EDISON

Sygnis

Q315 and rights issue

Rights issue to fund market development

Healthcare equipment & services

Sygnis sells its own-brand TruePrime and SunScript kits through its website and an international distributor network. A rights issue for €6.7m plus a €0.6m debt conversion was announced on 17 November. This will allow Sygnis to develop its brand, extend its product range of kits and enter the crucial US market. Kits may also be sold as OEM products for next-generation sequencing. A kit for cell-free DNA "liquid biopsy" analysis, a high growth area, is planned for 2016. Cash at 30 September was €0.6m with a €0.3m loan payment due by the year end.

Year end	Revenue (€m)	PBT* (€m)	EPS* (c)	DPS (c)	P/E (x)	Yield (%)
12/13	0.48	(3.05)	(32.1)	0.0	N/A	N/A
12/14	0.39	(1.92)	(19.3)	0.0	N/A	N/A
12/15e	0.65	(2.50)	(19.0)	0.0	N/A	N/A
12/16e	2.50	(0.93)	(5.91)	0.0	N/A	N/A

Note: *PBT and EPS are normalised, excluding intangible amortisation, exceptional items and share-based payments. FY16e EPS assumes 17.4m share post-rights.

Sales starting to build

Sales of €0.3m for the nine months to September 2015 (9M15) are mostly Caco-2 licensing fees, but with kit sales developing: 102 kits in H1 and 147 in Q3 including repeat orders. In 2016, Sygnis will target single cell genome amplification as a high growth area where its novel enzymes have a clear technical advantage. OEM kits may be sold with next-generation sequencing systems supplied by leading scientific equipment companies.

Innovative product range

Sygnis's core IP is a range of novel engineered enzymes for genetic analysis and genome sequencing. The two own brands are TruePrime and SunScript. TruePrime kits copy and amplify the whole genome before DNA analysis and gene sequencing. Sygnis has shown data on the advantages of avoiding random primers by using the TruePrime system. This gives better quality genomic DNA with much less contamination from extraneous DNA sources. The SunScript kit converts short-lived RNA messages in cells into DNA for analysis or sequencing. The enzyme is stable with high yields and sensitivity claimed; it can work together with TruePrime. A planned 2016 launch is for a cell-free DNA kit for liquid biopsy in research.

Valuation: Management expects a strong 2016

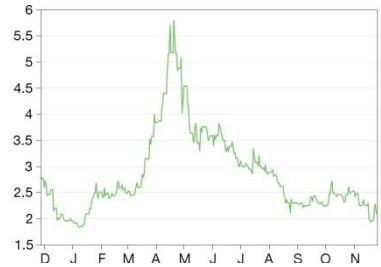
Value progression depends on the success of the TruePrime and SunScript kits with a set of new product launches and US entry planned for 2016. Sales are guided by management at between €0.5m and €0.7m in FY15 and at €2.5m in 2016. We maintain our revenue forecasts, but expect lower PBT than previously in FY15 and FY16. Guidance puts Sygnis on a prospective FY16 market cap to sales multiple of about 12x. Cash outflow for 9M15 was €3.4m. The rights issue at €1.90/share could raise €6.7m gross in cash. Some €0.6m of debt is being converted to equity with €0.3m remaining due in Q415. Cash at 30 September was €0.6m.

27 November 2015

Price	**€2.07**
Market cap	**€28m**

Net debt (€m) at 30 September 2015	2.3
Shares in issue at 17 November (excluding the planned rights issue)	13.5m
Free float	43%
Code	LIO1
Primary exchange	Frankfurt
Secondary exchange	NA

Share price performance



%	1m	3m	12m
Abs	(20.1)	(9.3)	(27.4)
Rel (local)	(23.7)	(19.9)	(36.4)

52-week high/low	€6.15 €1.82

Business description

Sygnis develops tools for molecular biologists. Its main focus is in the field of polymerases for the amplification and sequencing of DNA. Sygnis is launching a direct sale range of TruePrime and SunScript products over 2015 and 2016. A product, SensiPhi, is partnered with Qiagen.

Next event

FY15 results	April 2016

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Edison profile page

Novel enzymes, growth markets

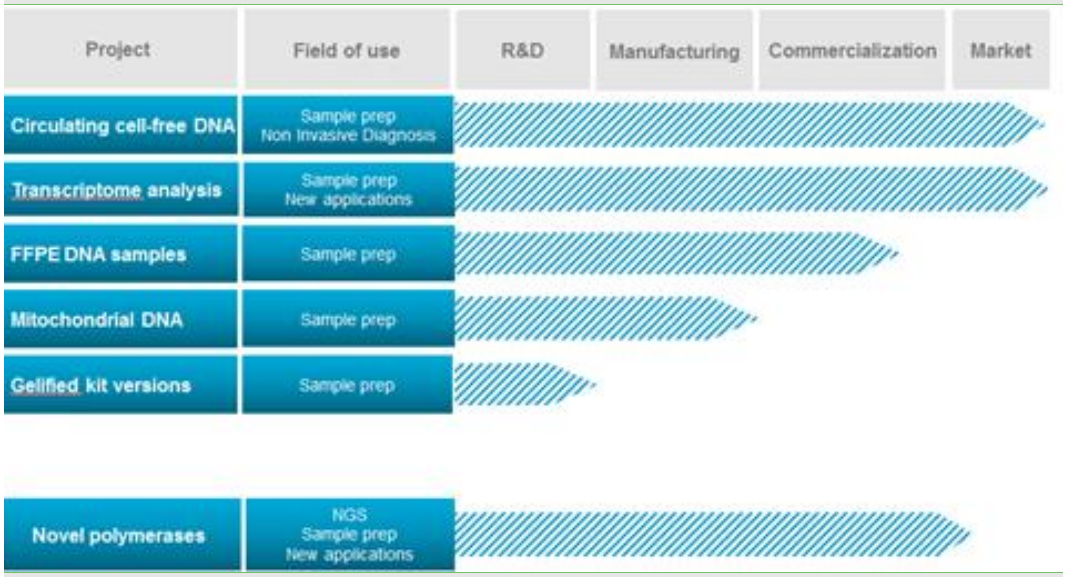
Sygnis has been transforming itself over 2015 from a supplier of enzymes that third parties incorporate into their own-brand kits to a standalone company with its own technology and brands sold through distributors and a direct web sales channel. Non-core technologies are out-licensed on non-exclusive deals. In 2015, two important new brands, TruePrime and SunScript, were launched. Exhibit 1 shows the timelines for each with multiple kits types. [1]

Exhibit 1: Branded kit launches in 2015

Source: Sygnis

Sygnis has a major set of new products in development, two of which are scheduled to reach the market in 2016 and two which should be in commercialisation in the same year, Exhibit 2.

Exhibit 2: 2016 development projects



Source: Sygnis

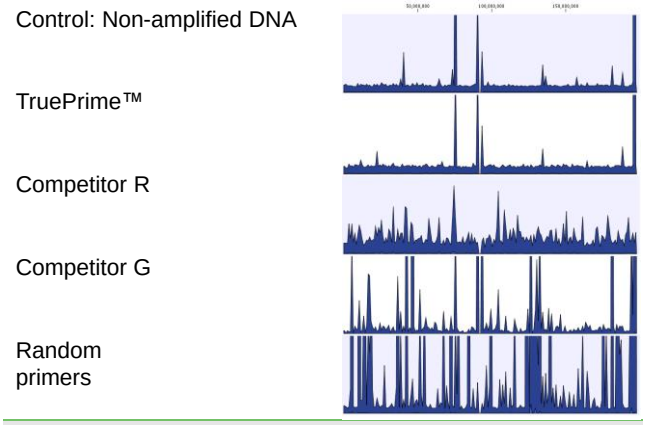
[1] In Exhibits 1 and 2, Gelified refers to freeze dried (lyophilised) enzymes. These are very stable in that format.

TruePrime

DNA has two strands. To amplify it, the double helix of DNA is separated into single strands. To copy these, polymerases (DNA copying enzymes) require a short double-stranded section. This double-stranded starting point is produced in most amplification kits by using random primers, chemically synthesised short strands of DNA that bind to the single strands. The polymerase enzymes bind to these double-stranded primer sections and add new DNA bases (the letters of the genetic code) onto the primer. This copies and amplifies the DNA.

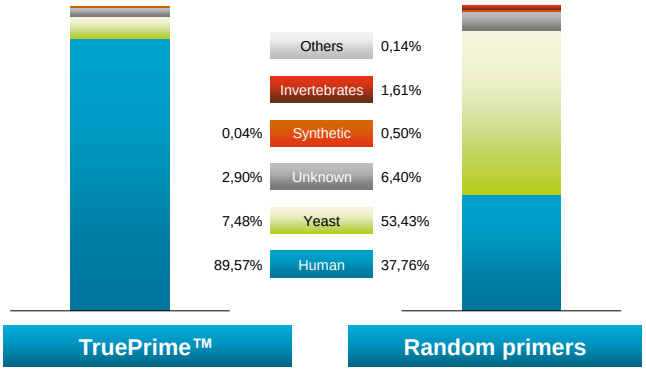
Random primers are still patent protected, for example US6124120 A, which expires in October 2017, covers random primers for multiple displacement amplification, the standard method. Sygnis has avoided the use of random primers using a new, highly stable enzyme: TthPrimPol. The commercial advantage could be that this allows other companies to enter the market sooner. There are also technical advantages. The TthPrimPol enzyme randomly binds to single-strand DNA and creates short, double-stranded, primed regions so no added random primers are required. The high-efficiency, proven Phi29 polymerase then extends the primer to create new copies of the DNA. By using TthPrimPol, Sygnis claims that more primers are created and that this increases the sensitivity of the amplification twofold. The quality of the copying is higher and better than competitors; Exhibit 3 shows fewer random over-copied sections (shown by spikes) relative to competitor-copied DNA. TruePrime is less sensitive to extraneous DNA contamination. Exhibit 4 shows that high-purity human DNA is obtained even with a contaminated starting material. When amplifying the genome of a single microscopic cell, the risk of contamination is high.

Exhibit 3: TruePrime produces high-quality DNA, comparable to native DNA, relative to competitors



Source: Sygnis based on amplification of Human Chromosome 3 Coverage (12m readout pairs)

Exhibit 4: TruePrime shows much less contamination from extraneous DNA as avoiding random primer use



Source: Sygnis

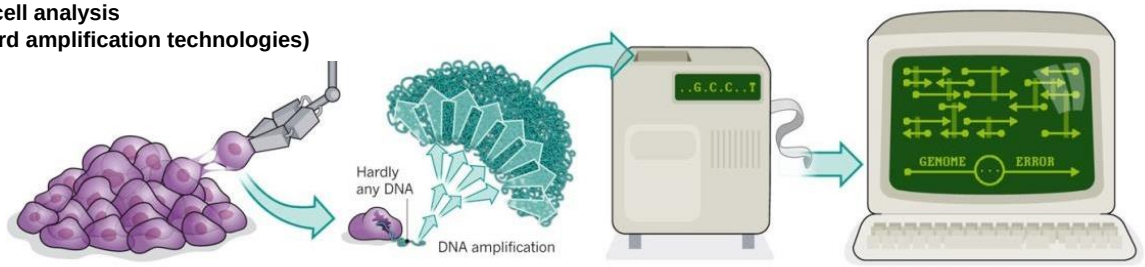
Highly sensitive amplification enables smaller amounts of DNA to be copied. This is why the first TruePrime kits with superior technical qualities are being aimed at the fast-growing and technical single-cell amplification market, Exhibit 5. In addition, since there are more primers generated by the enzyme, coverage of the genome is potentially 20% better.

The two current whole genome amplification (WGA) kits work with DNA and were launched in early 2015. One is for single cells (scWGA) while the other general-purpose WGA kit is used with more abundant DNA. Both use Sygnis's novel and patent-protected TthPrimPol polymerase enzyme. This does not require random primers – short sections of synthetic DNA needed to start the DNA copying (amplification) reaction. This cuts costs and has technical advantages in speed and accuracy with less copying bias. The SensPhi enzyme licensed to Qiagen does require random primers.

In early June 2015, a rolling circle amplification (RCA) TruePrime kit was launched. RCA is a standard method for preparing DNA for sequencing to make multiple copies of circular DNA and RNA from small samples such as single bacterial colonies, cell culture samples and various virus types (bacteriophages [cosmids] or RNA viroids). Current methods take up to 18 hours. The new TruePrime kit cuts this to one hour and is primer free with the advantages highlighted above.

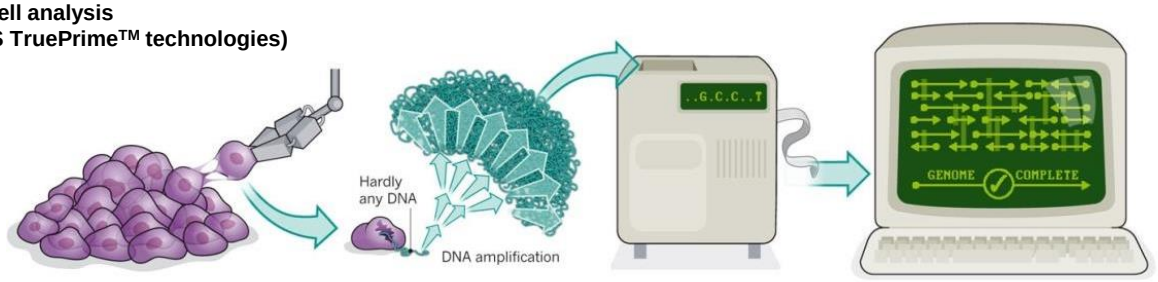
Exhibit 5: Need for better single cell analysis

Single cell analysis (standard amplification technologies)



Cancer tissue	Current technologies create errors during amplification by e.g. amplifying external DNA	Amplified DNA including amplified errors is sequenced	Errors introduced in earlier steps make sequence assembly difficult; final sequence can have gaps

Single cell analysis (SYGNIS TruePrime™ technologies)



Cancer tissue	**SYGNIS TruePrime™**: Complete absence of common artifacts linked to the use of oligonucleotides through primer free amplification	Amplified DNA is sequenced	The sequences are assembled to give a common "consensus" sequence

Source: Sygnis

SunScript

The SunScript range is complementary to TruePirime. SunScript is an enzyme isolated from HIV-1 (HIV uses RNA to carry its genes so it must be copied into DNA, called reverse transcription, when it infects cells). Cells copy (transcribe) their DNA-based genes into multiple RNA messenger molecules; these messengers are used to synthesise proteins. To find out what proteins cells are making, RNA messages are reverse transcribed into DNA for analysis or sequencing. RNA is easily degraded and cannot be sequenced directly; DNA is very stable.

SunScript comes in two varieties: H+ and H-. The natural H+ enzyme has a ribonuclease activity (H+) that automatically destroys the RNA after it has made a DNA copy. This is because RNA-DNA hybrid molecules cannot be read or copied by other enzymes so, for the DNA to be used in other processes, the RNA needs to be destroyed. This is ideal for short RNA messages.

Longer messages can be knotted up and are harder to copy as a whole. Here the SunScript H- reverse transcriptase (RT) is preferred as it does not destroy the RNA, which allows long RNA molecules to be copied at high accuracy. Higher temperatures unknot the RNA molecules, allowing better copying and separation of the RNA-DNA hybrids. SunScript is stable up to 83^{o}C.

The RT PCR kit is a real-time (RT) measurement so the relative abundance of a specific RNA gene message can be determined – even if only a few copies are present. It detects a specific sequence.

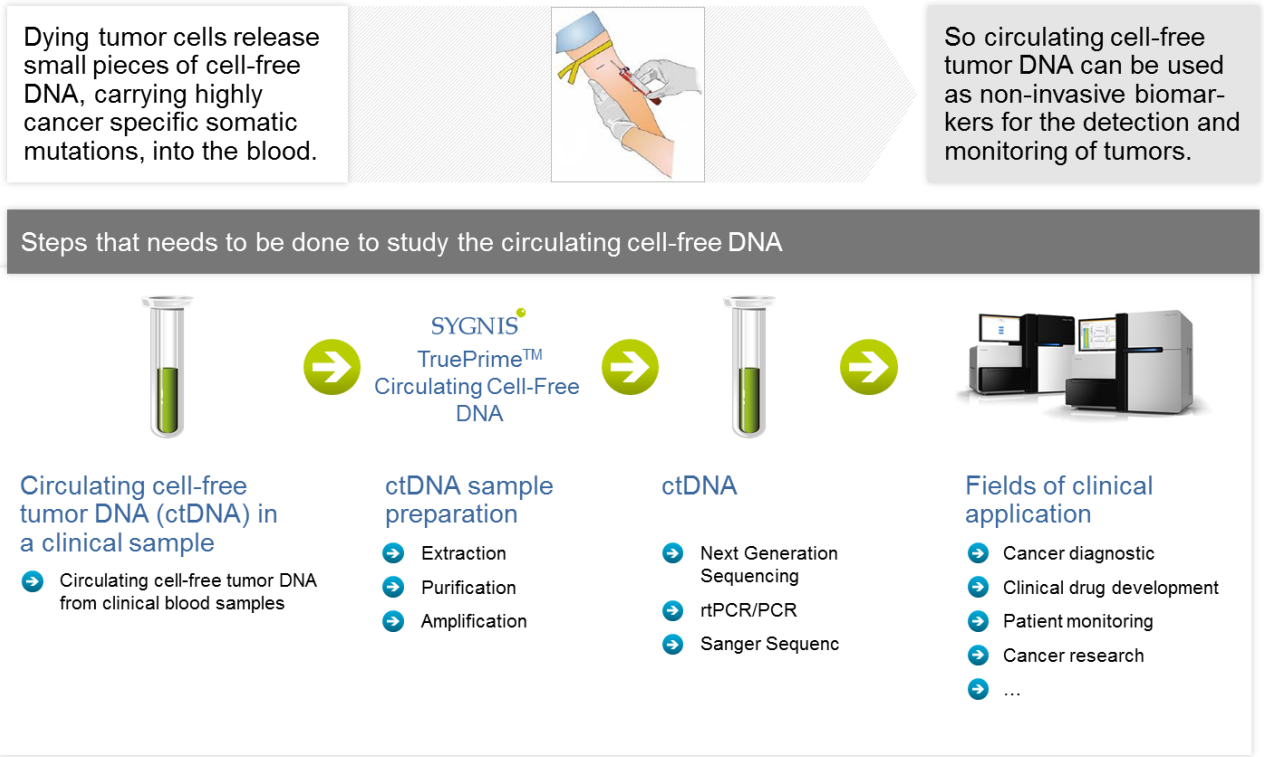
The TruePrime whole transcriptome amplification (WTA) kit combines both new enzymes. This allows RNA messages to be directly amplified into DNA for sequencing or analysis.

Cell-free DNA diagnostics

An important trend is the interest in detecting and monitoring cancer through the use of liquid biopsy. The same basic method can be used to screen pregnant women for foetal genetic abnormalities without the need to sample amniotic fluid – a risky procedure.

In cancer, there are various approaches, but the two current ones are either to detect mutated cancer DNA directly in blood or to isolate cancer cells by using antibodies or microfluidic devices. Sygnis is developing a kit for the direct, cell-free approach, Exhibit 6. In blood, cancer DNA may only be 0.01% of the overall cell-free DNA, so the signals need amplification. Sygnis is developing a TruePrime kit for research use only due for launch in 2016. These tests could be used for screening, but have an obvious eventual clinical role in monitoring treatment and in detecting cancer reoccurrence. Cancer diagnostics are one of the fastest growing market areas: management estimates a CAGR of 18%. There is a lot of current clinical research interest that could provide immediate sales and data. Clinical applications will require extensive validation.

Exhibit 6: Cell-free DNA diagnostics



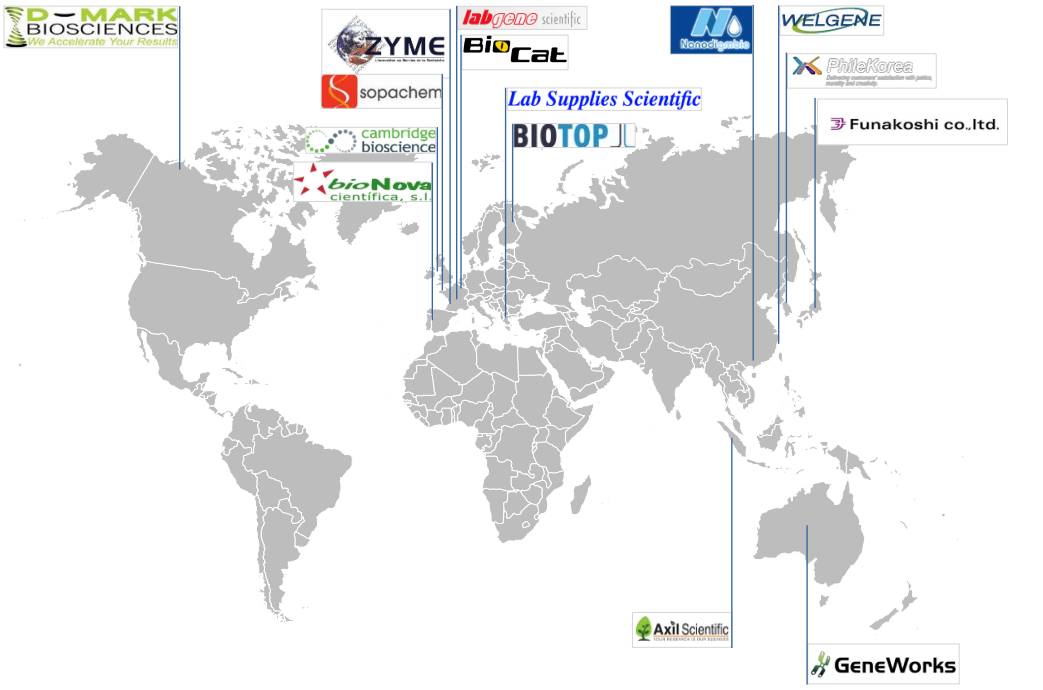
Source: Sygnis. Note both TruePrime and SunScript can be used depending on the application

In genetic testing in pregnancy, it may be necessary to test for genetic abnormalities. One such abnormality is Down's syndrome caused by an extra copy of chromosome 21. To be definitive, this test currently requires an amniocentesis, invasive sampling of the amniotic fluid to obtain some free floating foetal cells. This is risky. A developing alternative is to use cell-free DNA shed by the placenta (this is foetal material). This cell-free DNA can be amplified from the mother's blood. If excess foetal chromosome 21 DNA is present, this can be determined. Currently this is a research technique, but it is being increasingly investigated. It is applicable to other genetic conditions. Currently, there are no research publications showing Sygnis products in this indication, but the technique uses standard molecular biology methods.

Distribution and direct sales

The now extensive distributor network, which covers key EU countries and Japan, is being established, Exhibit 7. In H1, revenues were lowered by promotional discounts and 102 kits were sold. In Q3, 149 kits were sold (Q3 report, page 9).

Exhibit 7: Sygnis's distributor network



Source: Sygnis

According to management from Q3 results, the distributors are now selling the majority of the kits. Web sales are going well.

Entry to the US market is critical for 2016 and the rights issue will provide funds to facilitate this. The US is about 50% of the market for advanced research products and a major diagnostics market. There are very well-established competitors in the molecular biology area such as New England Biolabs and Bio-Rad. However, the market responds rapidly to innovation and if the TruePrirme and SunScript brands can be established – especially in growth areas like single cell sequencing and in clinical research into cell-free DNA – then sales could be significant with rapid growth. Sygnis estimates that the next-generation sequencing market is worth $2.5bn, with 23% growth potential. Reagents account for 30-40% of this market.

The appointment of Dr Viribay as vice president, sales and marketing in April 2015 is a crucial appointment since he has experience of direct scientific sales, most recently with Thermo Fisher. Any OEM arrangement with a major scientific instrument supplier could give a significant boost to 2016 sales, but is not currently in our forecasts.

SensiPhi

This is a novel Phi29 DNA polymerase. It has technical advantages, especially for single cell sequencing and amplification of transcribed RNA over the generically available Phi29 enzyme used by many kit manufacturers. The rights to SensiPhi are exclusively licensed to Qiagen. Qiagen uses SensiPhi in four kits in its REPLI-g range. These are the REPLI-g Cell WGA & WTA kits and the

REPLI-g WTA Single Cell Kit. A specific kit for transcriptome analysis using Illumina high-throughput sequencing systems is now available: REPLI-g Single Cell RNA Library Kit.

Double switch

Double switch is a non-core drug discovery technology acquired with Sygnis Pharma. It enables researchers to evaluate protein-protein interactions. It is used in drug discovery. In 2015, it was licensed to Thermo Fisher Scientific on a non-exclusive basis. This follows a sale of another patent in the portfolio to Systasy Bioscience in May 2014. Payments on this technology are not seen as material.

Finance

Although revenues in January to September 2015 were only €307k, a payment is expected from Qiagen in Q4 in respect of SensiPhi, kit sales are growing and Caco-2 cell licensing revenues remain buoyant. The forecast of €650k in 2015 revenues appears challenging, but potentially achievable and within current revenue guidance of €0.5-0.7m and revenues of up to €2.5m in FY16.

Costs were increased in H1 by a €363 one-off item due to restructuring the German operations and setting up a new, smaller lab in Heidelberg. Reported costs were €2.35m (9M15) before the one-off charges. Capitalised development costs were €295k.

Overall cash flow from operations (9M15) was €3.12m. Adding capitalised development gives outflow of €3.42m (9M15), or €3m on an ongoing basis excluding restructuring costs. This implies a €4.4m operating cash outflow for the year. There was some capital expenditure (€112k) and a small equity issue of €360k through a SEDA arrangement with YA Global Master; a new arrangement lasts until 30 September 2018.

We are leaving our 2015 revenue forecasts unchanged, but have adjusted the normalised pre-tax loss forecast to €2.5m for FY15 (from a €1.8m loss). The 2016 revenue expectation remains at €2.5m, but the pre-tax loss has been adjusted as costs are likely to rise to around €3.5m before non-cash charges. This would give a normalised loss of about €0.93m for FY16 (€0.1m loss previously forecast). After the rights issue, this could give 2016 year-end cash of about €3.8m.

The 30 September balance sheet shows a current loan of €923k comprising €600k to Genetrix and €113k to Hopp BioTech; both of which are shareholders. The capital repayment due on the Genetrix €600k loan will be converted to equity as part of the rights issue. The interest (12% pa) and the Hopp BioTech loan plus interest will be paid with cash by 31 December 2015; these total €323k as of 30 September. Interest charges therefore fall in 2016 following loan repayment. The balance sheet has other liabilities recognised as €2m in respect of soft loans from Spanish public institutions. These carry a very low interest rate with terms in excess of 10 years.

Rights issue

The 7-for-2 rights issue is targeted to raise €6.7m in cash. In addition, €0.6m of equity will be issued to Genetrix (as above). The issue could lead to 3.86m new shares issued at €1.90, following which there might be 17.35m shares in issue. We have adjusted the eps forecast based on the possible new share capital amount.

Valuation: A volatile price with growth expectations

Value progression depends on the success of the TruePrime and SunScript kits with more products planned. Forecasts in a launch period are subject to high uncertainty, but sales are developing. The €2.5m FY16 sales guidance from management puts Sygnis on a prospective FY16 market capitalisation to revenue of about 12x, implying high market growth expectations from 2017. In 2016 and 2017, it is possible that Sygnis will enter at least one OEM deal for high-volume kit supply and further develop its product range. Products like cell-free DNA liquid biopsy could be very important. Sygnis is in its early growth phase. so value benchmarks are very hard to apply.

Sensitivities

Sygnis is developing strong brands with a clear position in a crowded market despite well-established competitors. Its products have demonstrated clear technical advantages, which should give a competitive advantage if focused onto specific high-growth indications like single cell and cell-free DNA analysis. Coupled with consistent marketing and a wide distribution network, Sygnis could gain share rapidly if the products are adopted by leading research groups. The US research market remains crucial to longer-term success. The clinical market is much larger and more lucrative, but needs sustained investment.

Exhibit 8: Financial summary

€'000s	2013	2014	2015e	2016e
Year end 31 December	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS				
Revenue	482	392	650	2,500
Cost of Sales	0	0	0	0
Gross Profit	482	392	650	2,500
EBITDA	(2,800)	(1,724)	(2,334)	(900)
Operating Profit (before GW and except.)	(2,881)	(1,781)	(2,382)	(950)
Intangible Amortisation	(800)	(524)	(363)	(300)
Exceptionals	(587)	(283)	(363)	0
Other	(16)	(620)	(150)	(250)
Operating Profit	(4,284)	(3,208)	(3,258)	(1,500)
Net Interest	(169)	(137)	(115)	25
Profit Before Tax (norm)	(3,050)	(1,918)	(2,497)	(925)
Profit Before Tax (FRS 3)	(4,453)	(3,345)	(3,373)	(1,475)
Tax	1,252	(135)	(100)	(100)
Profit After Tax (norm)	(3,050)	(2,053)	(2,597)	(1,025)
Profit After Tax (FRS 3)	(3,201)	(3,480)	(3,473)	(1,575)
Average Number of Shares Outstanding (m)	9.5	10.7	13.7	17.4
EPS - normalised (c)	(32.1)	(19.3)	(19.0)	(5.9)
EPS - FRS 3 (c)	(33.7)	(32.7)	(25.4)	(9.1)
Dividend per share (c)	0.0	0.0	0.0	0.0
Gross Margin (%)	N/A	N/A	N/A	N/A
EBITDA Margin (%)	N/A	N/A	N/A	N/A
Operating Margin (before GW and except.) (%)	N/A	N/A	N/A	N/A
BALANCE SHEET				
Fixed Assets	8,789	8,419	8,622	8,872
Intangible Assets	1,634	1,678	1,709	1,909
Tangible Assets	178	169	221	271
Other	6,977	6,572	6,692	6,692
Current Assets	2,538	4,118	6,534	4,445
Stocks	12	19	41	41
Debtors	57	37	156	353
Cash	2,196	3,764	6,037	3,751
Other	273	298	300	300
Current Liabilities	(2,281)	(1,305)	(794)	(1,000)
Creditors	(519)	(316)	(114)	(500)
Current loans	0	0	0	0
Other	(1,762)	(989)	(680)	(500)
Long Term Liabilities	(3,092)	(2,890)	(2,012)	(2,012)
Shareholder and other loans	(2,804)	(2,890)	(2,012)	(2,012)
Soft loans	0	0	0	0
Other long term liabilities	(288)	0	0	0
Net Assets	5,954	8,342	12,349	10,304
CASH FLOW				
Operating Cash Flow	(3,599)	(3,495)	(3,573)	(1,801)
Net Interest	4	(84)	(115)	25
Tax	(6)	0	0	0
Capex	(19)	(621)	(493)	(600)
Acquisitions/disposals	0	0	0	0
Financing net of costs, inc debt conversion	2,840	5,923	7,325	0
Dividends	0	0	0	0
Other	369	(155)	(871)	90
Net Cash Flow	(411)	1,568	2,273	(2,286)
Opening net debt/(cash)	1,959	608	(874)	(4,025)
HP finance leases initiated	0	0	0	0
Other	1,762	(86)	878	0
Closing net debt/(cash)	608	(874)	(4,025)	(1,739)

Source: Sygnis reports, Edison Investment Research

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