EDISON

Quantum Genomics

Development update

Strong Phase IIb data in hypertension

Pharma & biotech

Quantum Genomics released data from the Phase IIb NEW-HOPE trial, which strongly suggests that firibistat is an efficacious, safe drug with a differentiated mechanism that will address a very large patient population. After eight weeks of treatment, patients saw a statistically significant reduction from baseline (p<0.0001) in systolic automated office blood pressure (AOBP) of 9.7mmHg. Importantly there was no oedema that was seen with some of the other major classes of hypertension treatments.

Year end	Revenue (€m)	PBT* (€m)	EPS* (€)	DPS (€)	P/E (x)	Yield (%)
12/16	0.0	(6.2)	(0.60)	0.0	N/A	N/A
12/17	0.0	(10.3)	(0.93)	0.0	N/A	N/A
12/18e	0.0	(13.1)	(0.86)	0.0	N/A	N/A
12/19e	0.0	(16.2)	(1.00)	0.0	N/A	N/A

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

Efficacy similar to major blockbusters

While it is hard to compare across trials as there are differences in clinical trial design, the NEW-HOPE data is fairly similar to the eight-week treatment data for Diovan (valsartan), which had peak sales of $6bn in 2010 (although this also includes sales in heart failure patients) and had shown 6–9mmHg reductions in systolic blood pressure in their eight-week hypertension studies.

Works across races

Black people have a higher prevalence of hypertension and are less likely to have it under control compared to their white counterparts as certain classes of hypertension medication are less effective in black people. In the NEW-HOPE trial, black people saw a 10.5mmHg decrease whereas non-black people saw a 9.1mmHg decrease in systolic AOBP.

A clean safety profile

Headache was the most common treatment-emergent adverse event, seen in 3.9% of patients, followed by 2.7% with some skin issues (dermatitis, eczema). The only serious related adverse event was erythema multiforme, a skin-related hypersensitivity reaction, often caused by exposure to a particular drug. Erythema multiforme has been reported in other hypertension medications as well as in other common therapeutics such as antibiotics and aspirin.

Valuation: Increased to €803m or €66.91 per share

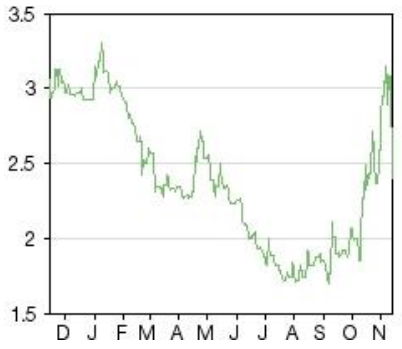
We have increased our valuation of Quantum Genomics from €284m or €23.71 per share to €803m or €66.91 per share, mainly due to increasing our probability of success for firibastat in hypertension from 20% to 50% due to the NEW-HOPE trial data. We also increased the probability of success in heart failure from 15% to 20% due to the innocuous safety profile so far. The probability of success for hypertension remains at a discount to where it would normally be as the company will require a partner to advance firibastat to approval.

13 November 2018

Price	**€2.40**
Market cap	**€29m**

Net cash (€m) at 30 June 2018	5.9
Shares in issue	12.0m
Free float	84%
Code	ALQGC
Primary exchange	Euronext Paris
Secondary exchange	OTCQX

Share price performance



%	1m	3m	12m
Abs	6.2	37.9	(25.5)
Rel (local)	7.0	47.9	(21.1)
52-week high/low		€3.3	€1.7

Business description

Quantum Genomics is a biopharmaceutical company developing firibastat, 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. The Phase IIb study in hypertension was recently very positive and the Phase IIb in heart failure should start by the end of 2018.

Next events

Phase IIb heart failure study initiation	Q418
Start of Phase III in hypertension	H119
Firibastat partnership	2019

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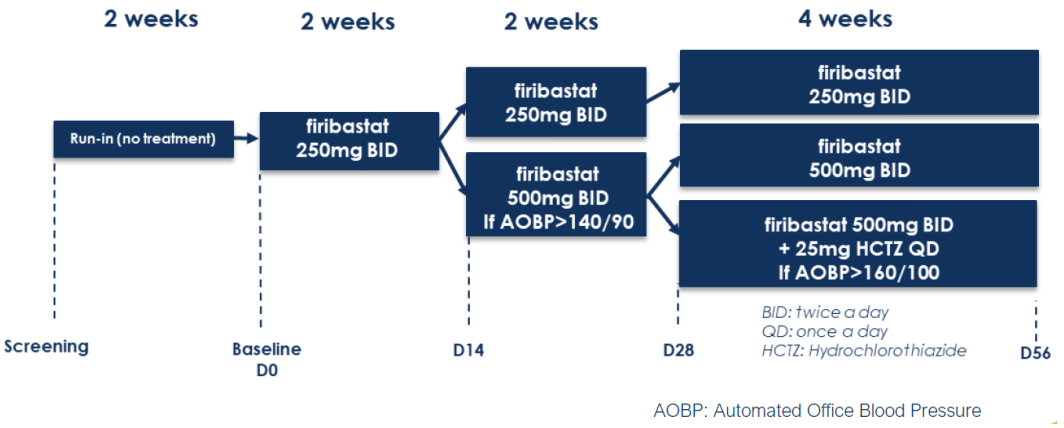
Edison profile page

NEW-HOPE hypertension data

The company announced the results of its NEW-HOPE study in a late-breaking presentation at the American Heart Association (AHA) annual meeting on 10 November 2018. As a reminder, the NEW-HOPE trial completed enrolment faster than expected, enrolling 256 patients (254 included in the intent-to-treat analysis) in just 10 months. NEW-HOPE focused enrolment on hypertensive overweight (BMI 25–45kg/m^2) patients (65% of patients were obese), with a primary endpoint of change from baseline in systolic AOBP at week eight.

Exhibit 1: NEW-HOPE study design



Source: Quantum Genomics

Following a two-week run-in period in which there was no treatment, systolic AOBP had to be 145–170mmHg. Patients start on 250mg twice a day (BID) for two weeks and then either continue at that dose or increase to 500mg BID, if their AOBP was still higher than 140/90, for another two weeks. Following that, patients go on 250mg BID, 500mg BID or 500mg BID with 25mg of hydrochlorothiazide, an often-used diuretic, if their AOBP was higher than 160/100. Ultimately 14% of patients stayed at the 250mg BID dose, 70% of patients stayed at the 500mg BID dose and 15% had to have hydrochlorothiazide added in.

Exhibit 2: NEW-HOPE efficacy data

	Baseline	Week 8	Improvement	P-value
Systolic AOBP, mean (primary endpoint, intent-to-treat analysis)	153.9	144.3	-9.7	<0.0001
Diastolic AOBP, mean (intent-to-treat analysis)	91.5	86.8	-4.5	<0.0001

Source: Quantum Genomics. Note: ND=not disclosed.

The results are quite strong and are in the vicinity of many of the standards of care (see Exhibit 3), but with a differentiated mechanism, which could be especially helpful in treating those currently not well controlled. One weakness to the data is that there was no placebo arm; however, hypertension trials typically do not have large responses with placebo patients, typically seeing declines of 2–4mmHg. Given the strength of the improvement in systolic AOBP, it is highly unlikely to be a result of a placebo response.

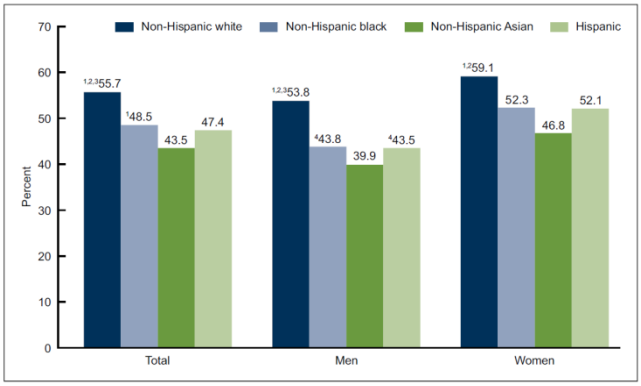
Exhibit 3: Competitor efficacy table

Drug	Class	Company (originator)	Peak sales (all indications)	Duration	Reduction in systolic blood pressure (mmHg)
Firibastat	BAPAI	Quantum Genomics	N/A	8 weeks	9.7
Diovan (valsartan)	ARB	Novartis	$6.0bn (2010)	8 weeks	5.6–9
Vasotec (enalapril)	ACE inhibitor	Merck	$2.5bn (1996)	4 weeks	10–14
Norvasc (amlodipine)	Calcium channel blocker	Pfizer	$4.9bn (2006)	8 weeks	12.1–16

Source: Quantum Genomics, FDA, company filings, Liu et al, (2010) Tolerability and effectiveness of (S)-amlodipine compared with racemic amlodipine in hypertension*; Current therapeutic research, clinical and experimental* 71, 1-29; Ruilope et al. (2010) Blood-pressure reduction with LCZ696, a novel dual-acting inhibitor of the angiotensin II receptor and neprilysin, *Lancet*; 375: 1255-66.

Hypertension is one of the most common medical conditions in the industrialised world and is associated with increased risk of major cardiac events (heart attack, heart failure, aortic dissection, etc) and stroke. The age-adjusted prevalence in the US is 29% of adults,[1] and between 17% and 24% in Western Europe.[2] Diagnosis and treatment rates for the disease are high (83% and 76%, respectively), although the rate of control is low at only 52%.[1] A large cohort of patients appears to be resistant to multiple interventions and 12–15% of diagnosed hypertensive patients are unsuccessfully controlled following treatment with three or more drugs.[3] Importantly, black people have a higher prevalence of hypertension compared to other groups but, along with Hispanic people, are less likely to have their hypertension under control compared to their white counterparts.

Exhibit 4: Percentage of adults with hypertension who have it controlled, by race and sex



Source: Yoon S et al., NCHS Data Brief, 2015 Nov;(220):1–8

As an example, in a pre-specified subgroup analysis of the 33,357-patient ALLHAT trial, which compared the efficacy of amlodipine (a calcium channel blocker), lisinopril (an ACE inhibitor) and chlorthalidone (a diuretic), differences in efficacy between black people and non-black people were consistently seen across timepoints with differences ranging from 1.8 to 6.1mmHg.

Exhibit 5: Differences in efficacy across races for hypertension drugs

	Black people			Non-black people		
SBP change from baseline (mmHg)	Chlorthalidone	Amlodipine	Lisinopril	Chlorthalidone	Amlodipine	Lisinopril
1 Year	-7.7	-5.7	-2.5	-9.8	-8.4	-8.1
2 Year	-8.6	-7.1	-3.4	-10.6	-9.8	-9.5
4 Year	-10.5	-8.8	-6.8	-12.3	-12.3	-12

Source: Wright et al., Outcomes in hypertensive black and nonblack patients treated with chlorthalidone, amlodipine, and lisinopril. *JAMA*, April 6, 2005 – Vol. 293, No 13.

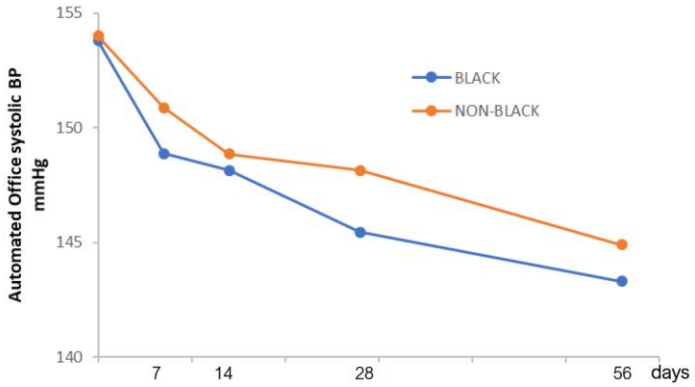
1 CDC

2 Kantar Health

3 Pimenta E and Calhoun DA (2012) Resistant Hypertension: Incidence, Prevalence and Prognosis. *Circulation* 125, 1594-1496.

Firibastat's efficacy in this underserved population, (10.5mmHg reduction in black people and 9.1mmHg reduction in non-black people) is helpful in setting it apart from other therapies.

Exhibit 6: Firibistat efficacy across races



Source: Quantum Genomics

Safety

Safety was innocuous and generally in line with competitors but without certain toxicities such as oedema and fatigue according to an analysis of the drug labels and FDA review documents (see Exhibit 7). Headache was the most common side effect, seen in 3.1% of patients, followed by some skin issues (dermatitis, eczema). The only serious related adverse event was erythema multiforme, a skin-related hypersensitivity reaction, often caused by exposure to a particular drug. Erythema multiforme has been reported in other hypertension medications as well as in other common therapeutics such as antibiotics and aspirin. Importantly, there were no changes in serum potassium or sodium levels observed and renal function was stable.

Exhibit 7: Competitor toxicity table

	Firibastat	Norvasc	Vasotec	Diovan
Oedema		5.1%		
Dizziness	2.0%*	2.6%	4%	3.6%
Flushing		1.6%		
Palpitation		2.2%		
Fatigue		4.5%	3%	2.1%
Nausea		2.9%		1.5%
Abdominal Pain		1.6%		
Somnolence		1.4%		
Headache	3.9%		5%	9.8%
Orthostatic effects			1%	
Asthenia			1%	
Diarrhoea	1.1%*		1%	2.1%
Cough			1%	2.3%
Rash/skin reaction	2.7%		1%	
Viral infection				3.1%
Upper respiratory infection				2.5%
Rhinitis				2.0%
Sinusitis				1.9%
Back pain				1.6%
Arthralgia				1.0%

Source: FDA, *disclosed as adverse events leading to discontinuation

Valuation

We have increased our valuation of Quantum Genomics from €284m or €23.71 per share to €803m or €66.91 per share, mainly due to increasing our probability of success for firibastat for

hypertension from 20% to 50% due to the NEW-HOPE trial data. We also increased the probability of success in heart failure from 15% to 20% due to the innocuous safety profile so far. The probability of success in hypertension remains at a discount to where it would normally be (for a Phase III asset we normally use a 60–70% probability of success) as the company will require a partner to advance firibastat to approval.

Exhibit 8: Quantum Genomics valuation table

Product	Main indication	Local	Status	Prob. of success	Launch year	Peak sales (m)	Patent protection	rNPV (m)
Firibastat (QGC001)	Hypertension	US	Phase II	50%	2023	$1,110	2031	€416.15
Firibastat (QGC001)	Hypertension	Europe	Phase II	50%	2023	$959	2031	€353.08
Firibastat (QGC001)	Development costs							-€132.33
Firibastat (QGC001)	Heart failure	US	Phase IIb	20%	2023	$574	2031	€106.26
Firibastat (QGC001)	Heart failure	Europe	Phase IIb	20%	2023	$687	2031	€126.08
Firibastat (QGC001)	Development costs							-€72.30
Total								€796.94
Net cash (30 June 2018) (m)								€5.91
Total firm value (m)								€802.85
Total shares (31 August 2018) (m)								12.00
Value per basic share								€66.91

Source: Edison Investment Research

Financials

The company ended H118 with €6.0m in cash and investments, adding approximately €0.7m from their €24.0m equity line from Kepler Cheuvreux during the half year. At the current run-rate, the company has stated it believes the equity line would fund it through to the end of 2020. We believe this will be dependent on whether additional trials are conducted by the company or a partner. As late-stage cardiovascular trials are extremely expensive, we expect any large Phase III trials to be financed via a partnership. However, it is possible the company may decide to at least start one of the Phase III trials as it is negotiating with potential partners to not lose any development time.

Exhibit 9: Financial summary

€000s	2016	2017	2018e	2019e
Year end 31 December	PCG	PCG	PCG	PCG
PROFIT & LOSS				
Revenue	0	0	0	0
Cost of Sales	0	0	0	0
Gross Profit	0	0	0	0
EBITDA	(6,216)	(10,292)	(12,622)	(14,792)
Operating Profit (before amort. and except.)	(6,216)	(10,292)	(12,622)	(14,792)
Intangible Amortisation	0	0	0	0
Other	1	0	4	0
Exceptionals	0	0	0	0
Operating Profit	(6,216)	(10,292)	(12,622)	(14,792)
Net Interest	0	0	(485)	(1,445)
Other	18	(176)	(61)	0
Profit Before Tax (norm)	(6,216)	(10,292)	(13,107)	(16,237)
Profit Before Tax (FRS 3)	(6,198)	(10,468)	(13,167)	(16,237)
Tax	958	1,150	1,482	2,111
Deferred tax	0	0	0	0
Profit After Tax (norm)	(5,258)	(9,142)	(11,625)	(14,126)
Profit After Tax (FRS 3)	(5,240)	(9,318)	(11,686)	(14,126)
Average Number of Shares Outstanding (m)	8.7	9.9	13.6	14.1
EPS - normalised (c)	(59.79)	(92.81)	(85.58)	(100.00)
EPS - FRS 3 (€)	(0.60)	(0.95)	(0.86)	(1.00)
Dividend per share (c)	0.0	0.0	0.0	0.0
BALANCE SHEET				
Fixed Assets	701	439	437	437
Intangible Assets	142	91	87	87
Tangible Assets	60	52	59	59
Other	500	296	292	292
Current Assets	13,809	13,478	16,421	14,295
Stocks	1,011	189	139	139
Debtors	1,599	2,197	3,127	3,127
Cash	11,198	11,089	13,155	11,029
Other	1	3	0	0
Current Liabilities	(3,481)	(4,572)	(5,759)	(5,759)
Creditors	(3,480)	(4,571)	(5,758)	(5,758)
Short term borrowings	(1)	(1)	(1)	(1)
Long Term Liabilities	(506)	(474)	(6,626)	(18,626)
Long term borrowings	(18)	(19)	(6,060)	(18,060)
Other long term liabilities	(488)	(454)	(566)	(566)
Net Assets	10,524	8,871	4,473	(9,653)
CASH FLOW				
Operating Cash Flow	(5,531)	(7,977)	(9,863)	(14,112)
Net Interest	0	0	0	0
Tax	0	0	0	0
Capex	(66)	32	(14)	(14)
Acquisitions/disposals	0	0	0	0
Financing	7,744	7,733	6,000	0
Dividends	0	0	0	0
Other	399	104	(57)	0
Net Cash Flow	2,546	(108)	(3,934)	(14,126)
Opening net debt/(cash)	(8,573)	(11,179)	(11,069)	(7,094)
HP finance leases initiated	0	0	0	0
Exchange rate movements	0	0	0	0
Other	60	-2	-41	0
Closing net debt/(cash)	(11,179)	(11,069)	(7,094)	7,032

Source: Edison Investment Research, company reports

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