EDISON

Transgene

Re-initiation of coverage

Worth a fresh look

Pharma & biotech

Transgene has successfully completed a major restructuring programme and secured fresh financing (up to €30m from the EIB and Institut Mérieux), which puts it in a strong position to advance its promising immunotherapy technologies once more. The focus is on conducting new Phase I/II studies for Pexa-Vec (oncolytic virus) and TG4010 (MUC1 cancer vaccine) in combination with immune checkpoint inhibitors, an eagerly anticipated approach for hard-to-treat cancers. Partner SillaJen has started a Phase III trial with Pexa-Vec for liver cancer. We re-initiate coverage of Transgene with a base-case valuation of €160m or €4.15 per share.

Year end	Revenue (€m)	PBT* (€m)	EPS* (€)	DPS (€)	P/E (x)	Yield (%)
12/14	11.1	(38.9)	(1.03)	0.0	N/A	N/A
12/15	9.6	(28.9)	(0.78)	0.0	N/A	N/A
12/16e	6.1	(27.2)	(0.71)	0.0	N/A	N/A
12/17e	7.8	(31.5)	(0.82)	0.0	N/A	N/A

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

Positive progression of lead candidates

The strategy of combining novel agents with immune checkpoint inhibitors (ICIs), to help increase the number of patient responders to ICIs beyond the current 20-40%, is a widely accepted concept that holds significant potential. Transgene plans to start Phase I/II combination trials of Pexa-Vec and TG4010 with ICIs (nivolumab + ipilimumab) in 2016, and positive data from these studies would significantly enhance fresh partnering and/or financing options.

Entering pivotal territory

Transgene restructured its partnership with SillaJen, with the Korean partner fully funding (save a $6m contribution from Transgene) a global pivotal Phase III study for Pexa-Vec in patients (n=600) with advanced first-line HCC, under a special protocol assessment (SPA). Positive data (headline read-out in 2018) should therefore be sufficient to gain FDA approval. Transgene will potentially be able to submit the trial data to gain EU approval, where it retains commercial rights.

Restructured and refinanced

A major restructuring programme has resulted in the disposal of its pharmaceutical development/bio-manufacturing business (for €3.5m), and potential significant long-term cost savings (c €10m annually) for €7.5m of restructuring costs. Meanwhile a €20m EIB loan, a €10m commitment from the Institut Mérieux (major shareholder), and €31.7m in cash at end-2015 provide a cash runway through to 2017.

Valuation: Re-initiation at €160m or €4.15/share

We re-initiate coverage of Transgene with an rNPV-based valuation of €160m, or €4.15 per share. This mainly includes the prospects for TG4010 in NSCLC in the US and Europe (combined peak sales of €2.4bn) and Pexa-Vec for HCC in Europe (€425m peak sales). We present a base-case scenario with upside potential.

13 April 2016

Price	**€2.76**
Market cap	**€106m**

Gross cash (€m) at 31 December 2015	31.7
Shares in issue	38.5m
Free float	43%
Code	TNG
Primary exchange	Euronext, Paris
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	(3.2)	(17.1)	(51.6)
Rel (local)	(0.5)	(16.7)	(42.1)
52-week high/low		€6.0	€2.4

Business description

Transgene is a French drug discovery and development company focused on the treatment of cancer and infectious diseases with immunotherapies. The lead products are Pexa-Vec (in Phase III for HCC) and TG4010 (Phase IIb complete for NSCLC).

Next event

Start of combination studies for TG4010 and Pexa-Vec	Mid-2016

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Edison profile page

Transgene is a research client of Edison Investment Research Limited

Investment summary

Company description: Immunotherapy focus

Transgene is a drug discovery and development company based near Strasbourg, France. It is developing immunotherapies for the treatment of cancers and infections. The company was founded in 1979 and was listed on the Nouveau Marche (now NYSE Euronext) in 1998. Transgene is 52% owned by Institut Mérieux, which is 68% owned by the Mérieux family. Alain Mérieux is the chairman of Institut Mérieux and sits on the board of Transgene and bioMérieux (an in vitro diagnostics company); Philippe Archinard (CEO of Transgene) is also on the board of bioMérieux.

Transgene has two lead clinical-stage programmes. Pexa-Vec (JX594/TG6006) is partnered with SillaJen and recently entered a Phase III study in hepatocellular carcinoma (HCC). TG4010 has completed a Phase IIb study for non-small cell lung cancer (NSCLC). Transgene is planning combination trials, with immune checkpoint inhibitors (ICI) such as nivolumab and ipilimumab for both Pexa-Vec and TG4010.

Valuation: Re-initiation at €160m or €4.15 per share

We re-initiate coverage of Transgene with an rNPV-based valuation of €160m, or €4.15 per share. This includes the prospects for TG4010 in NSCLC in the US and Europe (combined peak potential sales of €2.4bn), Pexa-Vec for HCC in Europe (€425m peak sales) and TG1050 for hepatitis B in the US and Europe. For TG4010 we assume a classical clinical development timeline, starting with the Phase I/II studies planned in combination ICIs, so there could be considerable upside should a conditional marketing authorisation (CMA) submission be possible in Europe based on the Phase IIb TIME trial. For Pexa-Vec the Phase III PHOCUS study being conducted by SillaJen will potentially be sufficient to file for approval in Europe, assuming a positive study result. As such, we suggest our valuation largely reflects a base-case scenario and therefore represents fair value for the stock today, ahead of a number of potential catalysts.

Sensitivities: Clinical execution risk

Transgene is subject to the usual risks associated with drug development, including clinical development delays or failures, regulatory risks, competitor successes, partnering setbacks, and financing and commercial risks. The key sensitivities relate to the clinical performance of Pexa-Vec in the Phase III trial (initial data expected in 2018) and the results of the ICI combination studies of Pexa-Vec and TG4010. The outcome of the TG4010 combination studies in particular will have an impact on its partnership and/or fresh financing prospects for the programme. Precise details of these trials have yet to be announced; we assume that they will commence in mid-2016, with results possible by late-2017.

Financials: A stronger financial position

Transgene held €31.7m in cash as of end-2015, and secured access to a further €30m in funds in January 2016: €20m via an EIB loan and a €10m commitment from its largest shareholder, Institut Mérieux. As a result, the company expects to have sufficient funds to conduct its pipeline development activities through 2016 and 2017, with a cash burn of €35m anticipated by the company for 2016. For modelling purposes, we have assumed that the €20m EIB loan is drawn in two tranches of €10m in H116 and H216. Limited details have been provided on the terms of the EIB loan, except that the loan will be released in two tranches (at Transgene's request), and it is a five-year loan, with the principal and accumulated interest reimbursable only from the fourth year. We then assume the additional €10m shareholder commitment is received in 2017, which we

nominally attribute to long-term debt, given that the timing and nature of this 'commitment' is unknown at this stage.

Targeted immunotherapy technologies

Transgene has a pipeline of immunotherapies for the treatment of cancer and viral indications. The two lead programmes include the oncolytic virus Pexa-Vec, which recently entered a Phase III trial in HCC, and TG4010, a therapeutic cancer vaccine in development for NSCLC. Exhibit 1 details Transgene's clinical development pipeline. The programmes utilise viral vector technology with the aim of killing infected or cancerous cells (directly or indirectly).

Exhibit 1: Clinical R&D pipeline

Product/target	Stage (indication)	Partner	Notes
TG4010	Phase IIb complete (Stage III/IV NSCLC)	N/A	Therapeutic vaccine, MVA-MUC1-IL2, which induces an immune response against tumour cells that express the MUC1 protein (IL-2 stimulates the immune response). It has potential in most epithelial cell cancers (including NSCLC, breast, colorectal and prostate cancer). Phase III in planning but partner required. Phase II studies in combination with immune checkpoint inhibitors (ICIs) to commence in 2016. In the Phase IIb TIME trial in NSCLC, TG4010 in combination with chemotherapy led to significant improvements in PFS and OS. Efficacy was greatest in patients with low levels of the TrPAL biomarker. In April 2014, Novartis decided not to exercise its option to in-license TG4010 in a €700m deal.
Pexa-Vec (JX594/ TG6006)	Phase III (Hepatocellular carcinoma, CRC, and other solid tumours)	SillaJen	Oncolytic virus, VVTK-/GM-CSF, which targets fast-dividing cells with an active EGFR/ras signalling pathway, causing those cells to lyse and stimulates a T-cell immune response against nearby cells. More than 10 Phase I and II studies have so far been conducted. Commenced Phase III study (PHOCUS) in HCC (agreed under Special Protocol Assessment with the FDA) in January 2016. Transgene will also independently conduct exploratory combination trials with ICIs in both first-line HCC and solid tumours. Partnered with SillaJen (formerly Jennerex) in September 2010; the deal terms were revised in November 2015. SillaJen will assume responsibility for conducting the PHOCUS trial; Transgene will pay $6m to SillaJen over four years. Transgene has development and commercialisation rights to Pexa-Vec in Europe.
TG1050	Phase I (Chronic hepatitis B virus infections)	N/A	Targeted immunotherapy candidate for the treatment of chronic hepatitis B (HBV), based on a viral vector expressing 3 HBV antigens. Phase I (n=48) randomised, multi-centre, double-blind, placebo-controlled safety and dose-finding study commenced in November 2015. The safety and tolerability of TG1050 in patients who are currently being treated for chronic HBV infection with standard-of-care antiviral therapy will be evaluated. Secondary objectives include the antiviral activity of, and immune responses to, TG1050.

Source: Edison Investment Research. Note: PFS: progression-free survival; OS: overall survival.

Combination trial data should improve pipeline's appeal

Transgene recently announced a shift in strategy to move away from monotherapies towards combination therapies with immune checkpoint inhibitors. There is recognition within the immunotherapy sector that a combination approach can provide substantial efficacy improvements over monotherapies. A Phase II combination trial of Nivolumab and Ipilimumab demonstrated that patients had an objective response of 61% compared with 11% in the Ipilimumab only cohort; however, safety is a concern. 54% of combination patients suffered a grade 3 or 4 adverse event, compared to 24% on the monotherapy treatment. Most significantly colitis was reported in 17% of combination patients. The hope is that a lower dose of two agents may avoid some of the toxicity associated with either agent alone at its full monotherapy dose.

To this end, Transgene plans to conduct combination studies of the Pexa-Vec and TG4010 with immune checkpoint inhibitors (ICIs). ICIs target antigens that tumour cells display periodically (eg PD-L1), or T-cell receptors that dampen cytotoxic activity (eg PD-1 or CTLA4) in order to overcome tumour-mediated immunosuppression. Immunotherapies such as vaccines (eg TG4010, TG4001) or oncolytic viruses (eg Pexa-Vec) cause tumour cell death, triggering the release of tumour antigens for presentation to the immune system, and also help drive the tumour into a more immunogenic state, so increasing its susceptibility to immunotherapy with ICIs. Success in the TG4010 studies would improve the attractiveness of the programme to potential partners and should improve Transgene's negotiating position in the future.

Clinical programme update

The last six months have seen two key milestones for Transgene's programmes: the start of the Phase III study of Pexa-Vec (HCC) and the first-in-human Phase I study of TG1050 (chronic HBV). Transgene has also commenced further exploratory trials for Pexa-Vec: one evaluating Pexa-Vec in combination with metronomic cyclophosphamide (repetitive, low doses; shown to potentiate the activity of other immunotherapies) in breast cancer and soft tissue sarcoma (sponsored by the Bergonié Institute) and a second evaluating Pexa-Vec in the pre-surgery setting for cancer patients to further document Pexa-Vec's mechanism of action (sponsored by the University of Leeds).

Pexa-Vec comes into PHOCUS

Pexa-Vec is an oncolytic virus armed with a GM-CSF gene that selectively targets and destroys tumour cells. It is designed to replicate in tumour cells, causing those cells to rupture or be targeted by the body's immune system, without affecting healthy cells. It also reduces the tumour's blood supply by disrupting the formation of blood vessels.

Phase III: Underway following revised agreement with SillaJen

The Phase III PHOCUS trial commenced in January 2016. It is a randomised (1:1), open-label study comparing Pexa-Vec followed by sorafenib (tyrosine kinase inhibitor) versus sorafenib alone in patients with advanced HCC who have not received prior systemic therapy (n=600). Pexa-Vec will be administered as three bi-weekly intratumoural injections at day one and weeks two and four, followed by sorafenib at week six; the comparator arm will receive sorafenib 400mg twice daily starting on day one. The primary endpoint is overall survival (OS); secondary endpoints include time to progression, progression-free survival and overall response rate. Initial OS data are expected in 2018.

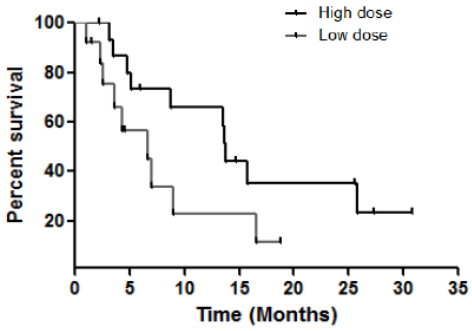
In November, Transgene announced a revised agreement for Pexa-Vec. SillaJen will now assume responsibility for conducting PHOCUS (previously Transgene was responsible for development costs in its licensed territories plus a fraction of central costs, estimated to cost $18m). In return, Transgene will pay a total of $6m to SillaJen over four years beginning this year; Transgene will now focus only on Europe, having returned the rights for all Middle Eastern countries, Russia, Ukraine, Belarus and Turkey. Transgene will also initiate and fund an independent exploratory trial evaluating Pexa-Vec in combination with ICIs. We view this outcome as positive; importantly it has enabled progression of Pexa-Vec's development, and while Transgene has had to return rights to certain areas, we believe that this is more than compensated for by the reduced financial burden, allowing it to focus on the remaining pipeline and commence combination trials.

Recap of Pexa-Vec data

Pexa-Vec has been evaluated in more than 10 trials in a number of tumour types; it has been well-tolerated in all trials. In the Phase II dose-finding study in HCC patients (n=30; 80% first-line), those receiving high-dose Pexa-Vec (intratumoural delivery) had a median OS of 14.1 months compared to 6.7 months for those on a low dose (HR: 0.39; p=0.02; Exhibit 2). However, the subsequent Phase IIb TRAVERSE study in second-line HCC was terminated early in 2013 as data from the first 80 events showed no evidence of OS benefit associated with Pexa-Vec.

The decision to continue development of Pexa-Vec was based on the detailed analysis of TRAVERSE and the prior Phase I/II trials with data from over 300 patients in total. The Phase III trial is in patients with first-line HCC, for which Pexa-Vec has previously shown promising data. This is also supported by the concept that immunotherapies are thought to be most effective when the tumour burden is low (ie less advanced) and in patients with functioning immune systems.

Exhibit 2: Results of Phase II study in HCC with Pexa-Vec



Source: Transgene

First oncolytic virus approved by the FDA and EMA

Regulators in the US and Europe have approved Amgen's Imlygic (talimogene laherparepvec), a genetically modified oncolytic herpes virus therapy indicated for the local treatment of unresectable melanoma lesions. The approval was based on the Phase III OPTiM study (n=436) comparing Imlygic to GM-CSF in patients with advanced, unresectable melanoma. The study met the primary endpoint of improving durable response rate: 16.3% of patients treated with Imlygic achieved a durable response versus 2.1% of patients treated with GM-CSF (p <0.0001). No OS benefit was demonstrated; however, there was a trend towards a 4.4-month longer median OS versus control.

Combinations: The logical approach

It is increasingly accepted that the advent of ICIs has changed the face of cancer treatment; approved antibodies targeting CTLA4 (Yervoy, BMS) and PD-1 (Opdivo, BMS and Keytruda, Merck) promise to be blockbuster therapies, with several other ICIs in late-stage development. ICIs target immune checkpoint pathways that have been co-opted to create immunosuppression within the tumour microenvironment, aiming to stimulate an immune response that results in long-lived tumour destruction. While these drugs can have a remarkable effect in a subset of patients, only one in five patients are likely to respond. The complex interplay between the tumour and the immune system, involving multiple immune-escape strategies, suggests that monotherapies are unlikely to be able to address all the mechanisms that impede anti-tumour immunity.

Attention is now turning to combination approaches in a bid to enhance the anti-tumour efficacy of each individual treatment. Transgene's active immunotherapy approach utilises viral vector technology to kill the cancerous cells, thereby improving recognition of tumours, increasing tumour immunogenicity and enhancing the subsequent immune response. This active approach is well-placed to act in combination with, and potentially synergistically with, the immunomodulatory approach of ICIs, which block negative stimulation of the immune system to enhance anti-tumour immune responses. Moreover, the fact that immune checkpoint mechanisms are thought to play a role in limiting the clonal expansion of T cells following vaccination, so potentially impeding the vaccination response, provides further rationale for a combined approach. In addition to carrying out combination trials with its lead candidates, Transgene will also conduct Phase II trials of therapeutic vaccine TG4001, for the treatment of HPV-related cancers.

Pexa-Vec

There is a growing consensus that oncolytic viruses will be best used as part of a combination approach with ICIs, serving to kill cancer cells and increasing neoantigen exposure for the ICI-primed immune system to target. In keeping with this, Amgen is testing Imlygic in combination with Yervoy and with Keytruda. In 2016, Transgene plans to conduct exploratory trials of Pexa-Vec in

combination with ICIs: the first in combination with Opdivo for the treatment of advanced HCC; the second in combination with Yervoy for the treatment of advanced solid tumours.

TG4010

Cancer vaccines are designed to elicit robust, durable, tumour-specific T cell immune responses, making them ideal partners for ICIs that aim to overcome T cell anergy. The synergy of these approaches has been demonstrated in pre-clinical models.[3] Preclinical data presented at the AACR Annual Meeting in April 2015 demonstrated that a combination of the therapeutic vaccine TG4010 with an anti-CTLA4 resulted in prolonged OS in a lung metastasis model, and, importantly, evidence of synergy on the control of tumour growth when used in combination with an anti-PD-1 in a MUC-1 positive tumour model.

Transgene plans to initiate exploratory Phase II trials in second-line non-small cell lung cancer (NSCLC) in combination with ICIs. These will be done independently of securing a partner for the Phase III trial in first-line NSCLC, but positive results would likely increase the attractiveness of TG4010 and could trigger the much-sought deal.

TG4010: Search for a partner continues

TG4010 is a therapeutic vaccine that causes patients to develop an immune response against cells that express the MUC1 protein (a large glycosylated protein). This protein is only expressed at low levels in normal tissues, but is expressed at high levels (often with reduced or aberrant glycosylation) in many tumours (70% of lung, 90% of breast, 60% of prostate and 70% of colorectal cancers). It is in development for the treatment of advanced non-small cell lung cancer (NSCLC).

Promising Phase II data

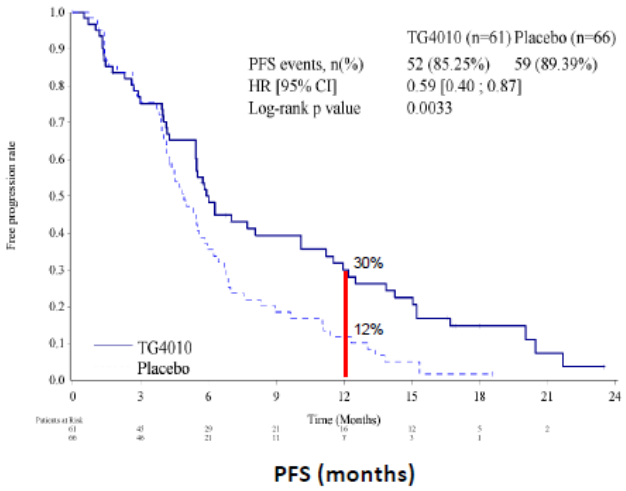
The Phase IIb stage of the Phase IIb/III TIME trial compared chemotherapy plus TG4010 to chemotherapy plus placebo in patients with advanced NSCLC (n=222). In the subset of patients with non-squamous tumours (n=196), TG4010 led to a significant improvement in progression-free survival (PFS; HR: 0.69, p=0.009) and OS advantage (HR: 0.75, p=0.0049). The benefit was greatest in those patients with low levels of the TrPAL biomarker (triple positive activated lymphocytes): at 12 months 30% of these patients remained progression-free (vs 12% on placebo); and at 24 months 40% of this group were still alive (vs 19% on placebo). See Exhibits 3 and 4.

The overall response rate (ORR) and duration of response (DR) data are also supportive of the potential of TG4010: for the total population (squamous and non-squamous NSCLC), those patients receiving TG4010 benefited compared to the placebo arm (ORR: 39.6% vs 28.8%; DR: 30.1 vs 18.7 weeks). Again, the benefit was greatest in those patients with non-squamous NSCLC and low TrPAL (ORR: 39.3% vs 30.3%; DR: 43.1 vs 18.1 weeks). See Exhibit 5.

In post-hoc analysis of all non-squamous NSCLC patients there was a similar level of PFS and OS benefit in the 97 patients with low levels of PD-L1 expression (<5%) to that observed with all non-squamous NSCLC patients. In various studies it has been shown that non-squamous NSCLC patients with low levels of PD-L1 will not benefit as much from ICIs targeting PD-L1 and PD-1 as those with high levels of PD-L1 expression. This suggests that TG4010 could potentially become a valuable treatment in those non-squamous patients less likely to benefit from treatment with PD1 or PD-L1 inhibitors, in addition to the potential synergistic approach discussed previously.

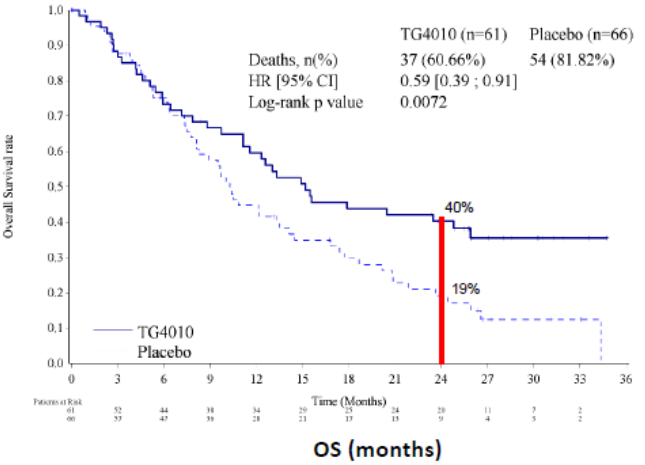
TG4010 was well tolerated; the most frequent TG4010-related adverse events were mild to moderate injection site reactions. To date, over 350 patients have been treated with TG4010.

Exhibit 3: Kaplan-Meier curve for PFS in patients non-squamous NSCLC and low levels of TrPAL biomarker



Source: Transgene

Exhibit 4: Kaplan-Meier curve for OS in patients non-squamous NSCLC and low levels of TrPAL biomarker



Source: Transgene

Exhibit 5: Key data from Phase IIb stage of TIME trial

Intent-to-treat subgroup	Total no. of patients (TG4010/placebo)	PFS HR (95% CI; p-value)	OS HR (95% CI; p-value)	Response rate TG4010 vs placebo	Duration of response (weeks) TG4010 vs placebo
Low TrPAL	147 (71/76)	0.66 (0.46-0.94; p=0.010)	0.67 (0.46-0.98; p=0.018)	39.4% vs 31.6%	41.4 vs 18.7
Non-squamous	196 (98/98)	0.69 (0.51-0.94; p=0.009)	0.73 (0.52-1.01; p=0.030)	39.8% vs 27.6%	40.9 vs 18.1
Non-squamous, low TrPAL	127 (61/66)	0.59 (0.40-0.87; p=0.003)	0.59 (0.39-0.91; p=0.007)	39.3% vs 30.3%	43.1 vs 18.1

Source: Transgene. Note: HR: hazard ratio; CI: confidence interval.

Waiting for a deal

Transgene continues to plan for the Phase III part of the TIME trial, which will enrol only patients with non-squamous NSCLC. However, Transgene has said in the past that it will not initiate the trial without a global development and commercialisation partner for TG4010. Transgene reports that discussions are ongoing with potential partners; however, in our view it is most likely that any deal will be signed once the planned Phase II studies in combination with ICIs have been completed. The extra data would reduce the risk for a potential partner and should improve Transgene's negotiating position.

First-in-human trial for TG1050 commences

In November, the first patient was dosed in the Phase I study with therapeutic vaccine TG1050 for the treatment of chronic HBV infection. It is an international, randomised, double-blind, placebo-controlled safety and dose-finding study evaluating single and multiple doses of TG1050 in patients who are currently being treated for chronic HBV infection with standard-of-care antiviral therapy (n=48). Secondary objectives include the antiviral activity of, and immune responses to, TG1050. Data is expected in H118.

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 240 million people have chronic HBV infection), Transgene will look to partner TG1050 once it has proof-of-concept data from this study.

Restructured and refinanced

Transgene has largely completed its restructuring programme announced in June 2015. In order to focus the business on research and development the company has closed the pharmaceutical development and bio-manufacturing business (which bought in revenues of c €1.7m in 2014). A reduction in future operating costs and new capital will enable Transgene to progress its pipeline through 2017.

Short-term loss for long-term gain

Restructuring that started in 2015 aims to generate significant savings from 2016. Operating costs for 2016 are expected to be c €10m below full year 2015. However, one-off restructuring costs of €7.5m will affect the short-term cash balance with a negative cash impact in 2016 of c €6m. Under the new strategy, Transgene's manufacturing plant and its associated assets were sold for €3.5m.

€20m EIB loan and €10m shareholder commitment

In January 2016 the European Investment Bank under its InnovFin IDFF (Infectious disease finance facility) agreed with Transgene a five-year €20m loan that will be realised in two tranches at the company's request. Both the interest and principal are repayable beginning in the fourth year of the loan. InnovFin was launched under the Horizon 2020 initiative in 2014 to help innovative firms access credit easily. Alongside the EIB loan, Institut Mérieux, Transgene's major shareholder has committed to providing additional funding of approximately €10m. Further details of the funding are expected later this year.

Valuation

We re-initiate coverage of Transgene with an rNPV-based valuation of €160m, or €4.15 per share. Our key inputs and assumptions are summarised in Exhibit 6 below. We note the following key assumptions on potential development timelines for TG4010 and Pexa-Vec:

- TG4010 – While the company has suggested that a CMA (conditional marketing authorisation) submission in Europe may be possible on the basis of clinical data collected so far, most notably from the Phase IIb TIME trial, we do not include this in our model. Instead we predict a more classical clinical development timeline for the project, starting with the Phase I/II studies planned in combination ICIs, and use NSCLC as a proxy for this opportunity. As such, there could be considerable upside should a CMA materialise, and/or development be expanded into other cancer indications. For illustration, should conditional approval be granted in Europe and TG4010 launched in 2017, the rNPV would rise to approximately €195m vs the €32m currently projected. Our probability of success if CMA was approved would increase to 65% compared to our current rate of 40%. Both the improved probability and accelerated launch timeline would contribute to the increased rNPV of €195m.
- Pexa-Vec – We have assumed that the Phase III PHOCUS study, which plans to include EU trial sites, will be sufficient to file for approval in Europe, assuming a positive study result. Transgene will be responsible for funding, compiling and submitting the regulatory application in Europe.
- TG1050 – Our valuation includes the EU and US market and we have assumed that TG1050 will be out-licensed on completion of a successful Phase II proof-of-concept study.

As such, we suggest this largely reflects a base-case scenario and therefore represents fair value for the stock today, ahead of a number of potential catalysts. Note that we also do not currently ascribe any value to the pre-clinical assets TG6002 and TG3003 or Phase I asset TG4001.

Exhibit 6: Transgene valuation model and key assumptions

Product	Status	Market launch	NPV (€m)	Peak sales (€m)	Probability of success	Royalty estimate	rNPV (€m)	rNPV/ share (€)	Key assumptions
TG4010 - NSCLC (EU)	Phase I/II	2025	88.5	1,062	40%	17.5%	32.3	0.84	c 313k annual EU incidence of lung cancer; 85% NSCLC; 75% MUC1 +ve; 66% normal NK cells; 20% peak penetration; €30k treatment price; €30m upfront on Phase IIb completion.
TG4010 - NSCLC (US)	Phase I/II	2025	78.8	1,299	40%	17.5%	31.5	0.82	c 221k annual US incidence of lung cancer; 85% NSCLC; 75% MUC1 +ve; 66% normal NK cells; 20% peak penetration; $50k treatment price
Pexa-Vec - HCC (EU)	Phase III	2020	99.4	425	50%	25.0%	47.1	1.22	c 52k annual EU incidence of liver cancer; 80% HCC; 25% peak penetration; €30k treatment price
TG1050 - HepB (EU+US)	Phase I	2025	190.5	2,054	15%	20.0%	17.5	0.45	c 5.4m chronic HepB prevalence in EU + US; 66% diagnosis rate; 33% require treatment; 5% peak penetration; €35k treatment price
Gross cash (31 December 2015)							31.7	0.82	
Total							160.0	4.15	

Source: Edison Investment Research. Note: Peak sales represent the largest one-year sales that occur over the projected product lifespan. Spot rate $1.1/€.

Sensitivities

Transgene is subject to the usual risks associated with drug development, including clinical development delays or failures, regulatory risks, competitor successes, partnering setbacks, and financing and commercial risks. The key sensitivities relate to the clinical performance of Pexa-Vec in the Phase III trial (initial data expected in 2018), the results of the ICI combination studies of Pexa-Vec and TG4010 and Transgene's ability to secure a partner to enable the continued development of TG4010.

The outcome of the TG4010 combination studies in particular will have an impact on its partnership and/or fresh financing prospects for the programme. Precise details of these trials have yet to be announced; we assume that they will commence in mid-2016, with results possible by mid-2017.

The revised agreement with SillaJen for the conduct of the Phase III trial of Pexa-Vec has reduced the financial burden on Transgene, which we see as more than compensating for the returned rights to Pexa-Vec for all Middle Eastern countries, Russia, Ukraine, Belarus and Turkey.

Financials

Transgene held €31.7m in cash as of end-2015, and secured access to a further €30m in funds in January 2016: €20m via an EIB loan and €10m commitment from its largest shareholder, Institut Mérieux. As a result, the company expects to have sufficient funds to conduct its pipeline development activities through 2016 and 2017 with a cash burn of €35m anticipated by the company in 2016.

For modelling purposes we have assumed that the €20m EIB loan is drawn in two tranches of €10m in H116 and H216. Limited details have been provided on the terms of the EIB loan, except that the loan will be released in two tranches (at Transgene's request), and it is a five-year loan, with the principal and accumulated interest reimbursable only from the fourth year. We then assume the additional €10m shareholder commitment is received in 2017, which we nominally attribute to long-term debt, given the timing and nature of this 'commitment' is unknown at this stage.

Revenues in FY16 are expected to drop to €6.1m (vs €9.6m in FY15) following Transgene's restructuring programme, which resulted in its withdrawal from outsourcing of process development and bio-manufacturing activities. A lower R&D spend, discussed below, will also reduce the R&D related tax credits that Transgene also books as revenue.

We forecast a reduction in R&D expenses for FY16 to €27.5m (vs €32.1m in FY15), following the restructuring programme and a relatively lower level of clinical activity in 2016 (combination studies projected to start in H216) compared to concluding the TIME Phase IIb study in 2015. Our R&D estimate includes the one-off $4m (c €3.7m) milestone payment made to SillaJen for the start of the PHOCUS Pexa-Vec study in January 2016, as well as $6m in Pexa-Vec development costs payable to SillaJen over the next four years (FY16-19). Similarly, G&A expenses are also expected to decline in FY16 to €4.3m (vs €5.8m in FY15) as a result of the restructuring programme and reduction in headcount. In total, Transgene is guiding to a €10m overall reduction in operating costs in FY16 compared to FY15.

Other exceptional items in FY16 include a €6m negative cash impact from restructuring costs, which was set aside as a provision on the balance sheet at end-2015, and €3.5m received from the recent sale of Transgene's manufacturing plant and associated assets.

Exhibit 7: Financial summary

€000s	2013	2014*	2015	2016e	2017e
Year end 31 December	IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS					
Revenue	15,735	11,099	9,565	6,086	7,835
Cost of Sales	0	0	0	0	0
Gross Profit	15,735	11,099	9,565	6,086	7,835
R&D expenses	(50,063)	(41,731)	(32,138)	(27,465)	(32,958)
G&A expenses	(6,769)	(7,578)	(5,798)	(4,339)	(4,469)
EBITDA	(38,287)	(35,453)	(25,671)	(23,943)	(27,858)
Operating Profit (before GW and except)	(40,813)	(38,127)	(27,957)	(25,584)	(29,488)
Intangible Amortisation	(385)	(365)	(350)	(135)	(105)
Exceptionals (restructuring costs / discontinued operations)	0	(8,440)	(15,965)	0	0
Operating Profit	(41,198)	(46,932)	(44,272)	(25,719)	(29,592)
Other	0	0	0	0	0
Net Interest	(730)	(801)	(930)	(1,579)	(2,034)
Profit Before Tax (norm)	(41,543)	(38,928)	(28,887)	(27,163)	(31,522)
Profit Before Tax (IFRS)	(41,928)	(47,733)	(45,202)	(27,298)	(31,627)
Tax	0	0	0	0	0
Minority interest	(930)	(823)	(1,172)	0	0
Profit After Tax (norm)	(42,473)	(39,751)	(30,059)	(27,163)	(31,522)
Profit After Tax (IFRS)	(42,858)	(48,556)	(46,374)	(27,298)	(31,627)
Average Number of Shares Outstanding (m)	31.9	38.5	38.5	38.5	38.5
EPS - normalised (€)	(1.33)	(1.03)	(0.78)	(0.71)	(0.82)
EPS - IFRS (€)	(1.34)	(1.26)	(1.20)	(0.71)	(0.82)
Dividend per share (c)	0.0	0.0	0.0	0.0	0.0
BALANCE SHEET					
Fixed Assets	64,501	61,715	49,841	49,440	49,135
Intangible Assets	1,329	1,056	485	350	245
Tangible Assets	23,988	23,641	16,559	16,293	16,093
Other	39,184	37,018	32,797	32,797	32,797
Current Assets	61,349	79,238	51,028	42,772	28,237
Stocks	975	1,149	1,164	1,164	1,164
Debtors	1,896	1,540	1,784	1,784	429
Cash	47,862	65,935	31,650	26,894	13,713
Other	10,616	10,614	16,430	12,930	12,930
Current Liabilities	(23,996)	(21,563)	(26,725)	(19,697)	(20,796)
Creditors	(9,364)	(8,296)	(6,521)	(5,493)	(6,592)
Short term borrowings	0	0	0	0	0
Short term leases	(8,830)	(8,992)	(9,396)	(9,396)	(9,396)
Other	(5,802)	(4,275)	(10,808)	(4,808)	(4,808)
Long Term Liabilities	(45,232)	(47,551)	(47,597)	(66,953)	(76,316)
Long term borrowings	0	0	0	(20,000)	(30,000)
Long term leases	(40,788)	(43,199)	(44,401)	(43,757)	(43,120)
Other long term liabilities	(4,444)	(4,352)	(3,196)	(3,196)	(3,196)
Net Assets	56,622	71,839	26,547	5,561	(19,740)
CASH FLOW					
Operating Cash Flow	(50,186)	(55,037)	(46,082)	(30,495)	(24,915)
Net Interest	244	801	930	(1,579)	(2,034)
Tax	0	0	0	0	0
Capex	(2,184)	(2,602)	(1,527)	(1,374)	(1,429)
Acquisitions/disposals	0	0	0	3,500	0
Financing	70	62,735	477	0	0
Dividends	0	0	0	0	0
Other	7,902	12,527	12,975	5,836	5,836
Net Cash Flow	(44,154)	18,424	(33,227)	(24,113)	(22,542)
Opening net debt/(cash)	(53,948)	1,756	(13,744)	22,147	46,260
HP finance leases initiated	(11,411)	(3,191)	(2,646)	0	0
Other	(139)	267	(18)	(0)	0
Closing net debt/(cash)	1,756	(13,744)	22,147	46,260	68,802

Source: Transgene accounts, Edison Investment Research. Note: *2014 company accounts were restated. For modelling purposes we have assumed that the €20m EIB loan is drawn in two tranches of €10m in H116 and H216. We also assume the additional €10m shareholder commitment is received in 2017, which we attribute to long-term debt.

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Management team	
Chairman & CEO: Philippe Archinard	EVP, Research & Development: Eric Quéméneur
Philippe Archinard became CEO in 2004. From 2000 to 2004, he was CEO of Innogenetics and previously he was at bioMérieux, where he held various positions including CEO of its US operations. He has a PhD in biochemistry from Lyon University.	Eric Quéméneur joined Transgene in 2014. Prior to this, he spent over 20 years at the CEA (Atomic Energy Commission) where he was director of research programs and industrial partnerships in the life science division. He has a PhD in biochemistry from the Claude Bernard University in Lyon.
VP, Finance: Jean-Philippe Del	VP, Business Development: Colin Freund
Jean-Philippe Del became VP, finance at Transgene in 2014, previously serving as finance senior director. He has previously worked at Mazars and Kronenbourg Breweries. He has a post-graduate degree in accounting and finance and a master's degree from the University of Strasbourg.	Colin Freund joined Transgene in 2013 as chief business officer. He has previously worked at Agennix AG, GPC Biotech AG, Double Twist, Inc. and Boston Consulting Group. He has a degree in economics and management studies from the University of Cambridge and an MBA from Stanford University.

Principal shareholders	(%)
Institut Mérieux	52

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Amgen (AMGN); Bristol-Myers Squibb (BMY); Merck & Co (MRK)

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