BRYAN, GARNIER & CO

FOCUS

16th March 2016

Transgene

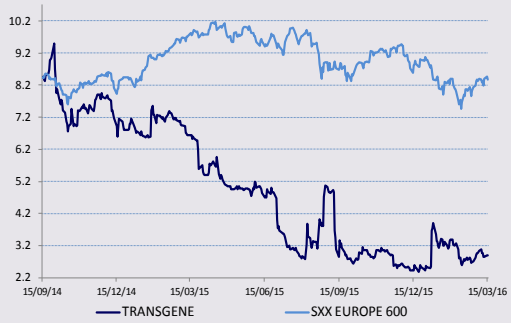
Data from combinations will be key

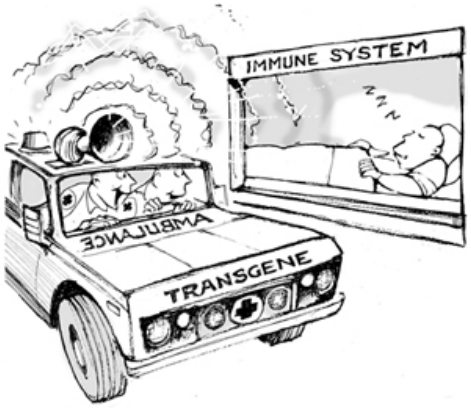
Healthcare

Fair Value EUR4.5(price EUR2.90) **CORPORATE**

Bloomberg	TNG.FP
Reuters	TRNG PA
12-month High / Low (EUR)	6.7 / 2.4
Market capitalisation (EURm)	112
Enterprise Value (BG estimates EURm)	169
Avg. 6m daily volume ('000 shares)	236.9
Free Float	48.0%
3y EPS CAGR	-8.4%
Gearing (12/15)	83%
Dividend yield (12/16e)	NM

YE December	12/15	12/16e	12/17e	12/18e
Revenue (EURm)	0.00	0.00	0.00	0.00
EBIT (EURm)	-35.81	-35.06	-26.00	-28.14
Basic EPS (EUR)	-0.98	-0.94	-0.70	-0.76
Diluted EPS (EUR)	-0.98	-0.94	-0.70	-0.76





Admittedly, the company has been through some pretty tumultuous times recently, hence the need to initiate a restructuring plan. But what's next? In our opinion, the future of Transgene lies in the different Phase I/II trials assessing its lead compound in combination with PD-1/PD-L1 blockers (and for which top-line results are expected by the end of 2017). Our Fair Value is EUR4.5.

- **TG4010's future lies in its potential combination with checkpoint blockers.** The dataset from the TIME study was definitely of quality, but the treatment paradigm has changed and will continue to. Targeting PD-1 or PD-L1 has resulted in practice-changing observations of safety coupled with impressive and durable anti-tumour activity in both already pre-treated and newly diagnosed patients with NSCLC (non-small cell lung cancer). So just like Bavarian Nordic did with its cancer vaccine (ProstVAC), we assume Transgene will need some proof-of-concept data implying TG4010 in combination with these immune checkpoint blockers to attract the attention of potential partners.

- **PexaVEC as a credible plan B**. While hepatocellular carcinoma (HCC) was initially seen as a very (too?) challenging indication for immuno-oncology agents, whether for checkpoint blockers or oncolytic virus, we have the feeling that our fears were overdone as 1/ nivolumab managed to induce tumour regression in already pre-treated patients (overall response rate: 20%) in a small study, 2/ in 2015, AstraZeneca and MedImmune entered a licensing agreement with Omnis Pharmaceuticals to develop an oncolytic virus for the treatment of HCC and other cancers that have metastasized to the liver. Apart from that, we see (i) the recent approval of Amgen's Imlygic (talimogene laherparepvec) and (ii) the responses obtained in combo with ipilimumab (anti-CTLA-4) in first-line melanoma as positive catalysts for the whole therapeutic class.

- **Our FV of EUR4.5 is derived from an SOTP**. Without going into too much detail, we are assuming 1/ that value creation will primarily stem from TG4010 and PexaVEC, both as part of a combination regimen with a checkpoint blocker (respective peak sales: EUR500m and EUR400m in their lead indication); and 2/ a probability of success of 35% for all these developments. Our WACC is 16.0%.

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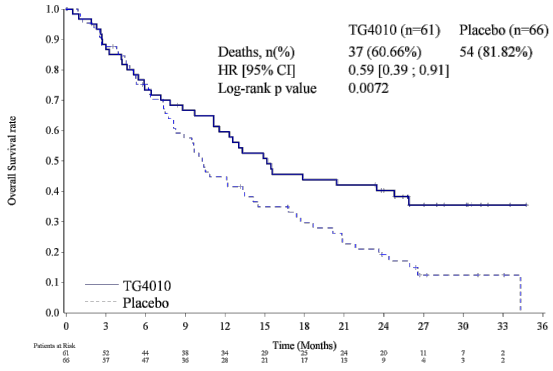
Transgene Major keys to focus on

1. TG4010



TG4010 is a cancer vaccine designed to elicit an immune response against cancerous cells overexpressing MUC1 and whose main indication is non-small cell lung cancer (NSCLC). Initially developed in combination with chemotherapies, the agent managed to elicit quite interesting responses and improved both progression-free survival (PFS) and overall survival (OS) in certain previously untreated patients, notably those with i) a non-squamous histology (for which the overexpression of MUC1 is said to be even higher), and ii) a low level of CD16, CD56, CD69 triple-positive activated lymphocytes or TrPAL at baseline.

However, tremendous changes have occurred within the treatment landscape of NSCLC. Targeting PD-1 or PD-L1 has resulted in practice-changing observations of safety coupled with impressive and durable anti-tumour activity in already pre-treated patients… That said, the medical need remains high and it is clear that one sole approach will not suffice to address all of the tumour's heterogeneity and adaptive ability (formation of an immunosuppressive microenvironment, immune-editing, etc.). The growing understanding of tumour mechanisms has naturally encouraged the development of new combination strategies to address this diversity while covering, as far as possible, the various avenues enabling the achievement of an optimal immune response. Active immunotherapies like TG4010 could notably be of interest in patients with low levels of activated immune cells (hence the usefulness of the TrPAL marker); but clinical data are needed to support this theory.

That said, note that **several other combinations of immune-oncology agents are currently being assessed for the treatment of NSCLC**. Whether IDO inhibitors, OX40 agonists, anti-NKG2A, anti-CD137 or anti-GITR, competition with other compounds is set to be fierce (especially since biomarkers are being assessed for some of them).

Last but not least, management is now considering a possible conditional marketing approval submission in Europe for TG4010 (and a Phase III implying a combo with chemotherapies would then be initiated to support the project).

2. Read-across from Bavarian Nordic

As a reminder, **Bavarian Nordic signed a collaboration agreement with BMS back in March 2015 involving its lead cancer vaccine (ProstVAC)**, which is currently developed as a treatment for metastatic castration-resistant prostate cancer (mCRPC). Interestingly, the compound managed to improve the overall survival in combination with an immune checkpoint inhibitor (namely ipilimumab, an anti-CTLA-4)… and we're pretty sure these PoC data were key in the negotiations with the big pharma.

On the one hand, this is quite positive for Transgene's TG4010 as it shows that a cancer vaccine can indeed potentiate the action of an ICI in patients with a quite low immunogenic tumour (and in which ipilimumab failed to improve the OS vs placebo in a previous Phase III trial (HR: 0.85, p=0.053)). On the other hand, it underlines how extended clinical data (ORR or maybe PFS/OS data) is needed to ink a collaboration agreement, at least when it comes to cancer vaccines (which unfortunately suffer from a long story of clinical failures).

This is certainly the reason why management has decided to initiate a set of different Phase I/II trials: 1/ one with nivolumab involving second-line patients with NSCLC, which by the way will be conducted in the US, 2/ another one with an undisclosed ICI (undoubtedly an anti-PD-1/PD-L1) in newly diagnosed patients in Europe. Given the likely design of these studies, we understand that **preliminary efficacy results should not be available before the end of 2017.**

3. PexaVEC as a credible plan B?

PexaVEC belongs to an emerging therapeutic class of living drugs called oncolytic virus. This kind of modified virus is engineered to replicate within and kill malignant cells (while sparing normal cells), and then favour an innate/adaptive response against a variety of cancer antigens. Very recently, an important milestone was reached with the approval of Amgen's Imlygic (talimogene laherparepvec) by both the FDA and the EMA for the treatment of adults with unresectable melanoma that is regionally or distantly metastatic (Stage IIIB, IIIC and IVM1a), with no bone, brain, lung or other visceral disease.

A Phase III has been initiated to assess PexaVEC as a single-agent for the treatment of newly diagnosed patients with hepatocellular carcinoma (HCC) against sorafenib (a multi-kinase inhibitor known as the current standard of care in this setting). But the most important part, at least to our eyes, is the initiation of an exploratory study evaluating PexaVEC in combination with nivolumab (an anti-PD-1) for this very same indication. Indeed, we see some fairly exciting synergies/complementarities between these two approaches (the first one boosting the innate response and potentially upregulating the PD-L1 expression, while the second one disinhibits the adaptive response). Importantly, Amgen has also published some quite interesting data in patients with previously untreated, unresected stage IIIB-IV melanoma (ORR: 56% with 33% of patients experiencing a complete response, disease control rate: 76%).

Very few I-O agents have been developed in this indication over the past few years, as the tumour microenvironment is said to be very challenging (upregulation of Tregs, alteration of macrophages to tumour-associated macrophage-like phenotype leading to immunosuppression and angiogenesis, etc.), and notably for oncolytic virus (presence of natural killer cells, cytokines supporting an anti-viral activity such as TNF-alpha and IL-6)… That said, we note that 1/ nivolumab indeed managed to induce tumour regression in already pre-treated patients (ORR: 20%); 2/ back in 2015, AstraZeneca and MedImmune entered into a licensing agreement with Omnis Pharmaceuticals to develop an oncolytic virus (which by the way is derived from a VSV) for the treatment of HCC and other cancers that have metastasized to the liver.

But as **clinical data remains the sole judge** (and is incidentally expected by the end of 2017, or during H1 2018), we are assuming a fairly low market penetration pending its publication or a potential positive read-across (25%e despite a fairly less competitive landscape).

4. BG Valuation

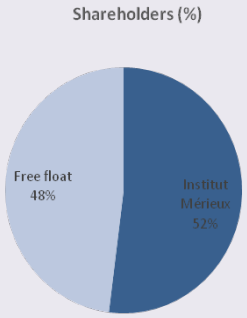
Our SOTP points to a FV of EUR4.5. Without entering into too much detail, we are assuming 1/ that value creation will primarily stem from TG4010 and PexaVEC, both as part of a combination regimen with a checkpoint blocker (respective peak sales: EUR500m and EUR400m in their lead indication); and 2/ a probability of success of 35% for all these developments. Our WACC is 16.0%.

Our valuation does not take into account early-stage compounds, whether TG1050 (a therapeutic vaccine developed for the treatment of HBV), TG6002 (a second generation of oncolytic virus) or TG3003 (a monoclonal antibody targeting CS1FR, which could be of interest in tumours known to exhibit an immunosuppressive microenvironment).

Next Catalysts

Period	Product	Area	
Q3 16	PexaVEC	Melanoma	Read-across from Imlygic in combo with pembrolizumab or ipilimumab
H1 18	TG4010	NSCLC	Phase I/II results in combination with an ICI
H1 18	PexaVEC	HCC	Phase I/II results in combination with an ICI
H1 18	PexaVEC	Solid tumors	Phase I/II results in combination with an ICI

Source: Company Data; Bryan, Garnier & Co ests.



Company description

Transgene is a biopharmaceutical company that develops immunotherapeutic products to treat cancers and chronic infectious diseases

Income Statement (EURm)	**2014**	**2015**	**2016e**	**2017e**	**2018e**	**2019e**
Revenues	0.0	0.0	0.0	0.0	0.0	0.0
Adjusted EBITDA	(44.0)	(33.2)	(25.8)	(23.8)	(26.0)	(28.3)
EBIT	(46.9)	(35.8)	(35.1)	(26.0)	(28.1)	(30.5)
Change (%)	*-13.9%*	*-23.7%*	*-2.1%*	*-25.8%*	*-8.2%*	*-8.4%*
Financial results	(0.80)	(0.93)	(1.0)	(1.0)	(1.0)	(1.0)
Pre-Tax profits	(47.7)	(36.7)	(36.1)	(27.0)	(29.1)	(31.5)
Exceptionals	0.0	0.0	(7.0)	0.0	0.0	0.0
Tax	0.0	0.0	0.0	0.0	0.0	0.0
Profits from associates	NM	NM	NM	NM	NM	NM
Minority interests	NM	NM	NM	NM	NM	NM
Net profit	(48.6)	(37.9)	(36.1)	(27.0)	(29.1)	(31.5)
Restated net profit	(48.6)	(37.9)	(36.1)	(27.0)	(29.1)	(31.5)
Change (%)	*-13.3%*	*-21.9%*	*-4.9%*	*-25.1%*	*-7.9%*	*-8.1%*
Cash Flow Statement (EURm)						
Operating cash flows	(41.9)	(32.5)	(33.8)	(24.8)	(27.0)	(29.3)
Change in working capital	12.4	12.7	0.0	0.0	0.0	0.0
Capex, net	2.5	1.5	1.0	1.0	1.0	1.0
Financial investments, net	(19.4)	34.2	0.0	0.0	0.0	0.0
Dividends	0.0	0.0	0.0	0.0	1.0	2.0
Other	NM	NM	NM	NM	NM	NM
Net debt	(13.7)	22.1	57.5	83.8	112	143
Free Cash flow	(56.7)	(46.7)	(34.8)	(25.8)	(28.0)	(30.3)
Balance Sheet (EURm)						
Tangible fixed assets	60.7	49.4	48.6	47.9	47.2	46.6
Intangibles assets	1.1	0.49	0.49	0.49	0.49	0.49
Cash & equivalents	65.9	31.7	26.3	0.05	(28.4)	(59.3)
current assets	13.5	19.4	19.4	19.4	19.4	19.4
Other assets	0.0	0.0	0.0	1.0	2.0	3.0
Total assets	141	101	78.4	51.4	22.2	(9.3)
L & ST Debt	52.2	53.8	83.8	83.8	83.8	83.8
Others liabilities	10.8	10.8	10.8	10.8	10.8	10.8
Shareholders' funds	71.8	26.5	(9.5)	(36.5)	(65.7)	(97.1)
Total Liabilities	141	101	78.4	51.4	22.2	(9.3)
Capital employed	62.4	51.9	51.1	50.4	49.8	49.1
Financial Ratios						
Operating margin	NM	NM	NM	NM	NM	NM
Tax rate	0.0	0.0	0.0	0.0	0.0	100
Net margin	NM	NM	NM	NM	NM	NM
ROE (after tax)	(67.59)	(143)	379	73.96	44.39	32.42
ROCE (after tax)	(77.76)	(73.06)	(70.49)	(53.53)	(58.56)	(64.13)
Gearing	(19.13)	83.43	(604)	(229)	(171)	(147)
Pay out ratio	0.0	0.0	0.0	0.0	(3.43)	(6.35)
Number of shares, diluted	36.43	38.53	38.53	38.53	38.53	38.53
Data per Share (EUR)						
EPS	(1.33)	(0.98)	(0.94)	(0.70)	(0.76)	(0.82)
Restated EPS	(1.33)	(0.98)	(0.94)	(0.70)	(0.76)	(0.82)
% change	*-2.1%*	*-26.2%*	*-4.9%*	*-25.1%*	*-7.9%*	*-8.1%*
BVPS	1.97	0.69	(0.25)	(0.95)	(1.70)	(2.52)
Operating cash flows	(1.15)	(0.84)	(0.88)	(0.64)	(0.70)	(0.76)
FCF	(1.56)	(1.21)	(0.90)	(0.67)	(0.73)	(0.79)
Net dividend	0.0	0.0	0.0	0.0	0.0	0.0

Source: Company Data; Bryan, Garnier & Co ests.

Price Chart and Rating History

Transgene

Ratings		
Date	**Ratings**	**Price**

Target Price	
Date	**Target price**
30/09/14	EUR12

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Stock rating

BUY — Positive opinion for a stock where we expect a favourable performance in absolute terms over a period of 6 months from the publication of a recommendation. This opinion is based not only on the FV (the potential upside based on valuation), but also takes into account a number of elements that could include a SWOT analysis, momentum, technical aspects or the sector backdrop. Every subsequent published update on the stock will feature an introduction outlining the key reasons behind the opinion.

NEUTRAL — Opinion recommending not to trade in a stock short-term, neither as a BUYER or a SELLER, due to a specific set of factors. This view is intended to be temporary. It may reflect different situations, but in particular those where a fair value shows no significant potential or where an upcoming binary event constitutes a high-risk that is difficult to quantify. Every subsequent published update on the stock will feature an introduction outlining the key reasons behind the opinion.

SELL — Negative opinion for a stock where we expect an unfavourable performance in absolute terms over a period of 6 months from the publication of a recommendation. This opinion is based not only on the FV (the potential downside based on valuation), but also takes into account a number of elements that could include a SWOT analysis, momentum, technical aspects or the sector backdrop. Every subsequent published update on the stock will feature an introduction outlining the key reasons behind the opinion.

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BUY ratings 64.4% NEUTRAL ratings 28.1% SELL ratings 7.4%

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