EDISON

Genkyotex

Reverse takeover

Targeting obNOXious fibrosis

Pharma & biotech

Genkyotex is a Euronext-listed company formed by the merger of Genticel and Genkyotex focused on NOX science and its application in fibrosis and other indications. The lead asset, GKT831, will start a Phase II trial in primary biliary cholangitis (PBC) in Q217, with data expected in 2018. Positive results could justify future development in other large fibrotic diseases including non-alcoholic steatohepatitis (NASH). GKT771 will be Phase I ready in late 2017 and will focus on inflammation and angiogenesis. A partnership for immunotherapies with the Serum Institute of India (SIIL) for up to $57m in milestone payments plus royalties is also in place. Cash of €21.8m at end March 2017 should be sufficient to fund operations for two years. Our valuation is €268m.

Year end	Revenue (€m)	PBT* (€m)	EPS* (c)	DPS (c)	P/E (x)	Yield (%)
12/16e	1.3	(21.7)	(27.8)	N/A	N/A	N/A
12/17e	0.0	(12.0)	(15.4)	N/A	N/A	N/A
12/18e	0.0	(13.0)	(16.7)	N/A	N/A	N/A

Note: *PBT and EPS are normalised, excluding intangible amortisation, exceptional items and share-based payments. 2016e is our pro forma estimate, based on available data.

Lead asset GKT831 to start Phase II in PBC in Q217

GKT831 is a first-in-class dual NOX1/4 inhibitor due to start a Phase II trial in PBC in Q217. The FDA has accepted the Investigational New Drug (IND) application which allows the study to start in the US. Initial data could be available in H118 with full results in H218. PBC is a rare autoimmune disease that causes liver fibrosis, cirrhosis and eventually liver failure. We estimate there are c 46,000 diagnosed patients in the US and EU and forecast peak sales for GKT831 of c $1.1bn.

Untapped market could hold significant value

Success in PBC could expand the clinical applications of GKT831 to other liver fibrosis opportunities such as NASH. There are currently no approved products for NASH, but prevalence data suggest c 60 million patients could be affected in the EU and US. Hence we see blockbuster potential for a product successfully developed for this market. Recent deals in the NASH space, with overall values up to $1.7bn, are indicative of the interest of large pharmaceutical companies in this indication.

More in the pipeline and a partnership

The second product, GKT771, is in preclinical stage and will be Phase I ready in late 2017; potential applications are angiogenesis and inflammation-related pain. Further NOX inhibitors are being investigated for oncology, hearing loss and neurology indications. The partnership with SIIL involves up to $57m of milestones and single-digit royalties on net sales. SIIL has rights to develop multivalent vaccines including pertussis antigens in emerging markets while Genkyotex retains rights to developed markets which represent a potentially larger opportunity.

Valuation: risk-adjusted NPV of €268m

Our valuation of the combined company is €268m based on an rNPV and includes the PBC indication, the SIIL deal and net cash. Additionally, should the company pursue NASH, we estimate this could add €30m to €90m, depending on the commercialisation strategy (via a partner or alone).

30 May 2017

Price	**€2.08**
Market cap	**€162m**

Net cash (€m) at 31 March 2017	20.8
Shares in issue	77.9m
Free float	50.6%
Code	GKTX
Primary exchange	Euronext
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	3.6	(6.5)	(55.5)
Rel (local)	2.0	(15.4)	(62.8)
52-week high/low		€5.2	€1.3

Business description

Genticel and Genkyotex have agreed to enter into a strategic combination. This shifts the focus to NOX science in fibrosis and other indications. It brings two main products: GKT831, planned to enter Phase II and GKT771, in preclinical stage. Genkyotex has a partnership with the Serum Institute of India.

Next events

GKT831 Phase II start	Q217
GKT771 Phase I ready	End 2017
GKT831 Phase II interim data	H118
GKT831 Phase II full data	H218

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Edison profile page

Investment summary

Company description: Focus on NOX science

Genticel's shareholders have approved the strategic combination with Genkyotex, a Swiss private company with extensive expertise in NOX science. The combined company has taken the name Genkyotex and is focused on the development of NOX inhibitors. Lead product GKT831 will start a Phase II clinical trial in PBC in Q217, with first interim data in H118. Its second product is GKT771, which is in preclinical stage and will be Phase I ready in late 2017, with a focus on inflammatory pain and angiogenesis. Furthermore, Genkyotex has a portfolio of early stage NOX inhibitors for other indications such as neurology, hearing loss and oncology. Finally, the new company is inheriting Genticel's agreement with SIIL for the use of GTL003 in the development of vaccine candidates and is eligible for up to $57m in upfront, development and sales milestone payments ($1.7m paid so far), as well as single-digit royalties on net sales. Genkyotex retains rights for the most profitable markets of Europe and the US among other developed regions.

Exhibit 1: Pipeline overview

Product	Indication	Phase	Comments
GKT831	PBC	Phase II ready	To start Phase II trial in Q217, interim data H118, full data H218
GKT771	Inflammation, angiogenesis	Preclinical	Phase I ready in late 2017
GTL003	Multivalent vaccines	Preclinical	SIIL to finish formal preclinical studies before starting clinical trials
ND	Neurology, hearing loss, oncology	R&D	Additional undisclosed NOX inhibitors

Source: Edison Investment Research, Genkyotex, Genticel. Note: ND = not disclosed.

Valuation: risk-adjusted NPV of €268m

We have updated our rNPV valuation to include the main assets of the combined entity, including GKT831 and GTL003 in addition to estimated net cash. No value for GKT771 is assumed prior to the start of its clinical development. Our valuation is €268m or €3.5/share (based on c 78m shares in the combined entity). For GKT831, we currently only include the potential in PBC, projecting peak sales of $1.1bn and launches in 2023. We do not typically include any contribution for indications until clinical development commences, hence our GKT831 estimates do not include any potential in NASH. However, a sensitivity analysis suggests NASH could add between c €30m and €90m, excluding milestones or upfronts, depending on the commercial strategy.

Financials: Sufficient cash to fund near-term catalysts

We estimate Genkyotex had c €20.8m net cash at the end of Q117, which should be sufficient to fund clinical development of both lead assets over the next two years, according to our forecasts. The company expects to receive an additional €3m in tax credits. Our updated forecasts for 2017 and 2018 include our assumed underlying R&D and G&A spend for the combined entity. We forecast R&D of €7m in 2017 and €10m in 2018, and G&A of $5.5m in 2017 and $5m in 2018. We also provide a simple estimated 2016 pro forma statement based on available information to date.

Sensitivities: GKT831 is the main value driver

We believe the main share price driver in the near term will be GKT831 interim data in PBC in H118. Positive results would justify further development in PBC and potentially support development in NASH. Conducting a full clinical programme in NASH would require significant funding. Therefore, positive data in the PBC indication is important to raise the interest of potential partners or capital markets to fund the NASH programme. In addition to that, liver fibrosis is a competitive environment, with one product on the market for PBC and several competitors in both

PBC and NASH ahead of Genkyotex. Progression of GKT771 and other early stage candidates to further clinical trials could also become value drivers.

NOX pipeline adds Phase II asset GKT831

As a result of the transaction, GKT831 and GKT771, developed by Genkyotex, will enter the pipeline of the new company. The leading product is GKT831, a NOX1 and NOX4 inhibitor due to start a Phase II clinical trial in PBC in Q217. The company recently announced the US FDA had accepted the IND application for the clinical trial. Interim data could be available in H118 and full data in H218. We estimate the number of PBC patients that could be eligible for treatment with GKT831 at c 46,000 and project peak sales of $1.1bn in this indication, with launch in 2023. The PBC trial, if successful, could also support development of GKT831 in the larger liver fibrosis opportunity, which could target c 60 million people in the EU and US. GKT831 is patent protected in the US, Europe and Japan until 2029.

PBC Phase II trial design

The study will enrol 102 patients with PBC. Patients will be administered placebo and two doses of GKT831, 400mg once a day or 400mg twice daily, during 24 weeks. The primary endpoint will be change in serum gamma-glutamyl transferase (GGT), a marker of liver injury. Secondary endpoints will explore other markers of cholestasis and liver injury,[1] inflammation[2] and liver fibrosis.[3]

Safety profile established in Phase I and Phase II studies

Genkyotex has conducted four Phase I studies that have established the safety of GKT831. These trials investigated GKT831 in 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.

A Phase II study in diabetic nephropathy did not meet the primary efficacy endpoint of reduction of proteinuria at 12 weeks, but results were statistically significant ($p<0.05$) in the pre-defined secondary endpoints of changes in liver enzymes such as GGT and markers of inflammation like high sensitivity C-reactive protein (hsCRP). Moreover, adverse events were significantly lower in the GKT831 arm vs placebo. The company concluded that the data supported further development in inflammatory and fibrotic indications.

Second asset GKT771 to be Phase I ready at end 2017

Genkyotex plans to start a Phase I study of second candidate GKT771, a NOX 1 inhibitor, if preclinical studies are positive. The product is expected to be ready for clinical studies by the end of 2017. The company has pointed to angiogenesis, inflammation and pain as potential applications. We are not including GKT771 in our valuation, as assessing its potential in the absence of clinical data is challenging.

NOX background

NADPH oxidase (nicotinamide adenine dinucleotide phosphate-oxidase, NOX) is an enzyme complex that generates reactive oxygen species (ROS) by transporting electrons through lipid

[1] Cytokeratin-18 (CK-18); bilirubin.

[2] Alkaline phosphatase (ALP); aspartate aminotransferase (AST); alanine aminotransferase (ALT); high sensitivity C-reactive protein (hsCRP) and interleukin-6 (IL-6).

[3] Enhanced Liver Fibrosis (ELF) score, collagen fragments and transient elastography.

membranes. It is involved in eliminating bacteria and other infectious agents. NOX comprises seven different isoforms and has a role in a number of biological pathways, as shown in Exhibit 2.

Exhibit 2: The NOX family

Isoform	Potential indications	Comments
NOX 1	Inflammatory pain, angiogenesis	Involved in VEGF, PI3K, TRPV1, NF-kB pathways. Mainly expressed in the colon. Generates superoxide.
NOX 2	Neurology	Involved in NMDA pathway. Mainly expressed in phagocytes and B lymphocytes. Generates superoxide.
NOX 3	Hearing loss	Involved in TRPV1 pathway. Generates superoxide.
NOX 4	Diabetes, fibrosis, cardiovascular	Involved in TGFb, RAS, RANKL, TLR4 pathways. Expressed in the kidney and blood vessels. Mainly produces H_2O_2.
NOX 5	N/A	Mainly expressed in lymphoid tissue and testis.
DUOX 1 & DUOX 2	Proliferation	Expressed in thyroid and lung tissue.

Source: Edison Investment Research, Genkyotex

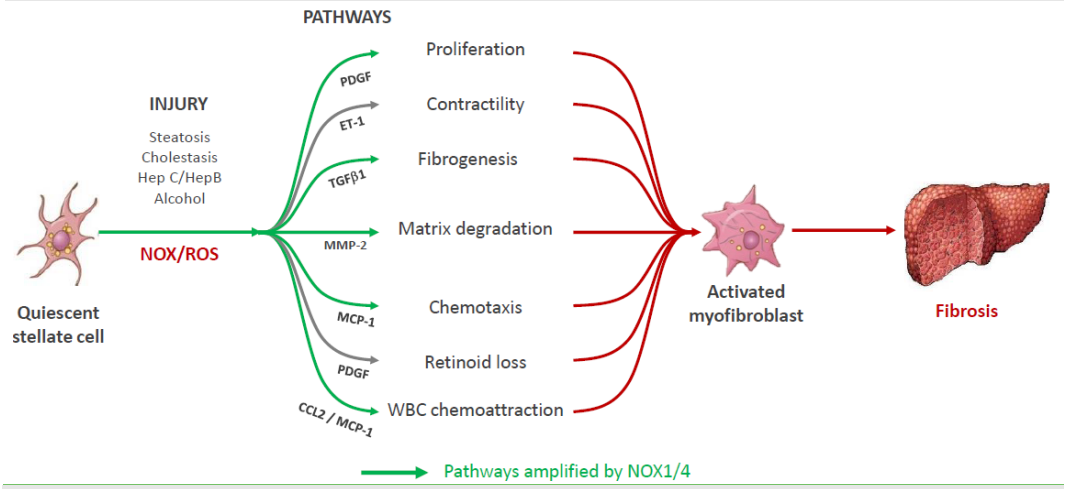
Increased NOX activity has been linked to various diseases, in particular to metabolic and cardiovascular diseases and neurodegeneration. Some isoforms are more present in certain tissues, which may lead to a particular phenotype in case of disease. Increased ROS in tissues contribute to fibrosis, hence targeting NOX has been proposed as a potential treatment for fibrosis in various organs such as the liver, lung or heart.

NOX1 and NOX4 are involved in validated fibrosis pathways

Fibrosis is a pathological condition in which scarring and thickening in an organ or tissue occurs in response to trauma and injury. The process is initiated when immune cells like macrophages release pro-fibrotic cytokines such as transforming growth factor-beta (TGFb) that stimulate fibroblasts. Activated fibroblasts are responsible for the deposition of collagen and extracellular matrix proteins. Although the process may be necessary for healing, in excess it may compromise the normal functioning of the organ. Fibrosis may affect various organs such as the lungs (idiopathic pulmonary fibrosis, cystic fibrosis), the liver (cirrhosis), heart (cardiac fibrosis) or the kidneys (renal fibrosis), among others.

Liver fibrosis is characterised by the accumulation of fibroblasts in response to injury. Accumulating evidence suggests a critical role of NOX in the activation process of hepatic myofibroblasts. NOX isoforms have been implicated to regulate hepatic stellate cells (HSC) activation and hepatocyte apoptosis, both of which are essential steps for initiating liver fibrosis.

Exhibit 3: NOX1/4 disease driving pathways in fibrosis



Source: Genkyotex

Only a handful of companies that we are aware of are developing NOX inhibitors for various indications; all are in the early stages of development (see Exhibit 4). In our view, Genkyotex is the most advanced among its peers as it is the only one that has a clinical stage compound.

Exhibit 4: Companies developing NOX inhibitors

Company	Product/s	Target	Proposed indication
Genkyotex	GKT831, GKT771	NOX1 and NOX4	Fibrosis, angiogenesis, inflammation
Alimera Sciences	Small molecule	Unspecified NOX	Dry AMD
ProNoxis	Small molecule	NOX2	Inflammation
Glucox Biotech	Small molecule	NOX4	Diabetes
Vasopharm	VAS2870	Pan-NOX	Cardiovascular

Source: Edison Investment Research, Evaluate Pharma

GKT831 has been shown to have dual NOX1 and NOX4 inhibiting effects. The half maximal inhibitory concentration (IC_{50}) is in the three-digit nanomolar range for NOX1 and NOX4, showing it is a potent inhibitor specific to these isoforms.

Solid animal proof-of-concept data in different disease models

To date, Genkyotex has generated 35 scientific publications showing the mechanism of action of its compounds *in vitro* and *in vivo*. Brenner D et al. (2015) reported that deletion of either NOX1 or NOX4 genes in mice attenuates induced liver fibrosis and showed that GKT831 suppressed signalling by a number of pro-fibrinogenic ligands in HSCs.

Furthermore, Genkyotex and collaborators have studied the role of NOX1 and NOX4 in liver tissue samples from patients with NASH and cirrhosis, and in and in mouse models of diet-induced NASH. They showed that NOX4 levels are increased in the NASH and cirrhosis liver samples compared with controls. Additionally, treatment with GKT831 reduced liver inflammation and fibrosis and increased insulin sensitivity in mice with diet-induced steatohepatitis.

The company has also studied the role of NOX4 and the effect of GKT831 in the bile duct ligation (BDL) model of PBC. Experiments concluded that BDL mice treated with GKT831 displayed less ROS production, decreased hepatocyte apoptosis and significantly attenuated fibrosis.

Animal data published in Science Translational Medicine showed that targeting NOX4 with GKT831 in an aging model of lung fibrosis led to a reversal of persistent fibrosis associated with aging and prolonged survival.

Differentiated profile and mechanism of action

Unlike most competitors, which focus on metabolic and cholestatic pathways, Genkyotex's GKT831 focuses on fibrosis and inflammation, as shown in Exhibit 5.

Exhibit 5: Mechanism of action competitive landscape in NASH and PBC

Fibrosis and inflammation		Metabolic and cholestatic	
Company	**Mechanism of action**	**Company**	**Mechanism of action**
Genkyotex	NOX 1/4 inhibitor	Intercept	Farnesoid X receptor (FXR) agonist
Tobira (Allergan)	Chemokine receptors 2 and 5 inhibitor	Genfit	PPAR α/δ inhibitor
Conatus	Apoptotic, inflammatory caspases inhibitor	Inventiva	PPAR α/δ and γ inhibitor
Gilead	Ask-1 inhibitor	Nimbus (Gilead)	Acetyl-CoA Carboxylase (ACC) inhibitor
Gilead	LOXL2 inhibitor	Galmed	SCD1 inhibitor

Source: Edison Investment Research, Genkyotex

Hence, the positioning of GKT831 in the NASH and PBC competitive landscape is unique as it is the only product that targets the NOX pathway with anti-fibrotic and anti-inflammatory effects.

A first step in the large fibrosis opportunity

Genkyotex plans to initiate a Phase II trial in PBC, formerly known as primary biliary cirrhosis. PBC is a rare autoimmune liver disease in which antibodies target and destroy biliary ducts causing leakage of bile fluids to the liver parenchyma, which eventually leads to fibrosis, cirrhosis and liver failure, which may cause death if left untreated. Most patients are middle-aged women and prevalence has been estimated at up to 40 cases per 100,000 people.

Exhibit 6: PBC background

What is PBC?	PBC is an autoimmune liver disease caused by a build-up of bile within the liver (cholestasis) and characterised by antimitochondrial autoantibodies (AMAs), infiltration of lymphocytes in portal tracts and progressive destruction of intrahepatic bile ducts, causing liver fibrosis, cirrhosis and eventually liver failure.
Epidemiology	Prevalence between two and 40 cases per 100,000 people. Incidence is 2.7 cases per 100,000 people. 90% of patients are women.
Symptoms	Usually asymptomatic at early stages and incidentally because of abnormal liver blood tests or incidental abdominal imaging. Fatigue, itch and scratching, dry mouth and eyes and right upper abdominal pain due to liver inflammation. In advanced disease, jaundice (yellow coloration of the skin and eyes), ascites (abdominal swelling) and oedema (fluid build-up in lower extremities).
Diagnosis of PBC	Diagnosis may be made incidentally after having a blood test for another reason. The main tests are: ■ Liver function tests: liver enzymes ALT, AST, GGT, alkaline phosphatase and bilirubin. ■ Imaging: ultrasound, CT scan, magnetic resonance imaging (MRI). ■ Liver biopsy and histopathology.
Treatment	The main treatments are: ■ Ursodeoxycholic acid (UDCA) is the first line treatment. Ocaliva is for patients with inadequate response or intolerant to UDCA. ■ Symptomatic treatment: antihistamines and cholestyramine for itching. ■ Liver transplant in advanced stage of disease.

Source: Edison Investment Research

Peak sales estimate of $1.1bn in PBC

We estimate that GKT831 could achieve peak sales of $1.1bn. Based on epidemiology data, we calculate that there could be up to 46,000 patients in the US and EU diagnosed with PBC and not responding to UDCA in the US and EU-5, which would represent a c $3bn opportunity, based on Intercept's Ocaliva US list price of $70,000. Allowing time to complete Phase III trials and regulatory reviews, we forecast initial launches for GKT831 in the US and EU from 2023. Our peak sales estimate of $1.1bn, which is based on a two-year duration of treatment and a 20% market penetration, assumes that GKT831 is able to demonstrate safety and/or efficacy benefits over Ocaliva. The company says this could be possible owing to its different mechanistic profile, which targets fibrosis/inflammation vs Intercept and Genfit's metabolic approach. However, if this benefit is not proved, we would assume duration of treatment (and hence sales revenues) more in line with Ocaliva. The consensus sales estimate for Ocaliva is $505m in 2022 (EvaluatePharma), when the patent expires.

Exhibit 7: Selected PBC competitors

Product	Company	Status	Comments
Ocaliva	Intercept	Market	Launched in US in Q216. Launch in EU expected early 2017.
Elafibranor	Genfit	Phase II	Randomised, double-blind, placebo-controlled trial in patients with PBC and inadequate response to ursodeoxycholic acid. Due to start in 2017.
GS-9674	Gilead	Phase II	Randomised, double-blind, placebo-controlled study in 75 PBC patients without cirrhosis. Primary completion August 2017. Treatment-emergent side effects. Acquired from Phenex Pharmaceuticals; total deal value $470m.
LJN452	Novartis	Phase II	Randomized, double-blind, placebo-controlled study in 95 PBC patients. Primary completion date December 2017. Endpoints: change in cholestatic markers, AEs, quality of life, change in itch, PK analysis.
MBX-8025	Cymabay	Phase II	Dose-ranging, open-label, randomised study in 36 patients intolerant or not responsive to UDCA. Primary completion date December 2017. Measure liver enzymes. AP, ALT AST, GGT, cholesterol, bilirubin.

Source: Edison Investment Research

NAFLD/NASH optionality

Non-alcoholic fatty liver disease (NAFLD) is the most common form of liver disease in the Western world. NAFLD represents a spectrum ranging from bland steatosis to NASH and is closely associated with obesity and metabolic syndrome. Research has recently been increasing in this

area due to the growing prevalence of NAFLD and the potential for NASH to progress to cirrhosis and liver-related mortality. NASH is becoming more prevalent with the increasing occurrence of obesity, diabetes mellitus and other components of metabolic syndrome. NASH is characterised as the hepatic manifestation of metabolic syndrome because as many as 90% of NAFLD cases have at least one component of metabolic syndrome and as many as 33% have three or more components; see Exhibit 8 for details. The development of NAFLD/NASH is associated with the diabetic pathophysiological process. NAFLD is believed to affect 80-100% of diabetic patients and progresses to NASH in 20-50% of cases. Mortality due to liver disease is thus two to three times higher in the diabetic population than in the overall population.

Exhibit 8: NASH background

What is NASH?	NAFLD is the most common form of liver disease in the Western world and represents a spectrum ranging from bland steatosis to NASH. Patients with bland steatosis typically follow a more benign course, whereas with NASH, the fat that accumulates in the liver causes inflammation and scarring, and has the potential to progress to cirrhosis and liver cancer. NASH seems to occur in the setting of insulin resistance or type 2 diabetes and is associated with increased coronary artery disease and cancer.
Prevalence	Worldwide: 10% of population (NAFLD: 25%). Found in all ethnic and age groups but peaks in fourth decade in men and sixth decade in women.
Symptoms	Usually asymptomatic and diagnosis of exclusion after evaluation for liver enzyme elevation or incidental abdominal imaging. Occasionally, fatigue, right upper abdominal pain and weight loss.
Diagnosis of NASH	■ Liver function tests. ■ Imaging: ultrasound, CT scan, magnetic resonance imaging. ■ Liver biopsy and histopathology remains the gold standard. No validated biomarker yet.
Treatment	No specific NASH drug treatment available, so treatment is aimed at associated conditions (only vitamin E and pioglitazone have shown beneficial effects in NASH): ■ Obesity: weight loss – diet, regular exercise, drugs (orlistat), bariatric surgery. ■ Insulin resistance: insulin sensitisers – thiazolidinediones (TZDs), metformin, meglitinides. ■ Hyperlipidaemia: lipid lowering agents – statins, fibrates, omega-3 fatty acids. ■ Oxidative stress: antioxidants – vitamin E, betaine, N-Acetyl-cysteine, lecithin, silymarin, beta-carotene. ■ Pro-inflammatory cytokines: anti-TNF agents (pentoxifylline, monoclonal antibodies). ■ Bacterial overgrowth: probiotics. ■ Apoptosis: cytoprotective agents (ursodeoxycholic acid), novel Rx (ACE/A2R inhibitors, oligofructose, incretin analogues).

Source: Edison Investment Research

We estimate that around 60 million people could be affected by NASH in the EU and US based on epidemiology data; hence, this represents a significant opportunity and we believe a product that is successfully developed could achieve blockbuster sales. Moreover, recent deals have reached overall values of up to $1.7bn (see Exhibit 9), which is indicative of the interest of pharmaceutical companies in this field. We typically do not include prospective indications within our valuation estimates until formal clinical plans are outlined and started. Hence, at this stage we are not including NASH in our valuation until the company outlines more definitive plans for this indication.

Exhibit 9: Selected NASH competitors

Product	Company	Status	Comments
Ocaliva	Intercept	Phase III	2,000-patient REGENERATE Phase III study; it will complete interim cohort enrolment in H117. Phase II CONTROL trial readout in 2017.
Elafibranor	Genfit	Phase III	2,000-patient RESOLVE-IT Phase III trial. Complete enrolment in H117. Readout in H218.
IVA337	Inventiva	Phase IIb	225-patient study. Two doses, randomised, placebo-controlled. Primary completion date June 2018.
Cenicriviroc	Tobira (Allergan)	Phase II	Currently in a Phase II study. Due to start a Phase III trial in 2,000 patients in April 2017. Acquired by Allergan for $1.7bn overall value.
Emricasan	Conatus	Phase II	Recruiting patients in two Phase II trials. Data in 2018. Option granted to Novartis for $50m upfront.
Selonsertib	Gilead	Phase II	Data in combination with mAb simtuzumab presented at The Liver Meeting in November 2016 showed regression of fibrosis and improvements in other measures of liver disease.
GS-9674	Gilead	Phase II	Phase I data presented at The Liver Meeting in November 2016. Safety profile and biological activity established. Acquired from Phenex Pharmaceuticals; total deal value $470m.
GS-0976	Gilead	Phase II	Programme acquired from Nimbus Therapeutics. $1.2bn total deal value ($600m paid to date).

Source: Edison Investment Research

A portfolio of discovery programmes and a partnership

Research and development

As increased NOX activity is involved in a number of pathways in different tissues, Genkyotex is pursuing research programmes to develop additional NOX inhibitors with applications in neurology, hearing loss and oncology. We are not including these projects in our model until clinical data are generated.

Partnering with the world's largest vaccine manufacturer

The new company is inheriting the collaboration agreement between Genticel and SIIL. SIIL sells more than 1.3 billion doses annually and is the largest vaccine producer in the world. SIIL manufactures the single shot DTaP vaccine, which protects against diphtheria, tetanus and pertussis (whooping cough). According to Genkyotex, around two-thirds of children immunised globally are vaccinated with a product manufactured by the Serum Institute.

Around 86% of children aged 12-23 months receive the DTP vaccine worldwide. Moreover, *Bordetella pertussis* antigens are included in multiple complex vaccination schedules such as hepatitis B (HB), polio (IPV) and influenza B (Hib).

The partnership involves the licence of Genkyotex's Vaxiclase used as an antigen (GTL003) to SIIL for its use in the development of acellular multivalent combination vaccines that include pertussis antigens. The licence covers all countries of the world except the US, Europe, Canada, New Zealand, Australia, Japan, Israel and Turkey. Genticel/Genkyotex is eligible for up to $57m in upfront, development and sales milestone payments, as well as single-digit royalties on net sales. To date, Genkyotex has received nearly $1.7m from SIIL. At present, SIIL is in the process of finishing formal preclinical testing before starting clinical trials. If they are able to strike a deal on similar terms for the more profitable western markets, the potential milestones could provide significant upside.

A synergistic contribution

The transaction between Genticel and Genkyotex was approved by Genticel's shareholders at their general meeting on 28 February 2017. As described in regulatory filings (*Traite d'Apport* and Document E), it is an all-share transaction in which Genticel will issue 62.3m shares to Genkyotex shareholders. They will receive 11.8355 new shares of Genticel for each contributed share of Genkyotex and hold 80% of the share capital and voting rights of Genticel, non-diluted.

Exhibit 10: Share transaction

Company	Current shares outstanding	Value (€)	New shares
Genticel	15,570,055	30,000,000	62,279,951
Genkyotex	5,262,133	120,000,000	N/A

Source: Edison Investment Research, Genticel

Genkyotex reported €21.8m gross cash at end March 2017, which we forecast should be enough to fund clinical development over the next two years.

Sensitivities

Genkyotex is subject to the usual drug development risks, including clinical development delays or failures, regulatory risks, competitor successes, financing and commercial risks. The main sensitivity in the near term relates to GKT831, in particular the successful completion and results from the PBC Phase II study. As PBC is considered the proof of concept in liver fibrosis that could

open the NASH opportunity, the investment case in the long term would be affected by a clinical setback in PBC.

Regulatory approval and competitive dynamics will be key for the commercial success of GKT831. Several competitors in PBC exist and while some of them will fail due to the inherent attrition rates associated with clinical development, GKT831 will not have a first to market advantage. A differentiated safety and efficacy profile will be key to garner market share.

Genkyotex is exploring the potential of GKT771 other NOX inhibitors in additional indications. At this stage, data from these studies are unlikely to be a major share price driver. However, as progress is made with these assets, they could gain more visibility and become more critical to the investment case.

Valuation: rNPV of €268m or €3.5 per share

Our valuation of Genticel was previously placed under review pending the in-licensing of assets as part of the strategic review that was initiated in Q316. This review has led to the strategic combination of Genticel and Genkyotex, with the combined entity called Genkyotex.

Edison's updated valuation for the new entity is based on GKT831 in the PBC indication and the SIIL deal, leaving all other product development opportunities and additional indications as upside. Taking conservative market share and pricing assumptions and using our standard 12.5% discount rate produces a risk-adjusted NPV of €268m or €3.5 per share, with 77.85m shares post-transaction. For the SIIL deal, we include the present value of the milestones according to our own assumptions on the likelihood and timing of receipt. At this stage we are not including royalties on sales of the product/s, which are undisclosed and it is therefore challenging to estimate future potential sales. A potential deal in western countries remains upside.

Our assumptions for PBC

Our assumptions for this programme are:

- The company develops the GKT831 itself, hence no upfront or milestone payments from a potential future licensing partner are assumed in our model.
- The company funds further clinical development, registration and launch in the EU and US in 2023. We assume c $30m clinical trial costs for a Phase III study in PBC, assuming c 200 patients.
- We assume a standard 90% gross margin and SG&A cost of 30% of sales revenues at peak sales of $1.1bn.
- We assume a 40% probability to reach the market, in line with standard success rates at this stage of development.

Exhibit 11: Valuation

Product	Peak sales ($bn)	Probability	rNPV (€m)	rNPV per share (€)
GKT831	1.1	40%	598.8	7.7
SIIL	N/A	N/A	7.7	0.1
Expenses		40%	(359.6)	(4.6)
Net cash		N/A	20.8	0.3
Total rNPV			**267.7**	**3.5**

Source: Edison Investment Research

NASH could add €30-90m

Although at this stage we do not include the NASH opportunity within our valuation (as we generally do not include programmes until more formal development plans are in place), we have also

examined the valuation potential if this indication is pursued in the future. We provide two scenarios: (1) the company conducts the programme itself; or (2) the company partners it with another company post Phase II data. For both scenarios we project launch in 2024 and a 10% probability of success. Given the size of the patient population, we believe that $2bn peak sales are achievable even if there are other competitors in this field. We consider two potential scenarios for NASH:

- A partnering strategy could add around €30m to our valuation. If the company partners GKT831 in the NASH opportunity once Phase II data are available, we estimate this could add around €30m to our valuation; this is based on assuming a fairly standard mid-teens royalty rate, although does not include any specific milestone payments. We also include Phase II trial-related costs in this scenario.
- A go-it-alone strategy could add around €90m. If the company retains full rights we estimate this could be worth around €90m. Although going it alone would likely require a higher capital outlay, which we have included in our estimation, to fund both full clinical development (including a Phase II and III trial) and the cost of building commercial infrastructure, in the longer term it should be significantly more profitable than a simple royalty on sales, potentially with a 50-60% pre G&A margin.

We will update our assumptions and valuation when there is guidance from the company on the path forward in NASH. We note that deals in the liver fibrosis area are indicative of the interest of large pharmaceutical companies in the anti-fibrotic approach. In particular, Tobira was acquired by Allergan for a c $595m upfront payment and an additional $1.1bn in potential milestone payments in September 2016, after Tobira announced its drug candidate had met the secondary endpoint of improving liver fibrosis without worsening NASH.

Financials

We have updated our financial forecasts (which were previously under review) following the strategic combination to form Genkyotex. To date, pro forma statements are available to end June 2016 (see Document E and Exhibits 12 and 13). We have provided a simple pro forma 2016 estimate (shown in Exhibit 14) based on available information; we expect the full pro forma 2016 accounts to become available around mid-2017 (and we will update our numbers accordingly). Our 2016 pro forma estimate includes: (i) reported Genticel FY16 financial results; (ii) H116 Genkyotex financial results, which we have extrapolated to arrive at estimated FY16 Genkyotex (pre-combination) financial results; and (iii) H116 transaction-related adjustments, which we have kept constant.

The main elements to consider for our 2017 and 2018 forecasts were operating expenses, as these will likely be the most significant financial components. Pro forma G&A spend for H116, excluding transaction-related adjustments, was €2.5m. Hence, we anticipate underlying G&A spend in 2017 and 2018, of around €5-6m per year (excluding any transaction-related costs).

In 2017 and 2018, we expect Genkyotex to fund the Phase II GKT831 PBC trial, which is expected to yield top-line data in 2018. We believe this trial, in around 90 patients, could cost around €10-12m over this timeframe. We also include R&D spend on the Phase I GKT771 trial, and R&D spend on earlier-stage programmes. We forecast R&D of €7m in 2017 and €10m in 2018.

Genkyotex reported gross cash of €21.8m at end of Q117. We estimate this should be sufficient to fund operations for around two years, including near-term milestones, namely clinical trials initiation and readout as well as R&D activities. Our estimated net cash of €20.8m at the end of Q117 includes c €0.9m Genticel debt from OSEO grants (French public funding) related to HPV research projects and a global industrial collaboration (Magenta). These grants are interest-free and

repayable according to a schedule that goes into 2023. Additionally, Genkyotex expects to receive an additional €3m in tax credits.

Exhibit 12: Summary pro forma profit and loss statement for H116

	Genticel €m	Genkyotex CHFm	Genkyotex €m	Adjustments €m	Pro forma €m
Revenue	0.000	0.000	0.000	0.000	0.000
Gross Profit	0.000	0.000	0.000	0.000	0.000
Other Revenues	0.220	0.000	0.000	0.000	0.220
R&D	(4.873)	(2.797)	(2.552)	(2.319)	(9.744)
G&A	(2.063)	(0.587)	(0.535)	(8.012)	(10.610)
Operating Income	(4.772)	(3.051)	(2.783)	(10.331)	(17.886)
Profit Before Tax	(4.751)	(3.131)	(2.857)	(10.331)	(17.939)
Net Income	(4.751)	(3.202)	(2.922)	(10.331)	(18.004)

Source: Genticel/Genkyotex Document E. Note: Exchange rate used is CHF1.0960/€ (average over H116).

Exhibit 13: Summary pro forma balance sheet (to end June 2016)

	Genticel €m	Genkyotex CHFm	Genkyotex €m	Adjustments €m	Pro forma €m
Total non-current assets	5.415	0.154	0.143	11.787	17.345
Total current assets	15.177	2.604	2.397	1.084	18.658
Of which cash	4.637	1.993	1.834	1.084	7.555
Total assets	**20.592**	**2.758**	**2.540**	**12.871**	**36.003**
Total equity	15.898	0.857	0.789	11.043	27.730
Total non-current liabilities	1.899	1.018	0.937	0.000	2.836
Of which non-current financial debt	1.599	0.000	0.000	0.000	1.599
Total current liabilities	2.795	0.884	0.814	1.828	5.437
Of which current financial debt	0.794	0.000	0.000	0.000	0.794
Total shareholders' equity and liabilities	**20.592**	**2.759**	**2.540**	**12.871**	**36.003**

Source: Genticel/Genkyotex Document E. Note: Exchange rate used is CHF1.0867/€ (at end June).

Exhibit 14: Financial summary

€000s	2016e	2017e	2018e
Year End December	IFRS	IFRS	IFRS
PROFIT & LOSS			
Revenue	1,304	0	0
Cost of Sales	0	0	0
Gross Profit	1,304	0	0
R&D expenses	(12,687)	(7,000)	(10,000)
G&A expenses	(14,324)	(5,500)	(5,000)
EBITDA	(21,698)	(12,000)	(13,000)
Operating Profit (before amort. and except.)	(21,698)	(12,000)	(13,000)
Intangible Amortisation	0	0	0
Exceptionals	0	0	0
Other	0	0	0
Operating Profit	(21,698)	(12,000)	(13,000)
Net Interest	23	13	2
Profit Before Tax (norm)	(21,675)	(11,987)	(12,998)
Profit Before Tax (FRS 3)	(21,675)	(11,987)	(12,998)
Tax	0	0	0
Profit After Tax (norm)	(21,675)	(11,987)	(12,996)
Profit After Tax (FRS 3)	(21,675)	(11,987)	(12,997)
Average Number of Shares Outstanding (m)	77.9	77.9	77.9
EPS - normalised (c)	(27.8)	(15.4)	(16.7)
EPS - (IFRS) (c)	(27.8)	(15.4)	(16.7)
Dividend per share (c)	0.0	0.0	0.0
Gross Margin (%)	NA	NA	NA
EBITDA Margin (%)	NA	NA	NA
Operating Margin (before GW and except.) (%)	NA	NA	NA
BALANCE SHEET			
Fixed Assets	11,995	11,995	11,995
Intangible Assets	11,829	11,829	11,829
Tangible Assets	167	167	167
Fixed term investments	155	155	155
Other	0	0	0
Current Assets	30,383	18,397	5,398
Stocks	0	0	0
Debtors	3,512	3,512	3,512
Cash	26,871	14,884	1,886
Other	0	0	0
Current Liabilities	(4,901)	(4,901)	(4,901)
Creditors	(4,303)	(4,303)	(4,303)
Short term borrowings	(598)	(598)	(598)
Long Term Liabilities	(1,384)	(1,384)	(1,384)
Long term borrowings	(336)	(336)	(336)
Other long term liabilities	(1,049)	(1,049)	(1,049)
Net Assets	36,093	24,106	11,108
CASH FLOW			
Operating Cash Flow	(22,693)	(12,000)	(13,001)
Net Interest	23	13	2
Tax	0	0	0
Capex	(13)	0	0
Acquisitions/disposals	0	0	0
Equity Financing	13,776	0	0
Other items	(345)	(600)	(601)
Net Cash Flow	(9,252)	(12,587)	(13,600)
Opening net debt/(cash)	N/A	(25,938)	(13,951)
HP finance leases initiated	0	0	0
Other	0	600	600
Closing net debt/(cash)	(25,938)	(13,951)	(950)

Source: Edison Investment Research, Genticel and Genkyotex accounts. Note 2016e relates to our pro forma estimates for the combined entity as described above.

Contact details	Revenue by geography
16, Chemin des Aulx CH-1228 Plan - Les-Ouates – Geneva Switzerland +41 (0) 22 880 10 25 www.genkyotex.com	N/A

Management team

CEO Genkyotex: Elias Papatheodorou	Deputy CEO: Dr Benedikt Timmerman
Elias Papatheodorou graduated from Ithaca College and Cornell University, US. He has had a 20-year career in public and private biotechnology companies. He has been senior VP business development at Medigene AG, CBO at Covagen, where he was instrumental in the CHF46m Series B fundraise and the subsequent sale of the company to J&J. Mr Papatheodorou joined Genkyotex in February 2015 as CBO and was named CEO in October 2015.	Dr Benedikt Timmerman has a PhD from the University of Ghent, Belgium, and an MBA from INSEAD, France. He has had a 20-year international career in life science companies. Previously he was senior director R&D of Novartis Seeds (1994-2000), a member of the EU Executive Committee (1995-2000) and a member of Novartis Agribusiness's (now Syngenta) global licensing and acquisitions team (1997–2000). He co-founded Genticel in 2001 (BT Pharma).

Principal shareholders	(%)
Edmond de Rothschild Investment	23.76
Eclosion 2	17.9
Luxemburgeoise Vesalius	8.88
Neomed Innovation V	6.84
Venture Incubator AG	5.57
Biomed Partners	5.45

Companies named in this report

Intercept (ICPT US), Genfit (GNFT FP), Allergan (AGN US), Gilead (GILD US), Novartis (NOVN SW), Alimera (ALIM US), CymaBay (CBAY US)

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