EDISON

BioPorto Diagnostics

Regulatory update

NGAL test hits a snag at FDA

Healthcare equipment & services

BioPorto announced on 3 October 2018 that it had received feedback from the FDA on its outstanding 510(k) application for The NGAL Test for risk use with acute kidney injury (AKI). The agency said that additional data would be required to support a 'rule-out' claim (ie that the test can exclude the risk of AKI). The company is engaged in discussions with the agency and has revised its timeline: an FDA decision in mid-2019.

Year end	Revenue (DKKm)	PBT* (DKKm)	EPS* (DKK)	DPS (DKK)	P/E (x)	Yield (%)
12/16	20.7	(22.4)	(1.57)	0.0	N/A	N/A
12/17	25.2	(33.7)	(2.03)	0.0	N/A	N/A
12/18e	29.6	(37.2)	(2.09)	0.0	N/A	N/A
12/19e	34.7	(17.0)	(0.91)	0.0	N/A	N/A

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

Reasons for delay unclear

It is difficult to assess the specific area of data deficiency for which the FDA requires more data, but the rule-out claim that was cited is contingent on the negative predictive value (NPV) of the test. This statistic depends upon on both the sensitivity and specificity of the test, as well as the underlying rate of the disorder (AKI). The latter is further complicated by the fact that AKI is defined in terms of serum creatinine, on which NGAL is aiming to improve. Any of these factors could be elements on which the agency requires clarification, albeit not limited to these.

Pathway forward depends on data needed

There are number of different paths forward for the company, which depend on the precise data requested. The FDA may want more confidence that the rate of AKI in the study reflects rates more globally (so that the NPV is representative), and this may be addressed using existing historical data, without a new trial. However, we cannot rule out the possibility that more clinical data may be needed. However, we see the FDA keeping the application open as an indication that there are no fatal flaws.

Changing claims is a possible way forward

The agency previously approved the product Nephrocheck with the claim that it was 'intended to be used in conjunction with clinical evaluation'. This is a weaker claim than the rule-out claim being examined, but the agency's openness indicates a potential pathway in which BioPorto adjusts its claims. We expect more detail following further discussions with the FDA, although the timeline is unclear.

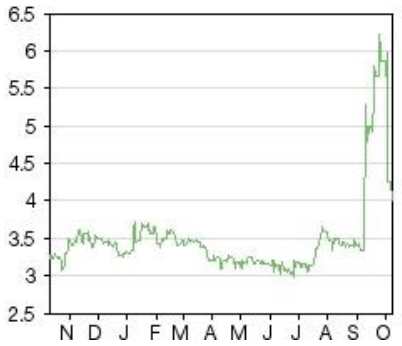
Valuation: Lowered to DKK895m or DKK5.76

We have reduced our valuation to DKK895m or DKK5.76 per basic share from DKK1,105m or DKK7.10 per basic share. This is driven by a delay in the commercialisation of The NGAL Test. We now expect potential approval in late 2019 with first significant sales in 2020 in the US, and this has similarly pushed back our follow-on indications. Our probability of success remains unchanged as we do not consider that this feedback reflects the ultimate approvability of the product.

9 October 2018

Price	**DKK4.01**
Market cap	**DKK624m**
	DKK6.38/US$
Net cash (DKKm) at 30 June 2018	22.5
Shares in issue	155.5m
Free float	83.8%
Code	BIOPOR
Primary exchange	NASDAQ Copenhagen
Secondary exchange	N/A

Share price performance



%	1m	3m	12m
Abs	20.4	26.7	22.3
Rel (local)	31.4	34.6	36.5
52-week high/low	DKK6.2		DKK3.0

Business description

BioPorto is a diagnostic company focused on the development and marketing of antibodies and other products for research and diagnostics. This includes a portfolio of products marketed for research use and The NGAL Test, which the company has submitted to the FDA for the prediction of acute kidney injury.

Next events

Paediatric AKI results	H119
FDA decision on The NGAL Test	Mid-2019

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More data needed for AKI approval

The company stated that 'additional data will be required to support the AKI rule-out claim in order to continue the application process'. The ability of a test to rule out a specific outcome is contingent on the negative predictive value (NPV) of the test. The NPV of a test is the rate at which a negative test result represents a true negative outcome (ie the patient does not develop AKI). Other commonly used diagnostic statistics like sensitivity and specificity are independent of the underlying rate of the condition being tested. However, NPV does depend on this rate (as well as incorporating sensitivity and specificity). Therefore, to support a rule-out claim, the company must provide some data regarding the rates of 'true AKI' observed in its study as well as in the broader population. There are additional complexities regarding what constitutes a 'true AKI' as the benchmark for this diagnosis is the flawed serum creatinine test, on which The NGAL Test aims to improve. In our initiation we detailed some of the issues involved in using a flawed benchmark to evaluate a better test.

It is important to note that the FDA's request for more data should not be interpreted as a rejection of the company's application. During the company's previous iteration of the 510(k) process for The NGAL Test in 2016, the FDA rejected two applications from the company. That is not the case in this instance, which suggests that the agency sees specific points of uncertainty in the application, but does not necessarily see the test as flawed. We have not seen the data being submitted to the FDA, so it is difficult to pinpoint the specific nature of the data deficiency, but we believe a deficiency in the sensitivity or specificity of the test would be a fatal flaw that would result in rejection. However, it should be noted that we cannot categorically exclude any of these possibilities at this time.

There are a number of potential pathways forward at this point, depending on the specific data requested by the FDA and how the company approaches it. In the best-case scenario, the agency wants more information on the underlying rate of AKI in ICU patients and the company can provide historical data. In this case, no additional clinical studies are needed. However, there is also the possibility, given the wide variation in the observed rates of AKI in studies, that these data are not sufficiently conclusive, or that the nature of the data deficiency cannot be addressed with historical data. In this case, the company may still be able to seek approval without additional clinical data if it modifies its claims. It could remove the rule-out claim, and the data could potentially support approval for a more broad risk assessment. However, this will affect how the company can market the test, but it may be able to add these claims in the future after approval with additional clinical data. Finally, there is the possibility that the data deficiency cannot be addressed without the company performing additional clinical studies.

We should note that the recently approved AKI test, Nephrocheck, has the specific labelling that it is 'intended to be used in conjunction with clinical evaluation'. This is a weaker claim than a rule-out claim because the test is only labelled to inform a diagnosis, as opposed to provide a definitive answer. We view the fact that the FDA was amenable to this labelling in this case as encouraging that the agency will exercise similar latitude with The NGAL Test. Although a change in labelling would not be ideal, it may be a viable way to avoid the need for additional clinical data.

Valuation

We have reduced our valuation to DKK895m or DKK5.76 per basic share from DKK1105m or DKK7.10 per basic share. This change is driven by the delay in commercialising The NGAL Test. We have delayed initial sales on the test in accordance with its new timeline (mid-2019 response

from the FDA) to initial commercialisation in the US in late 2019 and significant sales in 2020. Follow-on indications (emergency department and post-surgery) are similarly pushed back, and the paediatric test (although it is technically a different product) is also similarly delayed because we do not expect the retrospective trial to be sufficient to support approval before the supporting adult AKI approval. We also include in our model a 30% probability that they will need an additional clinical trial at a cost of approximately DKK6m. We may update this assessment of clinical costs and risk if we receive more data regarding the current submission. Our probabilities of success remain unchanged, because we do not believe the current communication reflects on the ultimate approvability of the product, although we may amend this view with more insight.

Exhibit 1: Valuation of BioPorto

Programme	Market	Prob. of success	Peak revenue ($m)	Valuation (DKKm)
The NGAL Test	ICU	50%	185.4	611.9
	ED	30%	173.8	278.4
	Post-surgery	30%	55.7	83.6
	Research	100%	2.6	21.8
	Paediatrics	45%	17.4	18.4
Other products	Research	100%	3.9	33.1
Unallocated costs				(174.8)
Total				872.4
Net cash and equivalents (Q218) (DKKm)				22.5
Total firm value (DKKm)				895.0
Total shares (m)				155.51
Value per share (DKK)				5.76
Dilutive warrants (m)				11.6
Total diluted shares				167.1
Value per diluted share (DKK)				5.58

Source: BioPorto reports, Edison Investment Research

Financials

We have adjusted our R&D spending schedule to match the new approval timeline. This has delayed the costs associated with follow-on studies for the emergency department and post-surgery markets until after potential FDA approval. This has reduced our expected R&D expenditures in 2019 to DKK10.0m from DKK35.5m, assuming that no additional studies are needed, although we may update this based on feedback from the company. Our funding requirement remains unchanged at DKK60m, which we model as illustrative debt in 2018.

Exhibit 2: Financial summary

DKK'000s	2016	2017	2018e	2019e
31-December	IFRS	IFRS	IFRS	IFRS
INCOME STATEMENT				
Revenue	20,720	25,155	29,561	34,650
Cost of Sales	(5,027)	(6,907)	(8,095)	(9,489)
Gross Profit	15,693	18,248	21,466	25,161
Sales	(18,041)	(18,545)	(19,033)	(19,603)
R&D	(9,669)	(21,930)	(27,533)	(9,959)
Administrative	(13,030)	(14,267)	(15,923)	(16,719)
EBITDA	(22,596)	(33,134)	(37,632)	(17,729)
Normalised operating profit	(22,596)	(33,134)	(37,632)	(17,729)
Amortisation of acquired intangibles	(182)	(329)	(329)	(329)
Exceptionals	0	0	0	0
Share-based payments	(2,061)	(2,856)	(2,856)	(2,856)
Reported operating profit	(24,839)	(36,319)	(40,817)	(20,914)
Net Interest	148	(570)	462	711
Joint ventures & associates (post tax)	0	0	0	0
Exceptionals	0	0	0	0
Profit Before Tax (norm)	(22,448)	(33,704)	(37,170)	(17,018)
Profit Before Tax (reported)	(24,691)	(36,889)	(40,355)	(20,203)
Reported tax	2,099	4,821	4,160	2,093
Profit After Tax (norm)	(20,538)	(29,297)	(33,336)	(15,251)
Profit After Tax (reported)	(22,592)	(32,068)	(36,195)	(18,110)
Minority interests	0	0	0	0
Discontinued operations	0	0	0	0
Net income (normalised)	(20,538)	(29,297)	(33,336)	(15,251)
Net income (reported)	(22,592)	(32,068)	(36,195)	(18,110)
Basic average number of shares outstanding (m)	131	145	160	168
EPS - basic normalised (ore)	(157)	(203)	(209)	(91)
EPS - diluted normalised (ore)	(157)	(203)	(209)	(91)
EBITDA Margin (%)	-109.1	-131.7	-127.3	-51.2
Normalised Operating Margin	-109.1	-131.7	-127.3	-51.2
BALANCE SHEET				
Fixed Assets	3,069	2,623	3,158	2,622
Intangible Assets	1,959	1,629	1,223	894
Tangible Assets	400	263	1,204	997
Investments & other	710	731	731	731
Current Assets	47,572	62,981	90,103	73,961
Stocks	3,941	3,434	2,661	3,120
Debtors	4,662	6,380	7,289	8,544
Cash & cash equivalents	35,641	47,080	72,412	54,556
Other	3,328	6,087	7,741	7,741
Current Liabilities	(5,146)	(8,653)	(9,751)	(8,533)
Creditors	(1,169)	(3,412)	(5,523)	(4,305)
Tax and social security	(242)	(182)	0	0
Short term borrowings	0	0	0	0
Other	(3,735)	(5,059)	(4,228)	(4,228)
Long Term Liabilities	(1,204)	(883)	(61,040)	(61,040)
Long term borrowings	0	0	(60,000)	(60,000)
Other long term liabilities	(1,204)	(883)	(1,040)	(1,040)
Net Assets	44,291	56,068	22,470	7,010
Minority interests	0	0	0	0
Shareholders' equity	44,291	56,068	22,470	7,010
CASH FLOW				
Op Cash Flow before WC and tax	(22,596)	(33,134)	(37,632)	(17,729)
Working capital	839	2,325	918	(2,930)
Exceptional & other	(239)	(595)	462	711
Tax	2,336	2,005	2,888	2,093
Net operating cash flow	(19,660)	(29,399)	(33,363)	(17,855)
Capex	(357)	(38)	(1,148)	0
Acquisitions/disposals	0	0	0	0
Net interest	0	0	0	0
Equity financing	20,858	40,921	0	0
Dividends	0	0	0	0
Other	(67)	(45)	(157)	0
Net Cash Flow	774	11,439	(34,668)	(17,855)
Opening net debt/(cash)	(34,867)	(35,641)	(47,080)	(12,412)
FX	0	0	0	0
Other non-cash movements	0	0	0	0
Closing net debt/(cash)	(35,641)	(47,080)	(12,412)	5,444

Source: BioPorto reports, Edison Investment Research

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