a launch in mCRC in the EU in 2020, the US in 2021 and Japan in 2021. We assume peak sales of $589m (EU), $308m (US) and $198m (Japan), which reflect lower reimbursement prices across the board and updated incidence numbers in Japan. The trial has been designed to take into account the insights gleaned from the IMPACT trial. The study is an open-label, randomised (1:1), controlled two-arm study (n=540; across >120 sites in eight European countries). The key differences from IMPACT include a more variable induction chemotherapy period (two to seven months), no constraints on the drugs used in chemo induction (any biological agent allowed), selection of responsive patients (PR/CR only; 50-60% estimated response; PR/CR is the primary inclusion criteria for patient selection, not duration of chemo), the use of a treatment control group ('doctor's choice') and a reinduction treatment (with chemo ± MGN1703) phase after first evidence of progressive disease (assessed by a local investigator). Patients in the lefitolimod treatment group will be dosed at the same level used in IMPACT, 60mg twice-weekly via subcutaneous injection. Patients will be stratified according to the biomarkers (CEA/NKT levels) identified in IMPACT (see Exhibit 2).

Exhibit 2: IMPALA Phase III study design



Source: Mologen. Note: PD: progressive disease, CT: Chemotherapy Treatment, PR: Partial Response, CR: Complete Response, mCRC: Metastatic Colorectal Cancer.

The primary endpoint is overall survival, the gold standard for a pivotal cancer study, which also allows for the open-label study design. Secondary endpoints include PFS, overall response rate, quality of life assessment and safety.

Preliminary data highlight stratification factors and confirm mode of action

At ASCO GI (gastrointestinal) 2016, Mologen gave preliminary demographic data, as well as stratification factors for the first 200 colorectal cancer patients. 101 patients were randomized into the treatment arm, with 99 in the control arm. 53 patients in the treatment arm (53 patients in the control arm) had CEA (carcinoembryonic antigen) levels below the upper limit of normal (ULN); it is thought that lower levels may be indicative of effective chemotherapy. Additionally, 66 patients had a presence of NK T-cells above 3.5% in the treatment arm (65 in the control arm), again an indicator that chemotherapy has been effective. Additional stratification factors included whether anti-VEGF and anti-EGFR were used as an induction therapy.

In November 2015, Mologen presented exploratory immunological data from a preliminary analysis of the IMPALA study at the Annual Meeting of the Society for Immunotherapy of Cancer. The profile of activated immune cells (monocytes, NK T-cells, NK cells and T-cells) identified in the analysis confirms the evidence already observed in IMPACT and the mode of action of Lefitolimod as an immune surveillance reactivator.

Limited treatment options for metastatic colorectal cancer

Colorectal cancer is both the third most common cancer diagnosed and the third leading cause of cancer-related deaths in both men and women in the US (cancer.org). The American Cancer Society estimates that there will be approximately 95,000 new cases of colon cancer and 39,000 cases of rectal cancer in the US in 2016. A cure is not possible for most patients with mCRC, although for those with limited involvement of distant organs surgery may be curative. For others, chemotherapy, often in combination with biological agents (VEGF and EGFR inhibitors), can improve symptoms and prolong life. However, the five-year survival rate of mCRC is just 11%.

There have been 56 Phase III trials in mCRC that are either open or have completed since 1 January 2015, according to clinicaltrials.gov. More recent approvals include Taiho Oncology's Lonsurf (trifluridine/tipiracil), which was approved for refractory mCRC in September 2015; median OS 7.1 months in the trifluridine/tipiracil plus best supportive care (BSC) arm (vs 5.3 months for BSC and placebo). Lilly's Cyramza (ramucirumab, approved in April 2015), a VEGF inhibitor, was approved for use in combination with the chemotherapy combination FOLFIRI (irinotecan with 5FU and folinic acid) in mCRC that has progressed after first-line treatment; median OS 13.3 months for patients on the FOLFIRI plus ramucirumab arm (vs 11.7 months for FOLFIRI plus placebo).

Capecitabine, an orally administered chemotherapeutic agent, is the most commonly prescribed treatment for CRC and registered sales in the US in 2015 of c $1B (source: Bloomberg), while Avastin (Roche), a VEGF inhibitor, tends to lead sales among biologics (approximately $6.8bn in 2015 across all indications). Avastin demonstrated an Overall Survival of 20.3 months when used alongside bolus-IFL compared to 15.6 months for bolus-IFL alone. Combinations of target therapies (TKIs, monoclonal antibodies and immunotherapies) and chemotherapy are increasingly becoming the best approach to treating the complex and constantly mutating disease that is cancer.

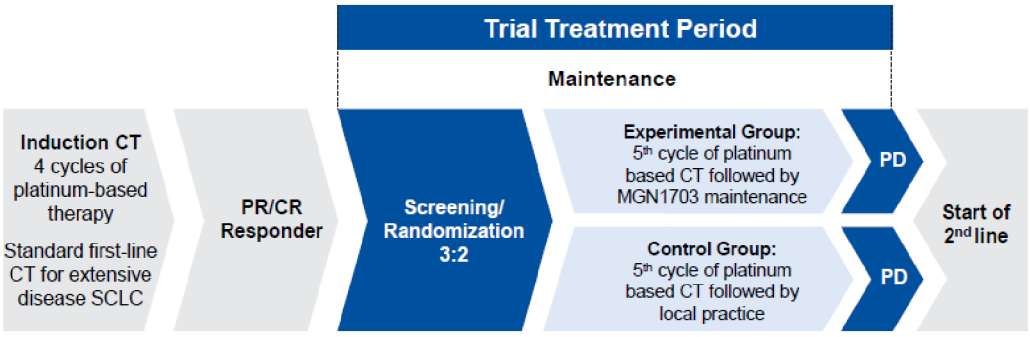
Phase II IMPULSE results near

IMPULSE is a randomized, controlled, two-arm, Europe-based study assessing lefitolimod as a maintenance therapy post-induction chemo in metastatic small-cell lung cancer (SCLC; n=100). Recruitment of patients was completed in October 2015. The trial was designed in a similar manner to both IMPACT and IMPALA, as demonstrated in Exhibit 3.

The response to first-line chemotherapy for SCLC is often good, but unfortunately the disease often progresses and five-year survival in the US has been shown to range from 31% for Stage I patients to just 2% for Stage IV patients. Therefore, a maintenance therapy such as lefitolimod could have a significant benefit in certain patient subgroups. Similarly to IMPALA, patients have been stratified according to biomarkers: NKT levels and neuron specific enolase (NSE, a tumour marker for lung cancer). The primary endpoint is OS and Mologen expects to begin the analysis by end-2016 and to present the data at ASCO in 2017. We assume lefitolimod will launch in SCLC in the US and the EU in 2022, with a launch in Japan in 2023. We assume peak sales of $207m (US), $216m (EU) and $57m (Japan).

The treatment paradigm for SCLC lung cancer is shifting; after decades with few advances, a new wave of immunotherapies holds promise. Chemotherapy agents like Etoposide and Cisplatin still lead first-line treatments, where others like Topotecan are often used as a second/third-line treatment in more aggressive cases. A wave of recent approvals for Immune Checkpoint Inhibitors (ICIs) in cancer is attracting ever greater investor interest in immunotherapies. A 1,125-patient Phase III trial being conducted by Bristol-Myers Squibb (BMS) is testing the ICI ipilimumab (Yervoy) in combination with chemotherapy for the treatment of SCLC. Initial data readouts are expected this year with the primary endpoint being OS. BMS is also conducting two other Phase III trials in SCLC.

Exhibit 3: IMPULSE Phase II study design



Source: Mologen. Note: PD: progressive disease, CT: Chemotherapy Treatment, PR: Partial Response, CR: Complete Response, mCRC: Metastatic Colorectal Cancer.

CheckMate 451 is investigating Nivolumab (Opdivo, BMS) alone and Nivolumab (Opdivo, BMS) in combination with ipilimumab (Yervoy, BMS) as maintenance therapy in patients with metastatic SCLC after completion of first-line chemo; the same target population as lefitolimod's. CheckMate 331 is investigating Nivolumab (Opdivo, BMS) vs chemotherapy in patients with relapsed SCLC. Both trials started recruitment in August 2015, with initial OS data expected in 2018.

TEACH study: Expansion study begun

Lefitolimod's broad activation of the immune system means that its potential may reach beyond oncology. A Phase I trial in HIV in collaboration with the Aarhus University Hospital, Denmark aims to assess whether lefitolimod can activate the innate and adaptive immune system in patients with HIV, leading to enhanced killing of HIV-infected cells. The study has received funding from the American Foundation for AIDS Research.

TEACH, the Phase I trial (initiated in June 2015), has enrolled 15 patients; the primary endpoint is to measure NK cell activation. Secondary endpoints include a collection of virological, immunological, pharmacodynamic and safety data. In March 2016 it was announced that the trial would be extended based on results that demonstrated lefitolimod generated broad immune system activation. This broad immune system activation was evidenced by the activation of plasmacytoid dendritic cells (pDCs), natural killer cells (NK) and T-cells. The first patients have recently been enrolled in the extension phase. Positive data could expand the licensing appeal of lefitolimod, as well as leading to further internal development. We expect final results from this investigator-led trial in H117.

Combination therapy

Lefitolimod is currently being tested in combination with the immune checkpoint inhibitor, ipilimumab (Yervoy). Combinations of immune therapies, particularly immune checkpoint inhibitors, have demonstrated remarkable efficacies in a range of cancers. Notable is the combination of Nivolumab (Opdivo) and ipilimumab (Yervoy) for the treatment of metastatic melanoma, approved by the FDA in October 2015. The objective response rate increased to 50% for the combination compared with 40% for Nivolumab (Opdivo) and 14% for ipilimumab alone. Progression-free survival increased to 11.5 months for the combination vs 6.9 months (Opdivo) and 2.9 months (Yervoy). However, adverse reactions in the combination arms were more severe and more common. 73% of patients in the combination arm had a serious adverse reaction (defined as grade 3 or 4, consisting of fatigue, edema, musculoskeletal pain, rash, pruritus, erythema, vitiligo and upper respiratory tract infection) compared with 37% in Opdivo alone.

A Phase I trial testing the combination of lefitolimod and Yervoy is being run by MD Anderson Cancer Centre in an investigator-led trial. The first of 60 expected patients was recently enrolled. The primary endpoint will be measured as maximum tolerated dose, with secondary outcomes measuring tumour response. The trial is expected to complete recruitment in 2017/18, with the start of primary analysis by 2019. Positive data readout could increase lefitolimod's licensing appeal, particularly if a solid safety profile is observed. If the immunotherapy combination had synergistic effects, active concentrations could potentially be reduced, allowing for reduced adverse reactions while maintaining efficacy.

Development pipeline realigned behind lefitolimod

Mologen's strategy is now focused on the commercialisation of lefitolimod; thus focus on the remaining product candidates has now shifted. While MGN1601's development is now on hold, successful out-licensing of lefitolimod would lead to a resumption of MGN1601's development programme. The MIDGE platform, which currently consists of two preclinical product candidates (MGN1331 and MGN1333) and a Phase I product candidate (MGN1404), will be divested or spun off. The preclinical EnanDIM product candidate will be advanced to Phase I.

EnanDIM: Next-generation product candidate

EnanDIM (Enantiomeric, DNA-based, ImmunoModulator) is a technology platform that consists of innovative linear DNA-based TLR9 agonists. The EnanDIM platform aims to provide the safety and

durability of lefitolimod with the ease of production of linear DNA. The use of linear single-stranded DNA in the body is problematic as degradation by enzymes means limited lifetimes. To counter this, EnanDIM family of molecules contains the stereoisomeric form (same molecular formula and bonding, but differ in three-dimensional orientation) of the ribose molecules at the end of the backbone. These cannot be recognised by DNA-degrading enzymes. Mologen plans to advance the preclinical assets into the clinic.

MGN1601: On hold, ready for the future

MGN1601, a Phase II-ready asset, has its development on hold as resources are focused on the commercialisation of lefitolimod. Development would be reinitiated on the successful out-licensing of lefitolimod. MGN1601 is a therapeutic cancer vaccine specific to renal cell carcinoma (RCC), cultured from a tumour cell line from one patient and genetically-modified using the MIDGE technology. This makes the product unique and difficult to copy by a potential generic competitor. The MIDGE transfected cells are also combined with lefitolimod (used as an adjuvant, at a lower dose) and the product can be stored and shipped frozen, providing an off-the-shelf cancer vaccine.

Encouraging outcomes in Phase I/II study

MGN1601 was evaluated in a small, open-label, single-arm Phase I/II study (ASET). The trial treated 19 patients with advanced RCC who failed prior systemic therapies (intent-to-treat, ITT). 10 patients completed the study per protocol (PP; intradermal injections of 10m cells per dose, administered once-weekly for four weeks, then bi-weekly until 12 weeks). Overall, two patients achieved disease control (1x PR; 1x SD) after 12 weeks and continued treatment in an extension phase (starting at week 24 through to 120 weeks). Subsequently, one patient had PD after 60 weeks, while the other completed all five further vaccinations and was still in tumour remission after 120 weeks. Median OS was 24.8 weeks in the ITT population and 115.3 weeks in the PP group. The two patients still alive at week 120 were in the PP group. The safety profile was favourable.

Valuation

Our valuation of Mologen has decreased to €201m (vs €337m) or €8.87/share. While further Lefitolimod indications (HIV and ASM) have been added, the early stage of these trials mean they currently only contribute 4.4% to the valuation. The protracted clinical timelines of MGN1601 and our new assumptions on treatment prices are the main contributors to our reduced risk-adjusted (r) NPV. Due to the changing reimbursement environment, we have remodelled our pricing across all indications, with lower base prices and growth where applicable. We assume Lefitolimod in particular, which is used as a maintenance therapy, will attract lower reimbursements in this new pricing environment. Our sum-of-the-parts DCF model applies a standard 12.5% discount rate. Our key assumptions and valuation metrics are summarised in Exhibit 4.

We assume that Lefitolimod is out-licensed in oncologic indications in 2018, while it is developed to a Phase III-ready state in HIV (2021) where it is subsequently out-licensed. Positive progression of the HIV pipeline could provide valuation uplift (see unadjusted NPV).

Our valuation assumes that a licensing partner will be secured in oncology on successful completion of the IMPALA study, with a 25% royalty rate in mCRC in the EU/US. Since the SCLC programme will have completed Phase II, we assume a more modest 15% royalty. In reality, the royalty rate may fall somewhere between the two levels. However, we have not included any upfront fees and/or milestones that would be expected on securing a partner and successful commercialisation of the product, which offers further potential upside to our valuation. While we assume a deal on completion of IMPALA, we note that a partnership could be secured ahead of IMPALA study data in 2017/18 (for example on the back of positive IMPULSE data in 2017).

On out-licensing of Lefitolimod, we assume that MGN1601's development will be resumed. The reduction in the probability of success for MGN1601 from 25% to 10% is due to uncertainties relating to its development, notably if and when development will be reinitiated. As the potential launch window has been extended, we assume more competition in the market and as such believe the peak market penetration will be reduced (12.5% compared to 15% previously), along with lower reimbursement rates.

For MGN1601, we assume Mologen would partner in the US, Europe and Japan after completion of a pivotal phase III. Therefore, royalties would be receivable (estimated at 25%). However, we do not model potential milestones and upfront payments which may result from any deal.

Exhibit 4: Mologen valuation metrics and assumptions

Product	Status	Market launch	NPV (€m)	Peak sales ($m)	Probability of success (%)	Royalty estimate (%)	rNPV (€m)	rNPV share (€)	Key assumptions
Lefitolimod - CRC - USA	Phase III-ready	2021	89	308	65	25	55.9	2.47	~135,000 CRC cases/yr; 25% metastatic + 5% regional; 60% chemo response; 25% peak share (2026); $40,000 treatment price; 2028 patent expiry
Lefitolimod - CRC - EU	Phase III	2020	200	589	65	25	128.1	5.66	~345,000 CRC cases/yr; 25% metastatic + 5% regional; 60% chemo response; 25% peak share (2026); $30,000 treatment price; exclusivity until 2030
Lefitolimod - CRC - Japan	Phase III-ready	2021	28	198	50	15	13.0	0.57	~112,000 CRC cases/yr; 25% metastatic + 5% regional; 60% chemo response; 25% peak share (2026); $35,000 treatment price; 8-yr exclusivity
Lefitolimod - SCLC - USA	Phase II-ready	2022	33	207	30	15	7.4	0.33	~225,000 lung cancer cases/yr; 15% SCLC; 75% advanced SCLC; 70% chemo response; 20% peak share (2027); $40,000 price; 2028 patent expiry
Lefitolimod - SCLC - EU	Phase II	2022	20	216	30	15	2.4	0.11	~310,000 lung cancer cases/yr; 15% SCLC; 75% advanced SCLC; 70% chemo response; 25% peak share (2028); $30,000 price; exclusivity until 2030
Lefitolimod - SCLC - Japan	Phase II-ready	2023	7	57	25	15	0.8	0.03	~38,000 lung cancer cases/yr; 15% SCLC; 75% advanced SCLC; 70% chemo response; 25% peak share (2028); $35,000 price; 8-yr exclusivity
Lefitolimod - HIV - WW	Phase I	2025	55	405	15	15	4.4	0.20	~ 36.7m cases (Prevalence), 46% treated, 5% peak share (2034), $20,000 price, patent expiry 2036 (expected - not yet granted)
Lefitolimod & ICI - ASM (SCLC used as model) - WW	Phase I	2028	48	511	15	10	5.8	0.26	~ 1.8m lung cancer cases worldwide, 12.50% SCLC, 5% peak share (2033), $30,000 price, patent expiry 2036 (expected - not yet granted)
MGN1601 - RCC -USA - On Hold	Phase II ready	2027	107	198	10	25	9.0	0.40	~63,000 RCC cases/yr; 25% advanced RCC; 12.5% peak penetration (2032); $60,000 treatment price; 12-yr BLA exclusivity (2038)
MGN1601 - RCC - EU - On Hold	Phase II ready	2027	58	116	10	25	3.9	0.17	~75,000 RCC cases/yr; 25% advanced RCC; 12.5% peak penetration (2032); $40,000 treatment price; 10-yr BLA exclusivity (2036)
MGN1601 - RCC - Japan - On Hold	Phase II ready	2028	3	23	10	25	0.2	0.01	~17,000 Kidney Cancer cases/yr, 80% RCC, 25% Advanced RCC, 12.5% peak penetration (2032), $50,000 treatment price, 8-year BLA exclusivity (2036)
Portfolio value			646				231	10.20	
Cash							-30	-1.33	Net cash 31 December 2016 including illustrative debt €30m
Total							201	8.87	22.6m shares out

Source: UNAIDS, Avert, WHO, GLOBOCAN, Ganjoho, Seer Cancer, Cancer Research UK, American Cancer Society. Note: An error occurred in the previous note and the wrong peak sales were displayed. This affected display only and had no effect on calculations relating to the valuation.

Product lifetimes have also been extended based on new patent expiry information. Patent expiry in both mCRC and SCLC is now expected in 2028 for the US and exclusivity until 2030 in the EU, while we assume patent expiries for the combination therapy and HIV will be in 2036. This has altered our assumptions on timelines in relation to peak penetration and pricing changes. We have remodelled some of our population and incidence rates, notably in Japan for CRC which has seen an increase in rNPV due to higher rates of incidence.

Sensitivities

The key sensitivities relate to the clinical performance of lefitolimod and the company's ability to secure the additional financing and/or a partner to complete the full clinical programme. Results from the IMPULSE and IMPALA studies will have a major bearing on lefitolimod's chance of regulatory approvals and commercial success. We have made assumptions about the potential market opportunity available to lefitolimod, which do not currently include significant stratification of patient populations. Lefitolimod may be most active in certain subgroups, which could reduce the target patient pool. However, confirmed activity in a patient subset may result in a higher treatment price, greater reimbursement rates and more favourable economic terms from any partnership. Lefitolimod accounts for 94% of our value and negative trial results would have a significant effect on our valuation. However, EnanDIM and MGN1601 which currently provide either no or little value in our model may contribute more to the value as they are clinically developed.

Financials

Cash at 31 March 2016 was €20.16m, which includes the capital raise in April 2015 when €28.3m gross (€26.2m net) was raised from the rights issue (one-for-three) of c 5.7m new shares at €5.00 per share. Our model suggests that current cash is sufficient to fund operations to early 2017, depending on the progress of the IMPULSE and IMPALA studies for MGN1703. Importantly, this provides a cash runway that accommodates some important milestones in H216, particularly the primary analysis of the IMPULSE study data in SCLC (expected H216 – data expected H117) and completion of patient recruitment in the IMPALA trial. However, a funding gap remains in respect of the IMPALA study (primary endpoint estimated by end-2018). We estimate this to be in the €25-35m range and include an illustrative €30m financing, nominally attributed to debt, in our FY16 forecasts to allow for completion of the study. Mologen has announced that funding will be covered by existing authorised capital, together with existing authorisation to use conditional capital.

A net loss of €4.5m for Q116 as reported (vs €3.2m in 2014) primarily reflects increased R&D expenditure in Q116 of €3.7m (vs €2.4m in Q115). R&D expense, as classified by Mologen, is mainly derived from "cost of materials" of €2.4m (€1.1m in Q115) and "personnel expenses" of €1.3m (€1.3m in Q115), as reported in the income statement. The increased R&D costs are expected to continue in FY16, mainly in support of the IMPALA and IMPULSE trials, with this expected to drive a higher net loss than in 2015. We forecast FY16 R&D (cost of materials) costs of €15.4m and SG&A (personnel expenses) of €5.2m. Our forecast net loss for FY16 remains unchanged at €24.9m.

Exhibit 5: Financial summary

€'000s	2013	2014	2015	2016e	2017e
Year end 31 December	IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS					
Revenue	227	12	39	40	50
Cost of Sales	0	0	0	0	0
Gross Profit	227	12	39	40	50
Research and development (cost of materials)	(2,904)	(8,687)	(11,011)	(15,415)	(16,186)
Selling, general & administrative (personnel expenses)	(4,364)	(5,113)	(5,074)	(5,175)	(5,227)
Other operating income/expense	(2,803)	(3,199)	(4,372)	(4,368)	(4,368)
EBITDA	(9,844)	(16,987)	(20,418)	(24,919)	(25,731)
Operating Profit (before GW and except.)	(9,923)	(17,059)	(20,499)	(24,943)	(25,762)
Intangible Amortisation	(935)	(38)	(40)	(88)	(53)
Exceptionals/Other	0	0	0	0	0
Operating Profit	(10,858)	(17,097)	(20,539)	(25,030)	(25,815)
Net Interest	30	19	3	25	8
Other	0	0	0	0	0
Profit Before Tax (norm)	(9,893)	(17,040)	(20,496)	(24,918)	(25,755)
Profit Before Tax (FRS 3)	(10,828)	(17,078)	(20,536)	(25,006)	(25,807)
Tax	0	0	0	0	0
Deferred tax	0	0	0	0	0
Profit After Tax (norm)	(9,893)	(17,040)	(20,496)	(24,918)	(25,755)
Profit After Tax (FRS 3)	(10,828)	(17,078)	(20,536)	(25,006)	(25,807)
Average Number of Shares Outstanding (m)	15.4	16.8	20.7	22.6	22.6
EPS - normalised (c)	(0.64)	(1.01)	(0.99)	(1.10)	(1.14)
EPS - FRS 3 (c)	(0.70)	(1.02)	(0.99)	(1.10)	(1.14)
Dividend per share (c)	0.0	0.0	0.0	0.0	0.0
BALANCE SHEET					
Fixed Assets	457	440	414	411	435
Intangible Assets	237	206	175	105	63
Tangible Assets	220	234	239	306	372
Other	0	0	0	0	0
Current Assets	15,480	14,613	25,981	31,523	6,248
Stocks	33	30	28	28	27
Debtors	0	0	0	0	0
Cash	14,765	13,563	24,592	30,134	4,860
Other	682	1,020	1,361	1,361	1,361
Current Liabilities	(943)	(1,747)	(6,886)	(6,886)	(6,886)
Creditors	(943)	(1,747)	(6,886)	(6,886)	(6,886)
Short term borrowings	0	0	0	0	0
Long Term Liabilities	(10)	(8)	(6)	(30,006)	(30,006)
Long term borrowings	0	0	0	(30,000)	(30,000)
Other long term liabilities	(10)	(8)	(6)	(6)	(6)
Net Assets	14,984	13,298	19,503	(4,958)	(30,209)
CASH FLOW					
Operating Cash Flow	(8,869)	(15,602)	(15,095)	(24,349)	(25,168)
Net Interest	0	3	0	0	0
Tax	0	(6)	12	0	0
Capex	(146)	(93)	(95)	(109)	(106)
Acquisitions/disposals	1	0	0	0	0
Financing	8	14,495	26,207	0	0
Dividends	0	0	0	0	0
Other	0	0	0	0	0
Net Cash Flow	(9,006)	(1,203)	11,029	(24,458)	(25,274)
Opening net debt/(cash)	(23,777)	(14,765)	(13,563)	(24,592)	(134)
HP finance leases initiated	0	0	0	0	0
Exchange rate movements	(6)	1	0	0	0
Other	0	0	0	0	0
Closing net debt/(cash)	(14,765)	(13,563)	(24,592)	(134)	25,140

Source: Company accounts, Edison Investment Research

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

Management team

Chief Executive Officer: Dr Mariola Söhngen	Chief Financial Officer: Walter Miller
Dr Söhngen joined Mologen on 1 November 2015, assuming the role of CEO. She is the co-founder of Paion and Paion Deutschland and served as MD at both. She also held the position of CMO of Paion from 2004 to 2015. Before founding Paion she worked for Grünenthal and Ferrer Internacional. She has a medical degree, a PhD in medicine, a diploma in pharmaceutical medicine and a master of business communication.	Mr Miller joined Mologen on 1 April 2016, assuming the role of CFO. He was most recently the CFO of Nuvisan, an international contract research organisation (CRO). He has also held various managerial positions at Santhera Pharmaceuticals, initially VP of finance and commercial operations in Germany and subsequently in Switzerland. He was also a member of the group's management team. He started his career at Isra Vision Parsytec in Aachen, Germany.

Principal shareholders	(%)
Global Derivative Trading	24
Deutscher Ring Krankenversicherungsverein	6
Baloise Holding	6
Deutsche Balaton Aktiengesellschaft	5
Salvator Vermoegensverwaltungs	5

Companies named in this report

Bristol Myers Squib, Taiho Oncology, Eli Lilly, Roche.