EDISON

Transgene

TG4010 data

Potential confirmed but checkpoint data needed

Pharma & biotech

The therapeutic potential of Transgene's TG4010 in non-squamous non-small cell lung cancer (NSCLC) was supported by the more mature overall survival (OS) Phase IIb data. However, we expect that additional data from combination studies with checkpoint inhibitors will be required for TG4010 to be out-licensed; these trials should start in H215. Transgene is also planning to initiate a Phase I study with TG1050 for chronic HBV infection. We maintain our valuation at €464m.

Year end	Revenue (€m)	PBT* (€m)	EPS* (c)	DPS (c)	P/E (x)	Yield (%)
12/13	15.7	(41.5)	(136.2)	0.0	N/A	N/A
12/14	11.8	(47.3)	(127.2)	0.0	N/A	N/A
12/15e	11.3	(56.1)	(145.6)	0.0	N/A	N/A
12/16e	11.6	(58.1)	(150.9)	0.0	N/A	N/A

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

TG4010 continues to demonstrate potential

The more mature OS data from the Phase IIb stage of the TIME study with TG4010 confirms the product's potential in non-squamous NSCLC, with an OS benefit of 3.8 months (14.6 vs 10.8) in patients receiving TG4010 with chemotherapy compared to those on chemotherapy alone. As seen previously, patients with low TrPAL biomarker expression benefited most from TG4010; the hazard ratio for this group was 0.64, with an OS benefit of 4.9 months versus placebo (15.2 vs 10.3 months).

Combination studies could attract new interest

Despite the good data from the TIME study it looks unlikely that Transgene will find a partner imminently for TG4010. However, a licensing deal could be triggered by data showing that TG4010 acts synergistically with checkpoint inhibitors. Preclinical data support the potential of TG4010 with this class of drug being used together. Transgene is in discussions with major pharma companies ahead of a Phase II trial in NSCLC with TG4010 and a checkpoint inhibitor that could start in Q415/Q116.

HBV therapeutic vaccine soon to enter the clinic

Transgene plans to initiate a Phase I trial with TG1050 for hepatitis B virus (HBV) in Q315. The therapeutic vaccine has been shown to stimulate a CD4 and CD8 response against three HBV proteins and have a sustained antiviral effect in preclinical studies. The WHO estimate that 240m people have chronic HBV infection, current therapies only cure 3-5% of patients, and most patients need lifelong antiviral treatments.

Valuation: DCF valuation of €464m unchanged

Our valuation of Transgene in unchanged at €464m (€12.03/share). The company has sufficient cash to operate to mid-2016, but we expect it to raise additional capital before the end of the year to support the TG4010 and checkpoint inhibitor combination trial and to advance its various programmes. Non-dilutive funding could come from the partnering of TG1050 or the preclinical asset TG3003.

3 June 2015

Price	**€4.95**
Market cap	**€191m**

Net cash (€m) at 31 December 2014	13.7
Shares in issue	38.5m
Free float	43%
Code	TNG
Primary exchange	Paris
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	(2.2)	(29.8)	(50.9)
Rel (local)	(1.5)	(31.2)	(56.1)

52-week high/low	€10.32	€4.80

Business description

Transgene is a French drug discovery and development company focused on the treatment of cancer and infectious diseases with immunotherapies. It has one product in Phase II development and two products about to enter Phase III.

Next events

AGM	11 June 2015
Start of TG1050 trial	Q315
H115 results	10 September 2015

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Update: Data improves, but checkpoint data needed

The more mature overall survival (OS) data from the Phase IIb stage of the Phase IIb/III TIME trial with TG4010 in NSCLC presented by Transgene at the ASCO meeting, shows that the therapeutic vaccine against cells expressing the MUC1 protein still has commercial potential, although we believe it is unlikely to trigger a licensing agreement in the near term. However, Transgene is planning a Phase II trial with TG4010 in combination with a checkpoint inhibitor (we anticipate either a PD1 or PD-L1 inhibitor) in NSCLC, which could lead to a partnering deal. To conduct this trial, Transgene will have to raise additional capital; it currently has sufficient capital to operate to mid-2016 and it could raise non-dilutive funding by out-licensing the HBV therapeutic vaccine TG1050 (about to start Phase I) or a promising immunotherapy preclinical asset TG3003. Our valuation is unchanged at €464m (€12.03/share).

TG4010 potential confirmed

The more mature data presented by Transgene at ASCO from the TG4010 Phase IIb study confirmed the findings of the interim data (Exhibits 1-6). There was a significant OS advantage in all patients with non-squamous NSCLC (HR=0.75, p=0.0093, n=196). The benefit was greatest in those patients with low levels of the TrPAL (triple positive activated lymphocytes, which express the CD16, CD56 and CD69 proteins), in this group the hazard ratio (HR) was 0.64 (p=0.0188, n=127) but, in those with high TrPAL, it was 1.01 (p=0.4805, n=69).

The overall response rate (ORR) and duration of response (DR) data (previously unreported, Exhibits 7-8) are also supportive of the potential of TG4010 in the treatment of non-squamous NSCLC in patients with low TrPAL levels. Consistent with previously reported results, the ORR and DR data for the total population (squamous and non-squamous NSCLC patients) showed that those patients receiving TG4010 benefited compared to the placebo arm (ORR: 39.6% vs 28.8%; DR: 30.1 vs 18.7 weeks). Again, those patients with non-squamous NSCLC and low TrPAL are shown to have benefited most compared to those receiving placebo (ORR: 39.3% vs 30.3%; DR: 43.1 vs 18.1 weeks).

Transgene also showed in post-hoc analysis of all non-squamous NSCLC patients that there was a similar level of progression-free survival (PFS) and OS benefit in the 97 people with low levels of PD-L1 expression (<5% of cells PD-L1+) to that observed with all non-squamous NSCLC patients. There is currently considerable interest in the potential of the PD1/PD-L1 inhibitors Bristol-Myers Squibb's (BMS) nivolumab (Opdivo), Merck's pembrolizumab (Keytruda), Roche's atezolizumab and other related inhibitors for the treatment of NSCLC, and it has been shown in various studies, that non-squamous NSCLC patients with low levels of PD-L1 will not benefit as much from these treatments as those with high levels of PD-L1 expression. Therefore, the activity seen with TG4010 in patients with low-PD-L1 NSCLC tumours indicates that the vaccine could become a valuable treatment in those non-squamous patients less likely to benefit from treatment with PD1 or PD-L1 inhibitors.

Although TG4010 appears to work equally well in non-squamous NSCLC patients regardless of PD-L1 expression, TG4010 could still work synergistically with PD1/PD-L1 inhibitors and other checkpoint inhibitors. In preclinical studies, a synergistic effect has been observed, as would be expected with TG4010 stimulating an immune response and checkpoint inhibitors removing a dampener on such a response. Transgene is in discussion with various companies developing checkpoint inhibitors (presumably AstraZeneca, BMS, Merck and Roche) with a view to a Phase II study (or studies) in non-squamous NSCLC with TG4010 in combination with a checkpoint inhibitor being initiated. Transgene hopes that such a trial will be started in Q415/Q116.

Exhibit 1: Kaplan-Meier curve for PFS in all patients with non-squamous NSCLC

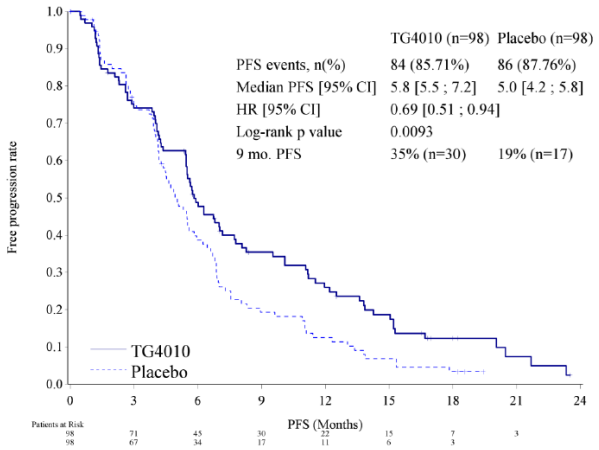


Exhibit 2: Kaplan-Meier curve for OS in all patients with non-squamous NSCLC patients

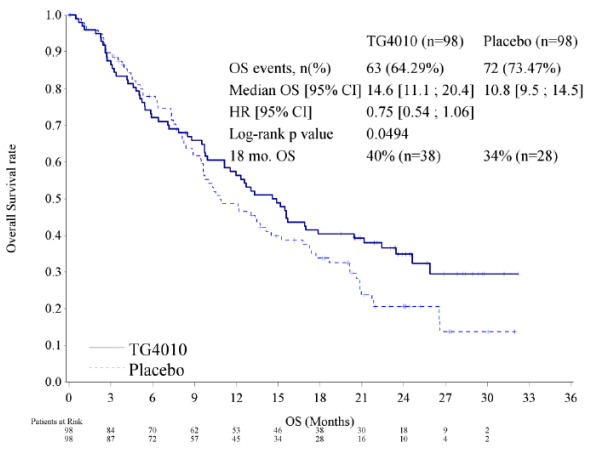


Exhibit 3: Kaplan-Meier curve for PFS in patients with low levels of TrPAL biomarker

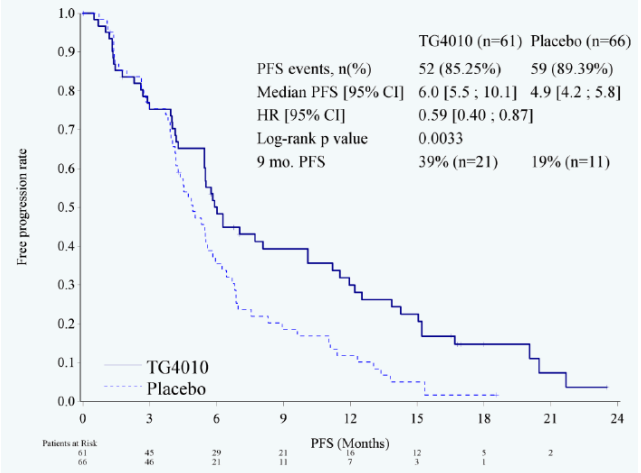


Exhibit 4: Kaplan-Meier curve for OS in patients with low levels of TrPAL biomarker

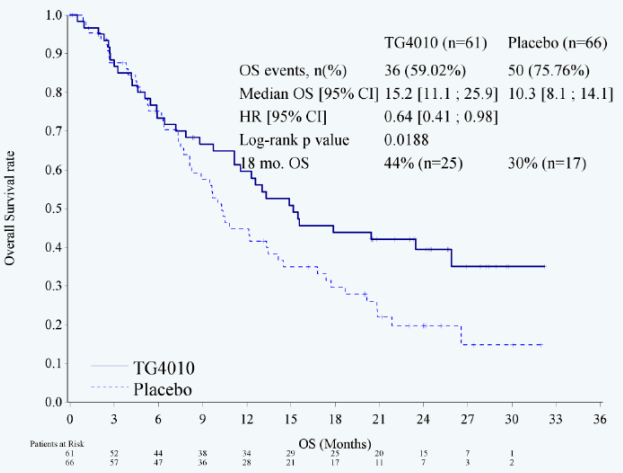


Exhibit 5: Kaplan-Meier curve for PFS in patients with non-squamous NSCLC high levels of TrPAL biomarker

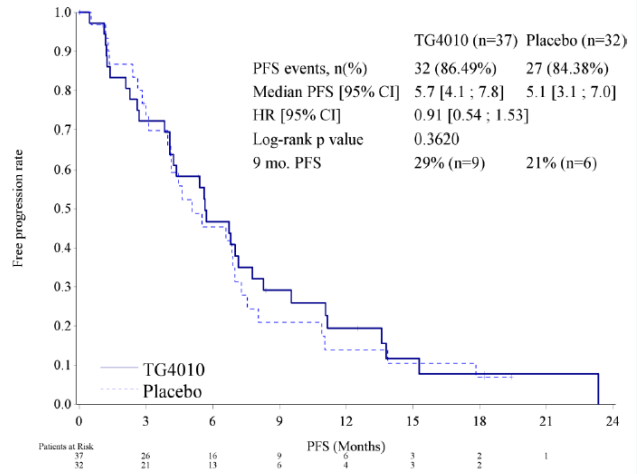
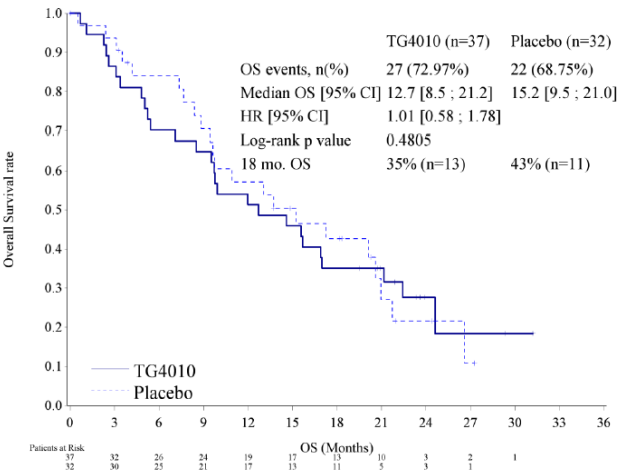


Exhibit 6: Kaplan-Meier curve for OS in patients with non-squamous NSCLC high levels of TrPAL biomarker



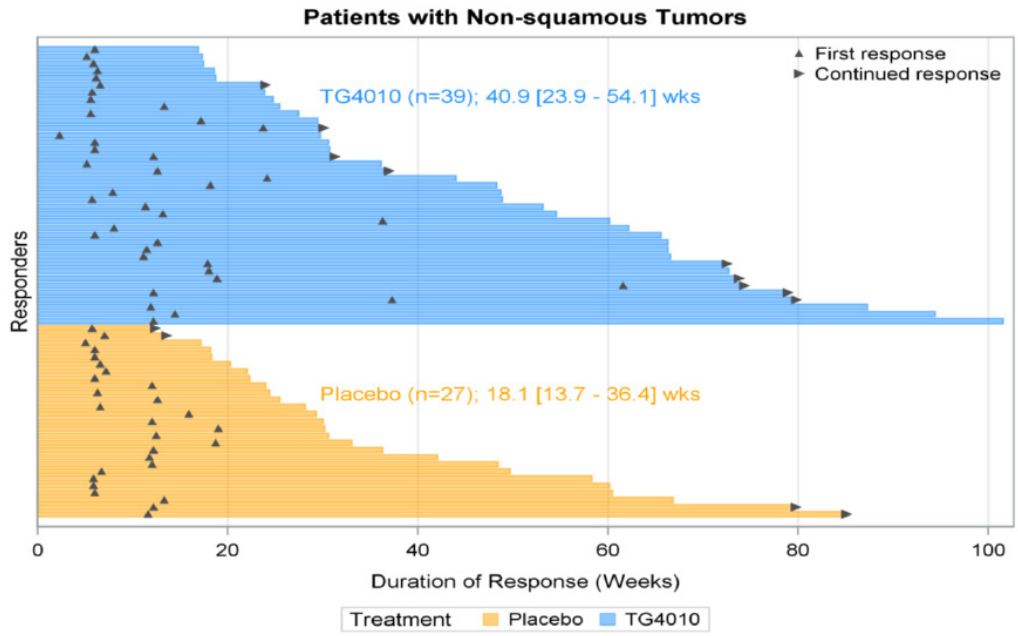
Source: Transgene

Exhibit 7: Overall response rates and duration of responses in Phase IIb TIME trial

	TG4010	Placebo
Overall population (n)	111	111
Overall response rate	39.6%	28.8%
Median duration of response (weeks)	31.1	18.7
Non-squamous NSCLC patients (n)	98	98
Overall response rate	39.8%	27.6%
Median duration of response (weeks)	40.9	18.1
Non-squamous NSCLC patients with low TrPAL biomarker (n)	61	66
Overall response rate	39.3%	30.3%
Median duration of response (weeks)	43.1	18.1

Source: Transgene

Exhibit 8: Duration of response for patients with non-squamous NSCLC



Source: Transgene

Discussions are reportedly still ongoing with potential partners; however, in our view it is most likely that any deal will be signed once the Phase II study in combination with checkpoint inhibitors has been completed. The extra data would reduce the risk for a potential partner and should improve Transgene's negotiating position.

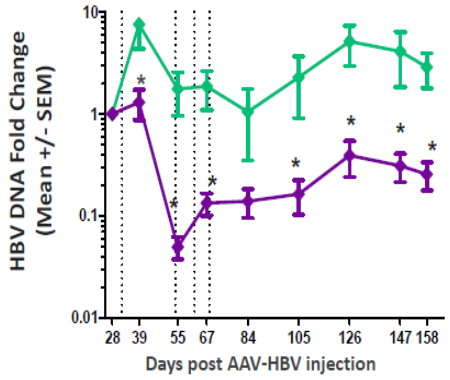
Transgene has said that it will not advance the TIME trial into the Phase III stage of the trial without a partner. This is probably still the case; however Transgene could decide to follow the approach of Bavarian Nordic with its therapeutic vaccine Prostvac. Bavarian Nordic raised capital and initiated a Phase III study in prostate cancer with Prostvac in 2011, having failed to find a partner; this strategy has paid-off as the company signed a $975m option deal for Prostvac with BMS in March 2015. The clinical sites for the TIME study are still open as it collects the final data from the Phase IIb stage of the trial, so Transgene could have a significantly faster route to market significantly by proceeding directly into Phase III.

Other pipeline news

A Phase III study with the oncolytic virus Pexa-Vec, Transgene's other Phase III-ready asset, is still expected to be initiated in Q415. Transgene and its partner Sillajen have an SPA (special protocol agreement) with the FDA for the design of the Phase III study in first-line hepatocellular carcinoma (HCC). We estimate that data from the trial could be reported in 2018.

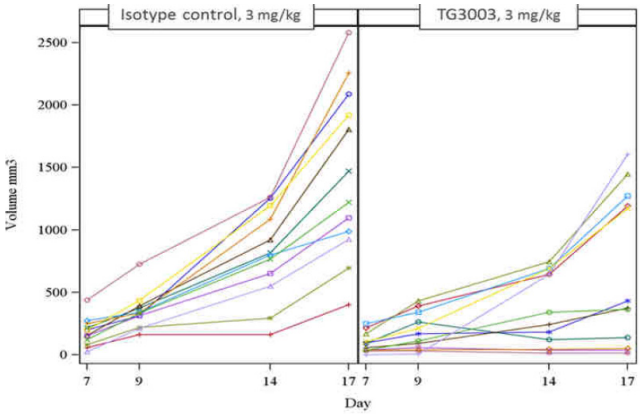
Transgene expects to initiate a Phase I study with therapeutic vaccine TG1050 in c 100 patients with chronic HBV infection in Q315. There are currently limited treatments for this infection, the cure rate from nucleotide analogues such as tenofovir (Viread) and entecavir (Baraclude) or pegylated interferon-α is only 3-5%, so that patients normally need long term anti-viral therapy to control their infection. Preclinical data with TG1050 suggest that the vaccine could produce a sustained immune response against the virus in chronic HBV patients, thereby preventing relapses without the need for antiviral therapies. Given the size of the potential market (the WHO estimates that 240m people have chronic HBV infection), Transgene will look to partner TG1050 once it has proof-of-concept data from the Phase I study that is about to start.

Exhibit 9: Preclinical data of the reduction in HBV DNA following vaccination with TG1050 (purple) or placebo (green)



Source: Transgene; Note: dotted lines indicate days of vaccinations.

Exhibit 10: Effect of TG3003 on tumour growth in preclinical studies



Source: Transgene

TG3003 is another promising preclinical asset for Transgene, and the company hopes to out-license the product before it enters clinical development in 2016. TG3003 is a monoclonal antibody against CD115 (CSF-1 Receptor), which acts as an immunomodulator and has potential in cancer immunotherapy. The antibody acts by binding to macrophages and pushing them towards becoming dendritic cells (antigen-presenting cells) instead of immune-suppressive M2-Type macrophages, thereby boosting the anti-tumour immune response. There are other CD116 antibodies in Phase I/II clinical development (including Roche's RG7155, Amgen's AMG820, Eli Lilly's IMC-CS4 and Daiichi Sankyo's PLX3397); but these other products act by blocking the CD115 receptor from binding to its ligand, whereas TG3003 down regulates CD116 signalling without interfering with ligand binding and is not cytotoxic to normal myeloid cells. Transgene has presented promising preclinical data (Exhibit 10) and reports significant interest from potential partners for TG3003, which could be used across a range of tumours in combination with other immunotherapy agents.

Financials and valuation

Our valuation of Transgene is unchanged at €464m (€12.03/share) and no changes have been made to our financial model. The next potential catalysts for the shares could be news regarding the Phase II trial with TG4010 and a checkpoint inhibitor, initiation of the Phase I/II trial with TG1050 in chronic HBV patients, and the partnering of TG3003.

Transgene had a gross cash position of €57.0m on 31 March 2015, which should allow the company to operate to mid-2016, without an equity raise or non-dilutive financing from a licensing deal. To enable the company to complete the Phase II combination trial with TG4010 and Phase I trial with TG1050, we expect Transgene to conduct an equity raise, although some financing could

come from the partnering of TG1050 or TG3003. We estimate that the company will have to raise €30m to operate into 2017.

Exhibit 11: Financial summary

€000s	2012	2013	2014	2015e	2016e
Year end 31 December	IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS					
Revenue	13,061	15,735	11,752	11,276	11,575
Cost of Sales	0	0	0	0	0
Gross Profit	13,061	15,735	11,752	11,276	11,575
EBITDA	(39,372)	(38,287)	(43,893)	(53,490)	(55,346)
Operating Profit (before GW and except)	(41,765)	(40,813)	(46,524)	(55,828)	(57,592)
Intangible Amortisation	(370)	(385)	(408)	(308)	(267)
Exceptionals	0	0	0	0	0
Operating Profit	(42,135)	(41,198)	(46,932)	(56,136)	(57,859)
Other	(488)	(691)	0	0	0
Net Interest	(106)	(39)	(801)	(260)	(546)
Profit Before Tax (norm)	(42,359)	(41,543)	(47,325)	(56,088)	(58,138)
Profit Before Tax (FRS 3)	(42,729)	(41,928)	(47,733)	(56,396)	(58,406)
Tax	0	0	0	0	0
Profit After Tax (norm)	(42,833)	(42,473)	(48,148)	(56,088)	(58,138)
Profit After Tax (FRS 3)	(42,729)	(41,928)	(47,733)	(56,396)	(58,406)
Average Number of Shares Outstanding (m)	31.8	31.9	38.5	38.5	38.5
EPS - normalised (c)	(136.4)	(136.2)	(127.2)	(145.6)	(150.9)
EPS - FRS 3 (c)	(136.0)	(134.5)	(126.2)	(146.4)	(151.6)
Dividend per share (c)	0.0	0.0	0.0	0.0	0.0
Gross Margin (%)	N/A	N/A	N/A	N/A	N/A
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	62,090	64,501	61,715	60,366	59,213
Intangible Assets	1,497	1,329	1,056	891	771
Tangible Assets	24,805	23,988	23,641	22,457	21,424
Other	35,788	39,184	37,018	37,018	37,018
Current Assets	98,374	61,349	79,238	36,704	18,278
Stocks	1,107	975	1,149	1,149	1,149
Debtors	2,012	1,896	1,540	1,540	1,540
Cash	92,915	47,862	65,935	23,401	4,975
Other	2,340	10,616	10,614	10,614	10,614
Current Liabilities	(19,402)	(23,996)	(21,563)	(25,158)	(55,515)
Creditors	(9,587)	(9,364)	(8,296)	(11,891)	(12,248)
Short term borrowings	0	0	0	0	(30,000)
Short term leases	(961)	(8,830)	(8,992)	(8,992)	(8,992)
Other	(8,854)	(5,802)	(4,275)	(4,275)	(4,275)
Long Term Liabilities	(41,484)	(45,232)	(47,551)	(46,927)	(46,308)
Long term borrowings	0	0	0	0	0
Long term leases	(38,006)	(40,788)	(43,199)	(42,575)	(41,956)
Other long term liabilities	(3,478)	(4,444)	(4,352)	(4,352)	(4,352)
Net Assets	99,578	56,622	71,839	24,985	(24,332)
CASH FLOW					
Operating Cash Flow	(51,294)	(50,186)	(54,236)	(49,152)	(54,225)
Net Interest	194	244	(4)	(260)	(546)
Tax	0	0	0	0	0
Capex	(1,945)	(2,184)	(2,602)	(1,298)	(1,360)
Acquisitions/disposals	0	0	0	0	0
Financing	725	70	62,735	0	0
Dividends	0	0	0	0	0
Other	7,086	7,902	12,527	8,800	8,324
Net Cash Flow	(45,234)	(44,154)	18,420	(41,910)	(47,807)
Opening net debt/(cash)	(111,178)	(53,948)	1,756	(13,744)	28,166
HP finance leases initiated	(11,593)	(11,411)	(3,191)	(0)	0
Other	(403)	(139)	271	0	(0)
Closing net debt/(cash)	(53,948)	1,756	(13,744)	28,166	75,973

Source: Edison Investment Research; company accounts. Note: Our FY16 forecasts include short-term borrowings of €30m, which is indicative of Transgene's funding requirement during that year. The other cash flow line primarily includes tax credits financing; FY14 also includes €3.1m from the disposal of Transgene's holding in Jennerex.

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