EDISON

Quantum Genomics

Clinical update

QGC001 clinical results

Pharma & biotech

Quantum Genomics announced the results from the 34-patient Phase IIa study of QGC001 for the treatment of mild to moderate arterial hypertension. It showed a 2.7 mmHg placebo-adjusted reduction in the primary endpoint of ambulatory systolic blood pressure (SBP, p=0.16) and a 4.7 mmHg reduction in in-office SBP (p=0.15). The p value improved to p=0.06 using a multivariate analysis, which is encouraging given the trial size, albeit slightly non-significant. Data from this study will be used in the design of the US-based Phase IIb hypertension trial, starting in H217.

Year end	Revenue (€m)	PBT* (€m)	EPS* (€)	DPS (€)	P/E (x)	Yield (%)
12/15	0.1	(4.5)	(0.55)	0.0	N/A	N/A
12/16	0.0	(6.2)	(0.60)	0.0	N/A	N/A
12/17e	0.0	(7.2)	(0.69)	0.0	N/A	N/A
12/18e	0.0	(12.5)	(1.15)	0.0	N/A	N/A

Note: *PBT and EPS are normalised, excluding amortisation of acquired intangibles, exceptional items and share-based payments.

Potential signal of efficacy despite suboptimal design

Although it is based on historical data and not head-to-head comparisons, the effect sizes seen in this clinical study were relatively low compared to those reported for approved hypertension medications, which produce placebo-adjusted changes in SBP in the range of 9-14 mmHg. However, the data on QGC001 are suggestive of activity and could potentially be improved with a more optimised clinical trial design.

Positive correlation with disease severity

Multivariate analysis of the trial data identified baseline hypertension as the strongest contributing factor to efficacy (p=0.01), suggesting that patients with more severe disease respond more strongly to treatment. The upcoming 250-person Phase IIb hypertension trial will enrol patients with “complicated hypertension” or those with elevated cardiac risk, and these criteria may improve effect size.

Potential to focus on patients with the highest need

One of the core premises of QGC001 is that it targets the brain renin-angiotensin system, which is specifically implicated in certain forms of resistant primary hypertension. One such class is the so-called low renin subtype, which is present in 25% of American hypertensive patients and 52% of hypertensive African Americans. The Phase IIb trial will have the potential to select exclusively for these patients who are expected to respond and have the highest unmet medical need.

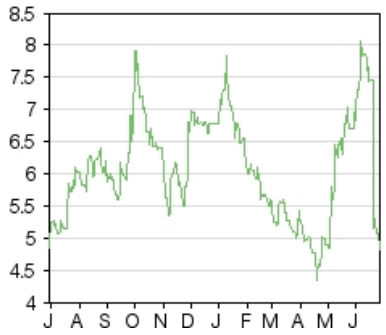
Valuation: €180m or €20.61 per share

We are maintaining our valuation of €180m or €20.61 per share. We believe the lack of statistical significance seen in this trial can be addressed in the Phase IIb, with improved clinical trial design, including enrichment of low renin sub-type patients and those with higher baseline blood pressure levels. We expect to update our valuation with the release of data from the Phase IIa heart failure trial in H118.

27 June 2017

Price	**€4.81**
Market cap	**€42m**
	$1.12/€
Net cash (€m) at 31 December 2016	11.2
Shares in issue	8.4m
Free float	51.3%
Code	ALQGC
Primary exchange	Alternext Paris
Secondary exchange	N/A

Share price performance



%	1m	3m	12m
Abs	(32.5)	(5.1)	(0.8)
Rel (local)	(32.2)	(10.8)	(23.6)
52-week high/low		€8.1	€4.3

Business description

Quantum Genomics is a biopharmaceutical company developing QGC001, a brain aminopeptidase A inhibitor for the treatment of hypertension and heart failure. Its mechanism is implicated in the 25% of patients resistant to treatment.

Next events

Hypertension Phase IIb start	H217
Heart failure Phase IIa data	H118

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Quantum Genomics is a research client of Edison Investment Research Limited

QGC001 Phase IIa results at long last

In June 2017, Quantum Genomics reported the results from the Phase IIa pilot study of QGC001 for the treatment of patients with mild to moderate essential hypertension. QGC001 is a brain aminopeptidase A inhibitor (BAPAI), a novel class of potential anti-hypertensives targeting the brain renin-angiotensin pathway. The study was previously completed in mid-2016, however the results were released as part of a presentation of the study's lead investigator at the 27th annual European Meeting on Hypertension and Cardiovascular Protection.

The trial was a randomised, double-blind, crossover study that measured the change in systolic blood pressure (SBP) in 34 patients over four weeks. Patients were dosed with 250mg of QGC001 twice a day for a one-week lead-in period, followed by 500mg per day. The primary outcome of the study was the reduction in ambulatory SBP measured over daytime hours using a blood pressure monitor. Patients showed a 2.7 mmHg improvement in this measure when compared to placebo, although the difference fell short of statistical significance (p=0.16). The patient's supine in-office blood pressure, measured by a clinician, improved more compared to placebo at 4.7 mmHg, although this measure also failed to reach significance (p=0.15). Other blood pressure measurements, including diastolic blood pressure (DBP) were generally insignificant (Exhibit 1).

Exhibit 1: Effect of QGC001 on different blood pressure measurements.

Measurement	Period	Placebo adjusted change (mmHg)			
		SBP	p	DBP	p
Ambulatory	Daytime	-2.70	0.16	-1.80	0.24
	Night-time	-0.51	0.85	0.64	0.67
	24h	-2.00	0.31	-1.04	0.48
Office		-4.65	0.15	-0.71	0.75

Source: Quantum Genomics

The study was small for a blood pressure study at only 34 patients (which can often reach into the thousands). It is therefore unfortunate, but not necessarily surprising, that statistical significance was missed. Also, approved blood pressure medications typically show an improvement in SBP (after placebo adjustment) from 9-14 mmHg. This effect size is seen across a range of classes treating patients with similar baseline SBP (Exhibit 2). We should note that there is potential for the treatment effect to increase with increased treatment duration, and this effect has been shown for instance with Diovan (valsartan).

Exhibit 2: Improvement in SBP from a selection of drugs*

Drug	Class	Measurement	Duration	Baseline SBP (mmHg)	Reduction in SBP, placebo adjusted** (mmHg)
QGC001	BAPAI	Daytime ambulatory	4 weeks	150	2.7
QGC001	BAPAI	Supine	4 weeks	148	4.7
Vasotec (enalapril)	ACE inhibitor	Seated	4 weeks	147	14
Norvasc (amlodipine)	Calcium channel blocker	Standing	24 hours	N/R	12
Diovan (valsartan)	ARB	Supine or Seated	8 weeks	151	9
Tekturna (aliskiren)	Renin inhibitor	Seated	8 weeks	151	12

Source: Quantum Genomics, FDA labels, FDA review documents. Note: *For illustrative purposes using historical data and not head-to-head comparisons. **Maximum effective dose reported. BAPAI = brain aminopeptidase A inhibitor. ARB = angiotensin receptor blocker. ACE = angiotensin converting enzyme. N/R = not reported in available documents.

Quantum Genomics did a multi-variate analysis that gives some insight into the variables contributing to drug response. The variable with the highest significance was the patient's baseline daytime SBP prior to entering treatment (p=0.01), because patients with the highest blood pressure when entering the study had the highest response. This is consistent with previous data in rats and

humans that suggests that the response correlates with disease severity. In previous studies, the drug had no effect on subjects with normal blood pressure.

The second most significant variable was the difference between patients during treatment and while on placebo at p=0.06, which is much better than in the more naive primary analysis. This suggests that other confounding imbalances between patients worsened the significance of the primary outcome. These issues can at least in part be addressed through future trial design, in particular a larger patient sample size enabling better randomisation.

The adverse event profile was similar between QGC001 and placebo and largely benign (Exhibit 3). Two patients discontinued from the trial due to adverse events, and one withdrew (during the placebo portion) due to severe hypertension. Importantly, the company also did bloodwork on participants and demonstrated that the treatment did not affect any hormones implicated in hypertension (such as renin or aldosterone, among others), suggesting that the drug's effect is the on-target action on BAPA.

Exhibit 3: QGC001 adverse events

	QGC001	Placebo
All Adverse events, n (%)	9 (28,1%)	7 (21,9%)
Serious Adverse events, n (%) Rash Vestibular disorder Arthralgia Severe hypertension	3 (9,4%) 1 1 1 0	2 (6,2%) 1 0 0 1
Change from baseline		
Potassium (mmol/L)	0,13 ± 0,48	-0,07 ± 0,46
Sodium (mmol/L)	0,20 ± 1,9	-0,10 ± 1,5
Creatinine (µmol/L)	-1,4 ± 8,4	0,6 ± 6,5
No significant changes in Haematological nor other biochemical parameters (neither in QGC001 nor in placebo)		

Source: Quantum Genomics

The next clinical step for the company is to initiate its planned Phase IIb hypertension study in the US, which is slated to begin in autumn 2017. The trial will build on the findings of this study and include 250 patients with so-called "complicated hypertension," or those with increased cardiovascular risk. There is potential for the company to enrich the study population for patients with low renin forms of hypertension. These patients are typically unresponsive to angiotensin receptor blockers (ARBs) and angiotensin converting enzyme (ACE) inhibitors, but are expected to respond to BAPAIs like QGC001. The company was previously unable to selectively enrol patients with this disease subtype due to restrictions on racial bias in clinical studies in France. Approximately 25% of hypertensive Americans have a low renin form, and up to 52% of the African American community. The company has stated that it will release the full details of the trial design on 27 June 2017. We currently forecast the trial costing between €5m and €6m, although we may adjust this based on these details. The company is also currently enrolling a European Phase IIa heart failure study, with a primary completion date around the end of 2017 and data expected in H118.

Valuation

We are maintaining our valuation of €180m or €20.61 per share. We believe the lack of statistical significance seen in this trial can be addressed in the Phase IIb trial, with improved clinical trial design, including enrichment of low renin sub-type patients and those with higher baseline blood pressure levels. We expect to update our valuation with the release of data from the Phase IIa heart failure trial in H118.

Exhibit 4: Quantum Genomics valuation

Product	Main Indication	Local	Status	Prob. of success	Launch year	Peak sales ($m)	Patent protection	rNPV (€m)
QGC001	HT	US	Phase IIa complete	15%	2023	1,110	2031	105.13
QGC001	HT	Europe	Phase IIa complete	15%	2023	959	2031	89.18
QGC001	Development costs							(110.90)
QGC101	HF	US	Phase IIa	15%	2023	574	2031	66.91
QGC101	HF	Europe	Phase IIa	15%	2023	687	2031	79.39
QGC101	Development costs							(60.64)
Total								169.07
Cash and cash equivalents (YE16) (€m)								11.20
Total firm value (€m)								**180.26**
Total shares (m)								8.75
Value per basic share (€)								**20.61**

Source: Edison Investment Research, Quantum Genomics reports

Financials

We are not making significant updates our financial forecasts at this time, but have made small adjustments to the timing of items on the balance sheet. We expect that the company will need €20m in additional financing to complete the Phase II trials for both programmes, at which time we expect the company to out-license the programme for further development. We may adjust our financing schedule with more details of the Phase IIb US hypertension study, if the scope of the trial exceeds our current estimates.

Exhibit 5: Financial summary

€000s	2014	2015	2016	2017e	2018e
Year end 31 December	IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS					
Revenue	324	144	0	0	0
Cost of Sales	0	(0)	0	0	0
Gross Profit	324	144	0	0	0
EBITDA	(2,418)	(4,310)	(6,216)	(7,172)	(10,948)
Operating Profit (before GW and except.)	(2,418)	(4,310)	(6,216)	(7,172)	(10,948)
Intangible Amortisation	0	0	0	0	0
Other	0	0	1	0	0
Exceptionals	0	0	0	0	0
Operating Profit	(2,418)	(4,310)	(6,216)	(7,172)	(10,948)
Net Interest	(20)	(222)	0	(2)	(1,601)
Other	(105)	54	18	0	0
Profit Before Tax (norm)	(2,537)	(4,503)	(6,216)	(7,174)	(12,549)
Profit Before Tax (FRS 3)	(2,542)	(4,479)	(6,198)	(7,174)	(12,549)
Tax	335	714	958	933	1,631
Deferred tax	0	0	0	0	0
Profit After Tax (norm)	(2,202)	(3,789)	(5,258)	(6,241)	(10,917)
Profit After Tax (FRS 3)	(2,207)	(3,765)	(5,240)	(6,241)	(10,917)
Average Number of Shares Outstanding (m)	4.8	6.9	8.7	9.1	9.5
EPS - normalised (€)	(0.46)	(0.55)	(0.60)	(0.69)	(1.15)
EPS - FRS 3 (€)	(0.46)	(0.54)	(0.60)	(0.69)	(1.15)
Dividend per share (€)	0.0	0.0	0.0	0.0	0.0
BALANCE SHEET					
Fixed Assets	623	520	701	711	719
Intangible Assets	66	108	142	142	142
Tangible Assets	32	54	60	70	78
Other	525	358	500	500	500
Current Assets	4,129	10,020	13,809	7,558	16,633
Stocks	0	14	1,011	1,011	1,011
Debtors	811	1,354	1,599	1,599	1,599
Cash	3,318	8,652	11,198	4,946	14,021
Other	0	0	1	1	1
Current Liabilities	(4,604)	(2,128)	(3,481)	(3,481)	(3,481)
Creditors	(1,296)	(2,128)	(3,480)	(3,480)	(3,480)
Short term borrowings	(3,308)	(1)	(1)	(1)	(1)
Long Term Liabilities	(279)	(390)	(506)	(506)	(20,506)
Long term borrowings	(6)	(78)	(18)	(18)	(20,018)
Other long term liabilities	(273)	(312)	(488)	(488)	(488)
Net Assets	(130)	8,022	10,524	4,282	(6,635)
CASH FLOW					
Operating Cash Flow	(2,791)	(3,142)	(5,531)	(6,227)	(10,901)
Net Interest	0	0	0	0	0
Tax	0	0	0	0	0
Capex	(304)	(72)	(66)	(25)	(25)
Acquisitions/disposals	0	0	0	0	0
Financing	3,699	12,150	7,744	0	0
Dividends	0	0	0	0	0
Other	116	(296)	399	0	0
Net Cash Flow	719	8,640	2,546	(6,252)	(10,925)
Opening net debt/(cash)	(724)	(5)	(8,573)	(11,179)	(4,927)
HP finance leases initiated	0	0	0	0	0
Exchange rate movements	0	0	0	0	0
Other	(1438)	(71)	60	0	0
Closing net debt/(cash)	(5)	(8,573)	(11,179)	(4,927)	5,998

Source: Edison Investment Research, Quantum Genomics reports

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