EDISON

Genkyotex

Business and financial update

Ready to make a dent in the fibrosis market

Pharma & biotech

Genkyotex has initiated a Phase II investigator-sponsored trial in patients with Type 1 diabetes (T1D) and kidney disease (DKD). Separately, it has announced the positive outcome of a safety review of its Phase II trial with GKT831 in patients with primary biliary cholangitis (PBC) with no adverse events or patient dropouts. Interim data have been pushed back slightly to autumn 2018 from mid-2018 and full data to H119 from end-2018 due to a slow rate of activation of a number of research centres. Additionally, the original deal with the Serum Institute of India Ltd (SIIL) has been expanded and Genkyotex is now eligible to an additional €100m in milestone payments plus royalties on sales. We include the DKD indication and the new terms with SIIL in our valuation, which is now €338.7m or €4.35/share.

Year end	Revenue (€m)	PBT* (€m)	EPS* (c)	DPS (c)	P/E (x)	Yield (%)
12/16	0.0	(5.7)	(37.1)	N/A	N/A	N/A
12/17	0.0	(13.9)	(21.0)	N/A	N/A	N/A
12/18e	0.0	(9.6)	(12.3)	N/A	N/A	N/A
12/19e	0.0	(9.7)	(12.4)	N/A	N/A	N/A

Note: *Normalised, excluding amortisation of acquired intangibles and exceptionals.

GKT831 starts clinical trial in diabetic kidney disease

An investigator-sponsored Phase II trial of GKT831 in T1D patients with DKD has started patient enrolment. The trial will be conducted at up to 15 centres in Australia. It will be fully funded by the Juvenile Diabetes Research Foundation Australia and the Baker Institute. Genkyotex will provide GKT831 under Good Manufacturing Practices (GMP). It is estimated that in 2015 there were 20.2 million cases of DKD in the US, EU5 and Japan. We project peak sales of c $1bn in the EU and US in 2028 and probability of success of 15%.

€100m deal expansion with Serum Institute of India

The original deal with the SIIL has been expanded to include developed countries (US, Canada and UE), significantly increasing the opportunity and covering virtually the whole market. SIIL is testing Genkyotex's Vaxiclase technology to develop new multivalent vaccines that contain *B. pertussis* (the whooping cough agent). Terms include a further €100m in development and sales milestone payments plus single-digit royalties on sales. So far, Genkyotex has received $1.3m.

Phase II study to open the liver fibrosis opportunity

GKT831 is currently undergoing an international Phase II study in PBC that will enrol 102 patients in over 50 centres in the US, Europe and Canada. The first safety review from the trial's ISMB has been successful; no serious or liver-related adverse events have been reported. Moreover, no patients have dropped out. The study continues towards first data in the fall of 2018 and full data in H119. We project $1.1bn peak sales for GKT831 in PBC with launch in 2023 in the EU and US. Furthermore, positive data would warrant investigation in additional fibrosis diseases such as NASH, idiopathic pulmonary fibrosis (IPF), or scleroderma.

Updated valuation of €338.7m or €4.35 per share

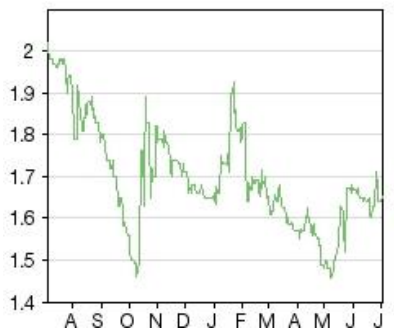
Our revised rNPV valuation of Genkyotex is €338.7m or €4.35/share (vs €268m, €3.4/share before). The main change is the addition of the DKD indication. As previously, we include GKT831 in PBC, the deal with the SIIL and updated net cash of €12.1m at 31 March 2018. We leave all additional indications as upside.

3 July 2018

Price	**€1.65**
Market cap	**€128m**

Net cash (€m) at 31 March 2018	12.1
Shares in issue	77.85m
Free float	50.55%
Code	GKTX
Primary exchange	Euronext
Secondary exchange	N/A

Share price performance



%	1m	3m	12m
Abs	(0.8)	5.2	(18.6)
Rel (local)	2.6	3.2	(20.3)
52-week high/low		€2.0	€1.5

Business description

Genkyotex is a biopharma company focused on NOX science in fibrosis and other indications. It has two main products: GKT831, in Phase II for PBC and DKD; and GKT771, in preclinical stage. Additionally, Genkyotex has a partnership with the Serum Institute of India.

Next events

GKT831 PBC Phase II interim data	Autumn 2018
GKT831 PBC Phase II full data	H119
GKT771 CTA submission	2018
Publication of additional NOX inhibition research	2018

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Edison profile page

Adding diabetic nephropathy to the equation

In late 2017 patient randomisation started in an investigator-sponsored Phase II study in patients with T1D and diabetic nephropathy. The primary endpoint of the study will be the change from baseline in urine albumin-to-creatinine ratio (UACR) after 48 weeks. A key secondary endpoint of the study will be changes in estimated glomerular filtration rate, which measure the effect of GKT831 on renal function. Patients will receive 200mg of oral GKT831 or placebo twice a day for 48 weeks. The study will be conducted at up to 15 centres in Australia under the leadership of Professor Mark Cooper, head of the department of diabetes at Monash University, and Professor Jonathan Shaw, deputy director at the Baker Heart and Diabetes Institute in Melbourne. We note that the study will have a limited impact on Genkyotex's financials as it will be entirely funded by the Juvenile Diabetes Research Foundation and the Baker Institute. Genkyotex will provide GMP-produced GKT831.

This trial has some important differences with respect to a previous Phase II study with GKT831 in Type 2 diabetes patients with diabetic nephropathy, which read out in 2015. In particular, the new trial is testing a higher dose (200mg twice/day vs the previous 100mg/day for six weeks followed by 200mg/day for six weeks) during a longer duration of treatment (48 weeks vs 12 weeks previously). The 2015 study did not meet the primary efficacy endpoint of reduction of proteinuria at 12 weeks, but results were statistically significant ($p<0.05$) in the predefined secondary endpoints of changes in liver enzymes such as gamma-glutamyltransferase (GGT) and markers of inflammation. We believe that increasing the duration of treatment and dose may bode well for improved efficacy in the new trial.

GKT831 has been proven safe in four Phase I studies in a total of 117 healthy subjects in a single ascending dose, in multiple ascending doses as well as the food effect and drug interaction. In these studies, GKT831 showed no safety issues and there were no dose-limiting toxicities. Furthermore, adverse events in the previous DKD Phase II trial were significantly lower in the GKT831 arm vs placebo.

Exhibit 1: DKD background

What is DKD?	DKD is one of the long-term complications of diabetes that leads to damage of the kidneys' filtering system. It is characterised by persistent albuminuria, progressive decline in the glomerular filtration rate and elevated arterial blood pressure.
Epidemiology	The main driver of the disease is the underlying epidemiology of diabetes. According to Datamonitor Healthcare in 2015, there were 20.2 million prevalent cases of DKD in the adult diabetic population in the US, EU5 and Japan. DKD is more prevalent in diabetics with longer disease durations, thus prevalence is strongly influenced by an ageing population.
Diagnosis	DKD is usually diagnosed in regular urine and blood tests conducted in diabetic patients. Assessment of kidney damage and function: kidney damage is usually detected through albumin leakage into the urine – typically a urinary albumin-to-creatinine ratio (UACR) over 30mg/g, which represents at least moderately increased albuminuria. Albuminuria is also a marker of CV risk and inflammation.
Staging based on eGFR	■ Stage I: Kidney damage with normal or increased GFR. eGFR ≥90 mL/min/1.73 m^2 ■ Stage II: Kidney damage with mildly decreased GFR. eGFR 60-89 mL/min/1.73 m^2 ■ Stage III: Moderately decreased eGFR 30-59 mL/min/1.73 m^2 ■ Stage IV: Severely decreased eGFR 15-29 mL/min/1.73 m^2 ■ Stage V: Kidney failure. eGFR <15 mL/min/1.73 m^2
Treatment	Current treatments include angiotensin converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs), which are recommended as first-line treatment in hypertensive DKD patients with severe albuminuria and also in patients with moderate albuminuria. CE inhibitors or ARBs control blood pressure, reduce proteinuria and slow the loss of renal function in patients with DKD and UACR >30mg/g or hypertension and normoalbuminuria. ACE inhibitor Capoten (captopril, from Bristol-Myers Squibb and Par Pharmaceuticals, 2016 sales $16m) and the ARBs Cozaar (losartan from Merck, generic, 2016 sales of $511m in hypertension and DKD) and Avapro (irbesartan from Sanofi, 2016 sales $849m in hypertension and DKD) are the ones that have demonstrated strong renal outcomes in patients with severe albuminuria. Data for these drugs are less strong in other patient segments, but ACE inhibitors and ARBs are still recommended to prevent progression in moderate albuminuria (also known as microalbuminuria), particularly for hypertensive patients

Source: Edison Investment Research. Note: eGFR = estimated glomerular filtration rate.

Exhibit 2: Selected DKD competitors

Product	Company	Status	Mechanism of action	Comments
Atrasentan	AbbVie	Phase III	Endothelin receptor antagonist	Current Phase III in 4k+ patients (PC date mid-2018). Significant UACR reduction 35-42% vs 11% placebo in Phase II trial.
Finerenone	Bayer	Phase III	Mineralocorticoid receptor activator	Dose-dependently reduced UACR. Mean ratios of UACR in the two highest doses vs placebo were 0.62 and 0.67 ($p < 0.0001$ either).
Canagliflozin (Invokana)	J&J/Tanabe	Phase III	SGLT2 inhibitor	Numerically greater reductions in UACR compared to placebo at 26 weeks (-20.9% and -29.9% for Invokana 150mg and 300mg versus -7.5% for placebo; statistical analysis was not provided.
Dapagliflozin (Farxiga)	AstraZeneca	Phase II	SGLT2 inhibitor	Approved in the EU and US for T2D. Phase II in CKD to start in October 2017.

Source: Edison Investment Research

Competitors' trials are being conducted in T2D patients with DKD, in addition to RAS blockade therapy.

Phase II study in PBC on track for first read out in 2018

GKT831 is undergoing a Phase II trial in primary biliary cirrhosis (PBC). The study is expected to enrol 102 patients with PBC in over 50 research centres in the US, Canada and Europe. Genkyotex will report interim data in the autumn of 2018 (vs mid-2018 previously) and full results in H119 (vs by the end of 2018 previously). The reason for this delay is a slower than expected rate of activation of clinical research centres in four of the nine participating countries. The company recently announced the study had successfully completed its first pre-planned safety review by the ISMB which recommended the trial continues without changes to the protocol. Importantly, no serious adverse events, liver-related adverse events or patient dropouts had been reported at the time of the review. PBC is a rare disease of the liver in which biliary ducts are targeted by antibodies. Bile ducts are blocked causing leakage of bile fluids to the liver parenchyma, which eventually leads to fibrosis, cirrhosis and liver failure. We estimate the number of PBC patients that could be eligible for treatment with GKT831 at c 46,000 in the EU and US and project total peak sales of $1.1bn in this indication, with launch in 2023. We believe that the PBC trial, if successful, could also support development of GKT831 in the larger liver fibrosis opportunity, in particular Nonalcoholic steatohepatitis (NASH), which could target c 60 million people in the EU and US. Other fibrotic indications are IPF, cystic fibrosis, or scleroderma. GKT831 is patent protected in the US, Europe and Japan until 2029.

GKT831 shows potential in preclinical oncology models

Preclinical data published in the Journal of the National Cancer Institute showed that inhibition of NOX4 with GKT831 effectively targeted CAFs, delaying tumour growth. CAFs are part of the tumour microenvironment and are thought to be involved in various cancer biological processes and correlate with poor survival in many cancers. Hence, targeting CAFs may be a potential treatment in cancer. Additionally, the authors showed a statistically significant upregulation of NOX4 expression in multiple human cancers strongly correlating with myofibroblastic CAFs. Moreover, the senior author of the study, Professor Gareth Thomas of the University of Southampton, has received a grant from Cancer Research UK (CRUK) to design a potential clinical trial with GKT831 in combination with other anti-cancer drugs.

Deal with SIIL expanded to developed countries

Genkyotex has announced that its licensing agreement with the Serum Institute of India has been extended to cover additional countries, in particular the US, Canada and Europe. This adds an additional €100m in development and commercial milestone payments to the $57m of the original deal. Genkyotex is also entitled to single digit royalties on sales. Out of the total c €150m value, Genkyotex has received approximately $1.3m in upfront payments associated with the preclinical development of Vaxiclase. The next milestone payments will come from the clinical development of

the vaccine. The partnership started in February 2015 and involves evaluating new multivalent vaccines using Genkyotex's Vaxiclase technology. Vaxiclase is a re-engineered version *Bordetella pertussis*'s adenlylate cyclase (CyA) enzyme. In this deal Vaxiclase is used as an antigen that aims to improve the duration of protection of acellular pertussis (aP) vaccines. Current aP vaccines are of short duration and there is a need for new aP vaccines that provide long-lasting protection and efficacy. Most pertussis vaccines are administered in combination with diphtheria and tetanus. Furthermore, *Bordetella pertussis* antigens are included in multiple complex vaccination schedules, often for hepatitis B (HB), polio (IPV) and influenza B (Hib).

SIIL is the world's largest manufacturer of vaccines, with more than 1.3 billion doses sold annually. We believe this extension adds a significant opportunity. With this expansion the partners will cover virtually the entire market, on top of the 20% of the market that emerging countries represent. We have included this deal expansion in our valuation applying the same modelling approach as before.

Financials: FY17 results and Q118 cash update

Genkyotex reported operating expenses of €14.8m for FY17 vs. c €6m in FY16, which includes warrants issued to the company's employees and converted into shares (almost €4m in FY17 vs €0.07m in FY16). The increase in expenses is related to the initiation of the Phase II study with GKT831 in PBC and preclinical work for GKT771. Other operating expenses of €11.4m (vs none in FY16) are associated with the reverse merger between Genticel and Genkyotex and restructuring costs. This results in a net loss of €25.8m in FY17 vs net loss of €5.9m in FY16. We now forecast a net loss of €9.9m in FY18e vs €13m before as we do not forecast further expenses associated with share based payments, restructuring or the strategic combination.

Genkyotex recently provided a corporate and cash update for Q118. At 31 March 2018 cash, equivalents and short-term investments were €12.5m which should be sufficient to fund the company into Q119, according to our forecasts. We project a funding shortfall of €15m at the end of 2019, which for illustrative purposes we include as long-term debt.

Updated valuation of €338.7m or €4.35 per share

Using our standard 12.5% discount rate produces a risk-adjusted NPV of €338.7m, or €4.35 per share, vs €268m or €3.4 per share before. Our updated valuation includes GKT831 in DKD. As in the previous valuation, GKT831 in PBC and the SIIL deal are included. We leave all other product development opportunities and additional indications as an upside. Our assumptions for DKD are as follows:

- The company partners GKT831 for clinical development, registration and launch in the EU and US in 2023. We assume a partner funds these activities in a back-loaded deal that we project has an 18% royalty on net sales that is a blend of upfront, milestones and royalties.
- We assume a maximum 20% market share leading to $1bn peak sales in the EU-5 and US in 2028. This is based on c 56k patients in the US (source: Centers for Disease Control) and 25k patients in the EU-5 (source: London School of Economics) at a cost per year of $70k and $40k respectively.
- We assume a 15% probability of reaching the market, which reflects the risks from the previous trial. We look to update this as data are released.

Exhibit 3: Valuation

Product	Peak sales ($m)	Probability	rNPV (€m)	rNPV per share (€)
GKT831 – PBC (USA)	646.3	40%	379.0	4.9
GKT831 – PBC (EU5)	463.0	40%	271.5	3.5
GKT831 – DKD (USA)	867.0	15%	31.0	0.4
GKT831 – DKD (EU5)	219.0	15%	8.0	0.1
SIIL	N/A	20%*	16.7	0.2
Expenses		40%	(379.6)	(4.9)
Net cash (at 31 March 2018)		N/A	12.1	0.2
Total rNPV			**338.7**	**4.4**

Source: Edison Investment Research. Note: EU5 = Germany, the UK, France, Italy and Spain. * Probability from 2023 onwards.

NASH potential

We do not typically include any contribution for indications until clinical development commences; therefore, our GKT831 estimates do not include any potential in NASH. However, we believe that positive results in PBC could justify future development in other large fibrotic diseases including NASH. Therefore, we have run a sensitivity analysis that suggests that NASH could add between c €30m and €90m, excluding milestones or upfront payments, depending on the commercial strategy. This is based on two scenarios. The first scenario, in which the company conducts the programme itself, would add €90m value. This requires a higher capital investment, but should be significantly more profitable than a simple sales royalty, potentially with a 50-60% pre-G&A margin. In the second scenario the company partners GKT831 after Phase II data, adding c €30m in value, which assumes a standard mid-teens royalty rate and excludes any specific milestone payments. For both scenarios we model launch in 2024 and a 10% probability of success. Given the size of the patient population, we assume that $2bn peak sales are achievable even if there are other competitors in this field.

Exhibit 4: Financial summary

€ 000	2016	2017	2018e	2019e
Year End December	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS				
Revenue	0	0	0	0
Cost of Sales	0	0	0	0
Gross Profit	0	0	0	0
R&D expenses	(4,813)	(9,475)	(7,000)	(7,000)
G&A expenses	(1,641)	(5,299)	(3,500)	(3,500)
EBITDA	(5,854)	(13,590)	(9,385)	(9,385)
Operating Profit (before amort. and except.)	(5,928)	(13,629)	(9,424)	(9,424)
Intangible Amortisation	0	(476)	(476)	(476)
Exceptionals	0	(11,408)	0	0
Other	0	0	0	0
Operating Profit	(5,928)	(25,513)	(9,900)	(9,900)
Net Interest	234	(255)	(188)	(271)
Profit Before Tax (norm)	(5,694)	(13,884)	(9,612)	(9,695)
Profit Before Tax (FRS 3)	(5,694)	(25,768)	(10,088)	(10,171)
Tax	(158)	(5)	0	1
Profit After Tax (norm)	(5,778)	(13,850)	(9,573)	(9,656)
Profit After Tax (FRS 3)	(5,853)	(25,773)	(10,088)	(10,171)
Average Number of Shares Outstanding (m)	15.6	66.1	77.9	77.9
EPS - normalised (c)	(37.1)	(21.0)	(12.3)	(12.4)
EPS - (IFRS) (c)	(43.0)	(39.0)	(13.0)	(13.1)
Dividend per share (c)	0.0	0.0	0.0	0.0
Gross Margin (%)	NA	NA	NA	NA
EBITDA Margin (%)	NA	NA	NA	NA
Operating Margin (before GW and except.) (%)	NA	NA	NA	NA
BALANCE SHEET				
Fixed Assets	112	10,336	10,336	10,336
Intangible Assets	0	10,221	10,221	10,221
Tangible Assets	93	51	51	51
Fixed term investments	15	64	64	64
Other	4	0	0	0
Current Assets	14,732	16,557	6,469	11,298
Stocks	0	0	0	0
Debtors	0	0	0	0
Cash	13,937	14,625	4,537	9,366
Other	795	1,932	1,932	1,932
Current Liabilities	(1,753)	(2,420)	(2,420)	(2,420)
Creditors	(1,753)	(2,132)	(2,132)	(2,132)
Short term borrowings	0	(288)	(288)	(288)
Long Term Liabilities	(874)	(937)	(937)	(15,937)
Long term borrowings	0	(115)	(115)	(15,115)
Other long term liabilities	(874)	(822)	(822)	(822)
Net Assets	12,217	23,536	13,448	3,277
CASH FLOW				
Operating Cash Flow	(5,315)	(9,027)	(9,360)	(9,360)
Net Interest	234	(255)	(188)	(271)
Tax	(39)	(81)	0	0
Capex	0	(2)	0	0
Acquisitions/disposals	0	7,593	0	0
Equity Financing	14,490	(248)	0	0
Other items	(96)	(572)	(540)	(540)
Net Cash Flow	9,273	(2,593)	(10,088)	(10,171)
Opening net debt/(cash)	N/A	(13,937)	(14,222)	(4,134)
HP finance leases initiated	0	0	0	0
Other	0	2,878	0	0
Closing net debt/(cash)	(13,937)	(14,222)	(4,134)	6,037

Source: Edison Investment Research and Genkyotex accounts

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