EDISON

Medigene

Q3 results

Successful manufacturing of first TCR therapy

Pharma & biotech

Medigene's MDG1011 trial in MM, AML and MDS is ongoing and the first MDG1011 TCR cell product has been successfully produced. Additionally, procedures to speed up patient enrolment are being rolled out, including the simplification of enrolment criteria and the addition of new trial centres. We continue to forecast that clinical data from both the Phase I part of the MDG1011 Phase I/II clinical TCR trial and the now fully enrolled Phase I/II dendritic cell (DC) vaccine trial will be available in 2019. Financials for 9M18 were above guidance, driven by a reduction in expected R&D costs. We now forecast a net loss of €16.9m in FY18 vs €18.4m previously. Additionally, Medigene announced an exclusive licence agreement with Leiden University to develop a TCR against HA-1, an antigen expressed in a range of cancers. We value Medigene at €457m.

Year end	Revenue (€m)	PBT* (€m)	EPS* (€)	DPS (€)	P/E (x)	Yield (%)
12/16	9.7	(13.4)	(0.66)	0.0	N/A	N/A
12/17	11.4	(12.4)	(0.60)	0.0	N/A	N/A
12/18e	10.4	(16.3)	(0.70)	0.0	N/A	N/A
12/19e	11.0	(17.1)	(0.70)	0.0	N/A	N/A

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

MDG1011 TCR trial: Patient screening ongoing

The first personalised MDG1011 TCR therapy has been manufactured in the Phase I/II clinical trial and met the requirements needed for patient administration. However, due to the progression of the patient's disease, the treatment could not to be administered. Screening of patients is ongoing, although strict enrolment criteria (eg PRAME+ and HLA-A*02:01+) mean that only 10–20% of potential patients are eligible for treatment. We forecast initial Phase I data in 2019.

Leiden University agreement expands pipeline

Medigene has announced an exclusive worldwide licence agreement with Leiden University Medical Center (LUMC) to develop, manufacture and commercialise an HA-1 specific TCR for cancer treatment. The HA-1 TCR has been tested in five patients by LUMC and was well tolerated. LUMC will receive a one-time payment from Medigene plus milestone payments and low-single digit royalties.

9M18 financials: Lower than expected costs

To reflect new guidance, we have lowered our FY18 R&D forecasts to €20.1 vs €21.6m previously, as H118 clinical trial costs continue to be lower than previously forecast due to slower patient enrolment. We now forecast an FY18 EBITDA loss of €16.7m vs a loss of €18.2m previously. Medigene's net cash at end September 2018 was €76.3m (including time deposits).

Valuation: €457m (€18.59/share)

We value Medigene at €457m (€18.59/share) vs €453m (€18.47/share) previously as a result of rolling forward our model and updating it for net cash. This is based on an rNPV of its TCR, DC and legacy assets in addition to deal metrics for the bluebird bio partnership and legacy asset, Veregen.

19 November 2018

Price	**€9.59**
Market cap	**€236m**

Net cash (€m) at 30 September 2018 (including time deposits)	76.3
Shares in issue	24.6m
Free float	80.3
Code	MDG1
Primary exchange	Xetra
Secondary exchange	Frankfurt

Share price performance

%	1m	3m	12m
Abs	(14.0)	(28.5)	(12.5)
Rel (local)	(10.7)	(22.9)	0.7
52-week high/low		€18.8	€9.5

Business description

Medigene is a German biotech company with complementary technology platforms in cancer immunotherapy. Its dendritic cell vaccines and T-cell receptors (TCRs) are both in Phase I/II clinical studies.

Next events

DC vaccine initial clinical data	H119
MDG1011 initial clinical data	2019

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Edison profile page

TCR trial: New protocols in place to drive enrolment

Medigene's lead TCR product candidate, MDG1011, is a TCR that targets preferentially-expressed antigen in melanoma (PRAME) and is currently in the Phase I stage of a Phase I/II clinical trial. The company is initially planning to enrol 12 patients into the Phase I trial with one of three relapsed or refractory blood cancers: r/r multiple myeloma (MM), acute myeloid leukaemia (AML) or myelodysplastic syndrome (MDS). An additional 80 patients are expected to be enrolled in the Phase II stage (total of 92 patients). Prospective patients will be genotyped to ensure they are HLA-A*02:01 positive and PRAME positive, and all patients enrolled will undergo a cyclophosphamide and fludarabine preconditioning regimen. The Phase I component of the trial is designed to test up to three dose cohorts (an optional fourth dose cohort may be utilised) in a 3+3 design (12 patients in total). Patient screening is currently ongoing with no patient having received treatment to date. However, Medigene has successfully manufactured the first MDG1011 TCR cell therapy but, due to the progression of the patient's disease, the treatment could not be administered.

After discussions with the German regulatory authority, Medigene has been granted permission to amend its trial enrolment criteria with the aim of speeding up enrolment by changing the inclusion criteria from one patient per disease in each dose cohort to at least one MM patient and at least one patient of either AML or MDS. Multiple myeloma has a higher incidence rate than that of AML or MDS, so this change should be beneficial as it could enable the inclusion of two MM patients per cohort.

We note that the inclusion criteria remain relatively restrictive (eg HLA-A*02:01 positive and PRAME positive) and only 10–20% of patients screened are likely to make it into the trial. To expand the eligible patient population, Medigene has optimised its analytical method for determining whether a patient is PRAME positive so that lower levels of clinically relevant PRAME expression can now be detected.

Additionally, as demonstrated by the first cell product manufactured, patients may progress in the time (approximately two months) between having their T-cells removed, genetically modified (to make MDG1011) and then infused back into them (known as the vein-to-vein time). At this point, patients are no longer eligible for treatment. This is a well-known problem with cell therapy clinical trials and has been observed in other TCR and CAR-T trials. We expect a gradual and small reduction in the vein-to-vein time as the trial progresses and Medigene's expertise with cell production increases. Medigene is also preparing to open both new clinical trial centres to increase the number of patients screened and to start screening some patients at referral centres instead of clinical trial sites (to speed up the time to treatment).

In addition to these time concerns relating to manufacturing and screening, there are numerous safety periods in the Phase I component of the trial where no new patients can be treated (notably, at each dosing level, once all patients have been treated, a four-week safety follow-up will be observed before an independent data and safety monitoring board decides if the next dosing level should be administrated).

For now we retain our assumption that initial data (Phase I data, potentially first dose group) from the trial will be available in 2019 and that the Phase II part of the trial is likely to start in 2020. However, based on the sensitivities discussed above, these timings could alter further.

For further details of the MDG1011 trial design, please see our outlook note, TCR enters the clinic, published on 27 March 2018.

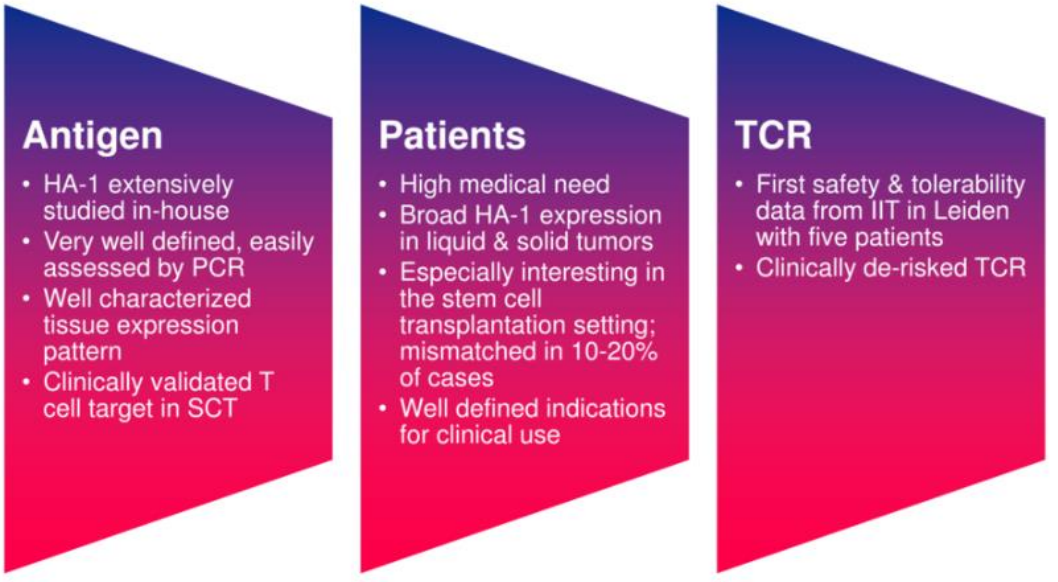
Minor histocompatibility antigen HA-1 potential across cancers

With the signing of an exclusive worldwide licence agreement with LUMC, Medigene has added an additional TCR asset to its pipeline. Under the agreement, Medigene will further develop an HA-1 specific TCR for the potential use in either solid or liquid cancers. The plans for development remain undisclosed at this time, but Medigene notes that it sees significant commercial and clinical opportunity with this antigen (Exhibit 1). We envision that a similar Phase I/II trial to the one currently being implemented with MDG1011 could be undertaken by the end of 2019. However, at this time we do not include HA-1 TCR in our valuation or financials and await more details on the product development strategy, at which point we will reassess the situation.

To date, an HA-1 specific TCR has been tested by LUMC in five patients (clinical trial registry). Data are yet to be published, but Medigene reports that the therapy was well tolerated. The trial was originally meant to enrol 20 patients, but was halted early due to slow enrolment as a result of complications in the trial design and manufacturing. Medigene will implement its own manufacturing processes and use the experience it is gaining with the MDG1011 clinical trial to try and bypass many of these previous issues. We note while LUMC has clinically tested the HA-1 TCR, Medigene will have to start the clinical trial development from scratch with a dose-escalation Phase I study. This is because Medigene is using its own manufacturing processes, which will classify the HA-1 TCR as a new product. We await the publication of efficacy data from the LUMC trial to further assess the potential of a HA-1 TCR.

While the proposed indications are currently undisclosed, Medigene is likely to focus on cancers where HA-1 is abundant, including leukaemias and lymphomas. Additionally the HA-1 TCR could potentially be utilised in solid cancers like renal cell carcinoma and breast cancer.

Exhibit 1: HA-1 TCR advantages



Source: Medigene Q318 company presentation

Technical investments for the future

In August 2018, Medigene announced a collaboration with Structured Immunity (SI), which will provide structural immunology expertise to aid Medigene's TCR selections. The collaboration will involve studying the interactions between a TCR and the corresponding MHC-peptide complexes. Additionally, the project will be supported by the expertise of the research laboratory of Dr Brian Baker at the University of Notre Dame and the IDEA (Innovation, De-Risking and Enterprise Acceleration) Centre.

SI has built a multifaceted platform that can determine TCR structure utilising x-ray crystallography, characterise TCR-peptide/MHC stability and affinity, asses TCR specificity, and provide structure-guided protein engineering solutions. Initially, the work will involve SI analysing the specificity and recognition properties of a Medigene-produced TCR selected against a solid tumour target.

In addition to seeking external expertise, Medigene continues to develop its internal platform (as noted by more than 15 patent applications in 2018). In March 2018, Medigene announced the grant of a European patent (EP2327763, expires in August 2026) that is based on the ability to discover antigen-specific MHC class-II-restricted CD4+ T-cells for use in the treatment of solid tumours. Based on internal and external research, Medigene believes that CD4+ T-cells will be able to enter and kill solid tumour tissue. This approach could broaden the number of potential tumour antigen targets and Medigene continues to refine the process with additional IP pending.

9M18 financials: Funded through trial readouts

Medigene reported 9M18 revenue of €6.0m (9M17: €5.2m) driven by increases in immunotherapy revenue (as a result of the bluebird collaboration), which rose 38% to €4.7m (9M17: €3.4m).

COGS and selling expenses in the period reduced to €0.7m and €1.4m respectively (vs €0.9m and €1.8m in 9M17). The reduction in costs was a result of the termination agreement with the API provider for Veregen in the previous year. General administrative expenses remained flat at €4.5m in 9M18.

R&D expenses increased to €13.3m (vs €11.1m in 9M17) as a result of the ongoing clinical trials, but were lower than forecast as the MDG1011 clinical trial costs continue to be below expectations due to both a later than expected trial start and slower than anticipated patient enrolment. Medigene has again (following Q2 revision) revised its forecast R&D costs downwards for FY18. As a result, we have adjusted our FY18 R&D forecasts to €20.1m vs €21.6m previously.

The 9M18 EBITDA loss increased by 5% to €10.7m (9M17: €10.14m). We now forecast an FY18 EBITDA loss of €16.7m vs a loss of €18.2m previously.

9M18 net loss increased to €12.2m vs €10.7m previously. We now forecast an FY18 net loss of €16.9m vs a loss of €18.4m previously.

The net cash position at end September 2018 of €76.3m (including time deposits) should enable the funding of Medigene beyond 2020 based on current forecast expenditure. We forecast a FY18 cash utilisation of €13.7m excluding the May 2018 €30.1m net capital raise.

Exhibit 2: Financial summary

€'000s	2016	2017	2018e	2019e
Year end 31 December	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS				
Revenue	9,749	11,375	10,409	11,018
of which: Veregen revenues (royalties/milestones/supply)	3,048	2,790	1,433	1,582
R&D partnering (SynCore/Falk Pharma/grants)	3,155	0	0	0
Non-cash income (Eligard)	2,493	3,699	3,699	3,699
Bluebird bio partnership	1,053	4,886	5,278	5,738
Cost of sales	(1,402)	(1,621)	(553)	(613)
Gross profit	8,347	9,754	9,856	10,405
Selling, general & administrative spending	(10,025)	(8,266)	(7,186)	(7,395)
R&D expenditure	(11,538)	(14,877)	(20,084)	(21,691)
Other operating spending	0	0	0	0
Operating profit	(8,974)	(13,389)	(17,414)	(18,680)
Goodwill & intangible amortisation	(525)	(524)	(523)	(522)
Exceptionals	4,242	0	0	0
Share-based payment	0	0	0	0
EBITDA	(12,371)	(12,122)	(16,666)	(17,933)
Operating Profit (before amort. and except.)	(12,691)	(12,865)	(16,891)	(18,158)
Net interest	(1,009)	(1,434)	(691)	(478)
Other (forex gains/losses; associate profit/loss)	263	1,884	1,278	1,546
Profit Before Tax (norm)	(13,437)	(12,415)	(16,304)	(17,090)
Profit before tax (reported)	(9,720)	(12,939)	(16,827)	(17,612)
Tax	228	(634)	(101)	(101)
Profit/(loss) from discontinued operations	0	0	0	0
Profit after tax (norm)	(13,209)	(13,049)	(16,405)	(17,191)
Profit after tax (reported)	(9,492)	(13,573)	(16,928)	(17,713)
Average number of shares outstanding (m)	20.0	21.6	23.4	24.6
EPS - normalised (c)	(66.20)	(60.42)	(70.03)	(70.01)
EPS - Reported (€)	(0.48)	(0.63)	(0.72)	(0.72)
Dividend per share (c)	0.0	0.0	0.0	0.0
BALANCE SHEET				
Fixed assets	47,742	48,595	47,460	47,357
Intangible assets & goodwill	35,767	36,292	35,769	35,247
Tangible assets	3,323	4,329	4,717	5,136
Other non-current assets	8,652	7,974	6,974	6,974
Current assets	63,973	63,342	78,717	58,829
Stocks	7,866	7,724	7,724	7,724
Debtors	1,175	1,699	680	680
Cash	52,630	51,724*	68,119*	48,230*
Other	2,302	2,195	2,195	2,195
Current liabilities	(11,966)	(9,808)	(8,699)	(8,699)
Trade accounts payable	(973)	(725)	(798)	(798)
Short-term borrowings	0	0	0	0
Deferred income	(3,575)	(3,575)	(3,495)	(3,495)
Other	(7,418)	(5,508)	(4,406)	(4,406)
Long-term liabilities	(21,157)	(15,962)	(20,379)	(17,042)
Pension provisions	(408)	(405)	(405)	(405)
Long-term borrowings	0	0	0	0
Other liabilities (Deferred taxes; Trianta milestones)	(2,395)	(3,672)	(3,672)	(3,672)
Deferred revenues (Eligard non-cash income & bluebird bio)	(18,354)	(11,885)	(16,302)	(12,965)
Net assets	78,592	86,167	97,099	80,446
CASH FLOW				
Operating cash flow	(3,611)	(20,729)	(15,987)	(19,465)
Net interest	(45)	(45)	109	322
Tax	(102)	(75)	(101)	(101)
Capex	(1,677)	(1,533)	(613)	(644)
Expenditure on intangibles	0	0	0	0
Acquisitions/disposals	10,537	480	1,242	0
Equity financing	(77)	19,329	30,078	0
Other	846	1,667	1,667	0
Net cash flow	5,871	(906)	16,395	(19,888)
Opening net debt/(cash)	(46,759)	(52,630)	(51,724)	(68,119)
HP finance leases initiated	0	0	0	0
Other (foreign exchanges differences)	0	0	0	0
Closing net debt/(cash)	(52,630)	(51,724)	(68,119)	(48,230)

Source: Company accounts, Edison Investment Research. Note: *Cash consists of cash in addition to both long- and short-term time deposits.

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