BRYAN, GARNIER & CO

INDEPENDENT RESEARCH

SOBI

17th October 2016

Brace yourselves… Winter is coming

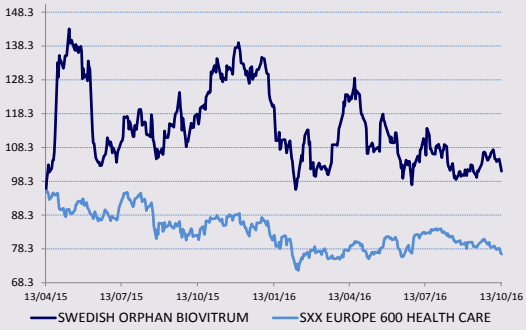
Healthcare

Fair Value SEK90 (price SEK101.30)

SELL
Coverage initiated

Bloomberg	SOBI SS
Reuters	SOBIV.ST
12-month High / Low (EUR)	139.3 / 95.9
Market capitalisation (SEKm)	27,391
Enterprise Value (BG estimates SEKm)	28,557
Avg. 6m daily volume ('000 shares)	1 234
Free Float	60.4%
3y EPS CAGR	ns
Gearing (12/15)	35%
Dividend yields (12/16e)	NM

YE December	12/15	12/16e	12/17e	12/18e
Revenue (SEKm)	3,228	5,066	5,966	7,243
EBIT(SEKm)	146.04	860.05	1,290	1,995
Basic EPS (SEK)	0.25	2.38	3.62	5.65
Diluted EPS (SEK)	0.25	2.38	3.62	5.65
EV/Sales	9.00x	5.64x	4.60x	3.60x
EV/EBITDA	62.5x	23.9x	16.5x	10.9x
EV/EBIT	198.9x	33.2x	21.3x	13.1x
P/E	NS	42.6x	28.0x	17.9x
ROCE	1.0	9.4	14.6	22.2



We are initiating coverage of SOBI with a Sell recommendation and a FV of SEK90. Although our EPS estimates are generally positive, they are noticeably lower than the consensus figures, especially due to our caution concerning Eloctate/Elocta… Or at least until its potential in "desensitisation" of patients with inhibiting antibodies has been confirmed. Pending this, we consider that forthcoming quarterly publications are likely to result in sharp cuts to earnings forecasts.

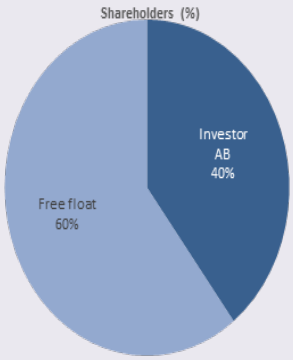
- **Overly optimistic in the haemophilia franchise?** We clearly agree that Elocta and Alprolix are attractive sales successes in the US and it is undoubtedly for this reason that consensus estimates are as high as they are for SOBI's territories (combined peak sales of between USD700m and USD1bn, vs. BG at USD500m). However, this should not mask the fact that 1/ these two BIIB molecules had no direct rivals in the US for more than a year, 2/ other geographical regions have historically preferred plasma options, 3/ in contrast, the competitive backdrop is already far less beneficial in Europe.

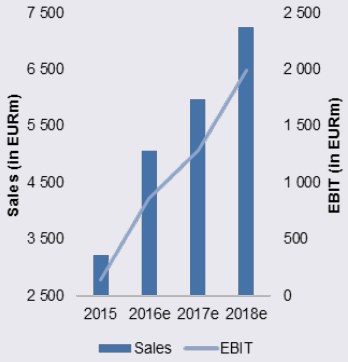
- **Elocta in ITI: significant potential. Still uncertain.** Note nevertheless that Elocta could potentially stand out from other long-acting FVIIIs by showing a benefit in immune tolerance induction (potential impact on our peak sales of USD400m). While initial data looks fairly promising, we would nevertheless underscore the fact that 1/ this proof of concept was only obtained on a small number of patients (n=3); 2/ for the moment, no clinical study has been initiated in order to confirm this positioning.

- **Initiation at Sell with a FV of SEK90.** Earnings momentum should be generally positive in coming years, but estimates look slightly too high especially for 2017e and in view of the lack of confirmation of Eloctate's potential in immune tolerance induction.

Analyst:
Mickael Chane Du
33(0) 1 70 36 57 45
mchanedu@bryangarnier.com

Sector Analyst Team:
Eric Le Berrigaud
Hugo Solvet
Marion Levi





Company description

SOBI is a Swedish healthcare company developing and commercializing rare disease-oriented drugs

Simplified Profit & Loss Account (USDm)	2014	2015	2016e	2017e	2018e	2019e	2020e
Revenues	2,607	3,228	5,066	5,966	7,243	8,435	9,158
Change (%)	*-%*	*23.8%*	*57.0%*	*17.8%*	*21.4%*	*16.5%*	*8.6%*
Adjusted EBITDA	257	465	1,194	1,666	2,394	2,934	3,429
EBIT	(325)	146	860	1,290	1,995	2,512	3,008
Change (%)	*-%*	*-%*	*489%*	*50.0%*	*54.7%*	*25.9%*	*19.8%*
Financial results	6.4	(58.4)	(36.6)	(36.6)	(35.8)	(35.8)	(35.8)
Pre-Tax profits	(319)	87.7	823	1,254	1,960	2,476	2,972
Exceptionals	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Tax	(50.7)	19.3	181	276	431	545	654
Net profit	(268)	68.4	642	978	1,529	1,931	2,318
Restated net profit	(268)	68.4	642	978	1,529	1,931	2,318
Change (%)	*-%*	*-%*	*839%*	*52.3%*	*56.3%*	*26.4%*	*20.0%*
Cash Flow Statement (USDm)							
Operating cash flows	299	411	977	1,354	1,927	2,353	2,740
Change in working capital	65.6	(96.0)	290	21.8	276	617	145
Capex, net	183	146	203	239	290	337	366
Financial investments, net	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Dividends	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Other	19.6	24.9	(480)	(495)	(400)	(379)	0.0
Net debt	345	1,651	1,167	73.3	(1,288)	(2,686)	(4,915)
Free Cash flow	50.6	361	484	1,093	1,361	1,398	2,229
Balance Sheet (USDm)							
Tangible fixed assets	115	109	194	297	435	604	794
Intangibles assets	4,247	5,787	5,672	5,550	5,448	5,364	5,302
Cash & equivalents	519	904	908	1,507	2,467	3,487	5,716
current assets	1,416	1,413	1,705	1,677	1,996	2,294	2,475
Other assets	592	1,003	906	1,385	2,201	3,052	5,097
Total assets	6,371	8,311	8,476	8,909	10,081	11,314	13,668
L & ST Debt	864	2,555	2,075	1,580	1,180	801	801
Others liabilities	983	1,067	1,070	1,020	1,063	743	779
Shareholders' funds	4,523	4,689	5,332	6,310	7,838	9,770	12,088
Total Liabilities	6,371	8,311	8,476	8,909	10,081	11,314	13,668
Capital employed	5,153	6,662	6,820	6,704	6,872	7,405	7,495
Ratios							
Operating margin	(12.47)	4.52	16.98	21.63	27.55	29.78	32.85
Tax rate	15.93	22.01	22.00	22.00	22.00	22.00	22.00
Net margin	(10.27)	2.12	12.68	16.39	21.10	22.90	25.32
ROE (after tax)	(5.92)	1.46	12.05	15.50	19.50	19.77	19.18
ROCE (after tax)	(5.20)	1.03	9.42	14.59	22.24	26.08	30.93
Gearing	7.63	35.21	21.88	1.16	(16.43)	(27.49)	(40.66)
Pay out ratio	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Number of shares, diluted	270	270	270	270	270	270	270
Data per Share (USD)							
EPS	(0.99)	0.25	2.38	3.62	5.65	7.14	8.57
Restated EPS	(0.99)	0.25	2.38	3.62	5.65	7.14	8.57
% change	*-%*	*-%*	*839%*	*52.3%*	*56.3%*	*26.4%*	*20.0%*
BVPS	16.73	17.34	19.72	23.34	28.99	36.13	44.71
Operating cash flows	1.11	1.52	3.61	5.01	7.13	8.70	10.13
FCF	0.19	1.34	1.79	4.04	5.03	5.17	8.24
Net dividend	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Source: Company Data; Bryan, Garnier & Co ests.

Table of contents

1. Investment Case 74

2. Why initiate coverage now? 75

2.1. A call on the European ramp-up of Elocta and Alprolix 75
2.2. Caution for the short term as well 76
2.3. Initiation at SELL with a FV of SEK100 77
2.4. A FV of SEK150 in a more optimistic scenario 78

3. Haemophilia A: the need to stand out from the crowd 80

3.1. Eloctate slowing in the US… 80
3.2. … and the risk of disappointment in Europe is far from zero 81
3.3. An opportunity in ITI… to be confirmed! 82

4. Idelvion set to weigh on Alprolix ramp-up 85

5. Appendix 86

Bryan Garnier stock rating system 89

1. Investment Case

Pourquoi investir maintenant?

Pourquoi s'intéresser au dossier maintenant :

The fact that Biogen announced the spin-off of its haemophilia business helped highlight the products for which SOBI has rights outside the US, namely Eloctate/Elocta and Alprolix. That said, our analysis of the segment suggests that short-term disappointment risk is far from negligible.

Attractif ou non?

Valorisation

It is difficult to base ourselves on multiples given that the company has only exceeded breakeven point very recently. Note however that our FV stands at SEK100 per share implying slight downside risk.

Horizon d'investissement?

Catalyseurs

Recent publications by BIIB have already shown a slowdown in growth at Eloctate and Alprolix in the US… And we have the feeling that coming quarters are very likely to show similar trends. We estimate that European revenues, which concern SOBI especially, could disappoint as of Q3 2016.

Valeur ajoutée?

Différentiation face au consensus *:*

Although our EPS estimates are generally positive, they are noticeably lower than the consensus figures (around 10% as of 2017e), especially in view of our caution on Eloctate, at least until its "desensitisation" potential in patients with inhibiting antibodies against FVIII has been confirmed.

Quels risques?

Risques

The main risk to our investment case would be higher than expected growth by Elocta and Alprolix in Europe.

2. Why initiate coverage now?

2.1. A call on the European ramp-up of Elocta and Alprolix

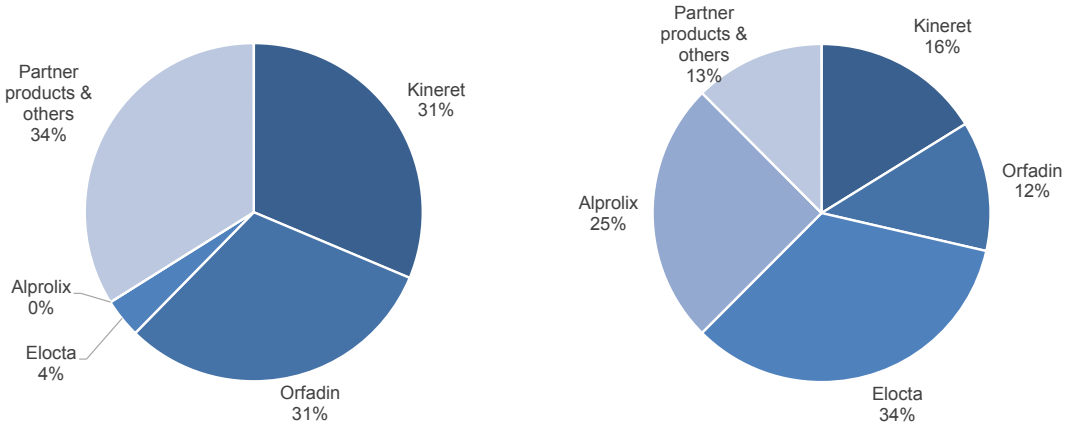
Since 2014, SOBI has been Biogen's partner in the development and marketing of Elocta and Alprolix in a well-established zone including Europe, North Africa, Russia and a part of the Middle-East (with BIIB nevertheless keeping the rights to North America). Thanks to this agreement, we would say that **SOBI could become the Swedish counterpart to Shire, namely a group focused on rare diseases field and also with high exposure to the haemophilia field.**

Fig. 1: SOBI - Commercial and clinical portfolio

Project	Indication	Partner	Clinical stage
Elocta (rFVIII Fc)	Haemophilia A	Biogen	Registered
Alprolix (rFIX Fc)	Haemophilia B	Biogen	Registered
Orfadin oral suspension	Hereditary Tyrosinaemia Type 1	Proprietary	Registered
Orfadin 20 mg capsule	Hereditary Tyrosinaemia Type 1	Proprietary	Registered
Nitisinone	Alkaptonuria	DevelopAKUre	Phase III
SOBI003	Enzyme replacement therapy	Proprietary	Preclinical
IL-1 Affibody	IL-1 driven disease	Affibody	Preclinical
C5 inhibitor	Complement C5 driven disease	Affibody	Preclinical
XTEN	Haemophilia	XTEN	Preclinical

Source: SOBI; Bryan, Garnier & Co. ests

Fig. 2: Sales - change in mix from 2015 to 2020e



Source: Bryan, Garnier & Co. ests

Today still, this franchise only plays a small role in earnings generation in that the two products that make up the division were only very recently approved by the European watchdog (November 2015 for Elocta and May 2016 for Alprolix). However, we estimate that it should represent almost 60% of the group's revenues in 2022e (excluding royalties and revenues linked to manufacturing as is the case with PFE's Refacto), with combined sales of almost EUR500m. Note also that the two companies pay each other royalties as a percentage of sales and net profit generated in their respective regions, according to the following scheme:

Fig. 3: Financial terms of the SOBI-Biogen agreement

% Royalties/Reimbursement between companies	Method	Before 1st sales in SOBI's territory	Base rate	After 1st sales in SOBI's territory
From SOBI to BIIB based on net sales in SOBI's territories	Royalty on sales	n/a	12%	17%
BIIB to SOBI based on net sales in North America	Royalty on sales	2%	12%	7%
BIIB to SOBI based on net sales in BIIB's territory ex-North Am.	Royalty on sales	2%	17%	12%
BIIB to SOBI based on net profit from BIIB's distribution territory*	Royalty on net profit	10%	50%	35%
** BIIB's distribution territory pertains to the territory in which sales are conducted through a third party*				

Source: SOBI; Bryan, Garnier & Co ests.

Fig. 4: Haemophilia - SOBI's addressable market

	Haemophilia A pop.	Haemophilia B pop.
Central and eastern Europe	6,839	1,155
Germany, Austria and Switzerland	4,616	876
Belgium, Netherlands and Luxembourg	1,875	379
Italy and Greece	4,651	980
Nordics and Baltics	1,670	384
France	5,400	1,201
UK and Ireland	6,229	1,394
Spain and Portugal	2,217	388
TOTAL Europe	**33,497**	**6,757**
Middle East	16,770	3,632
North Africa	2,959	610
Russia	5,801	992
TOTAL SOBI's territory	**59,027**	**11,991**

Source: SOBI; Bryan, Garnier & Co ests.

While these two projects look fundamentally promising, we nevertheless believe that consensus forecasts are slightly too optimistic, whether in terms of peak sales or ramp-up. Admittedly Biogen's figures are very attractive: barely a year after approval in the US market, Eloctate (Elocta's commercial name in the region) and Alprolix generated combined sales of USD500m. We ask ourselves to what extent these figures have inspired analysts' forecasts whereas underlying momentum on either side of the Atlantic is very different (the appeal for recombinant approaches and the share of patients under prophylactic treatment in Europe are well below US standards for example).

2.2. Caution for the short term as well

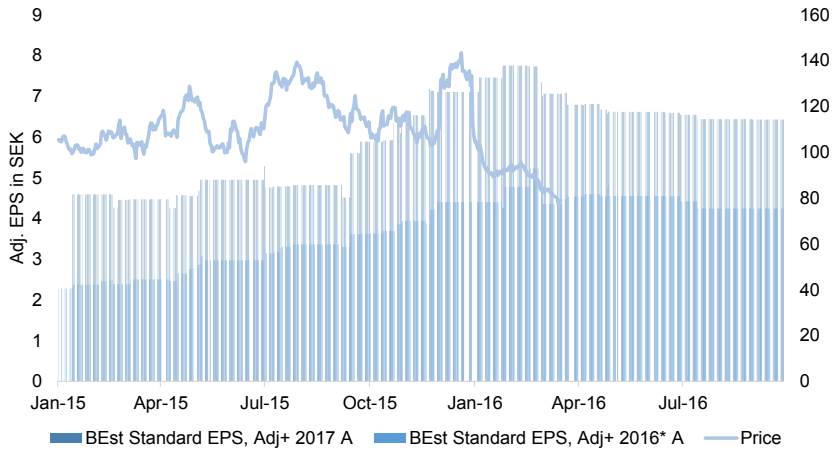
We will focus especially on Elocta's ramp-up in view of its relative weight in valuations (around 30-40% in our case). And as we stated in the first part of this study, the risk of disappointment should not be underestimated, especially in view of 1/ the recent change in the competitive backdrop (Kovaltry having been approved recently, and we believe that it should benefit from the large base of patients built up by Bayer with Kogenate), and 2/ the lower appetite for recombinant factors in Europe.

Fig. 5: 2016 guidance vs BG and consensus estimates

(in SEKm)	SOBI Guidance	Consensus	BG
Revenues (including royalties, manufacturing income, etc.)	4,800-5,000	5,178	4,850
Gross margin (%)	68% -70%	71%	70%
EBITA	1,200-1,300	1,134	1,161
in % of revenues	25-26%	22%	24%

Source: Bloomberg; Bryan, Garnier & Co ests.

Fig. 6: Change in 2016e and 2017e EPS since January 2015



Source: Bloomberg; Bryan, Garnier & Co. ests

2.3. Initiation at SELL with a FV of SEK100

We are initiating coverage of SOBI with a Sell recommendation and a FV of SEK100. Growth momentum that we expect for the company is generally very positive, since Elocta and Alprolix are two projects that should enable the group to double in size by the start of the next decade. However 1/ in our humble opinion, short-term market forecasts are slightly too high concerning the ramp-up of this franchise, 2/ the risk of disappointment during upcoming publications is far from zero, whether for SOBI or BIIB, and this is likely to result in a downgrade to the consensus average.

Fig. 7: BG estimates vs the consensus (2015-2019e)

(in SEKm)	2015	2016e	2017e	2018e	2019e
Total revenues (in EURm)	**3,228**	**5,065**	**5,868**	**7,006**	**8,173**
% growth y-o-y	0%	57%	16%	19%	17%
% Δ vs Bloomberg consensus	0.0%	-2.2%	-6.7%	-10.5%	-10.4%
Bloomberg consensus	3,228	5,178	6,286	7,830	9,120
Reported EBITA (in EUR)	**433**	**1,161**	**1,612**	**2,268**	**2,762**
% growth y-o-y		n/s	39%	41%	22%
% Δ vs Bloomberg consensus		2.3%	-8.0%	-13.4%	-18.0%
EBITA Bloomberg consensus	433	1,135	1,753	2,620	3,367

Source: Bloomberg; Bryan, Garnier & Co ests.

Our DCF valuation also points to a Fair Value of SEK100 and based on the following factors:

- A discount rate (WACC) of 9% based on 1/ a risk-free rate of 1.6%, 2/ an equity risk premium of 7% and 3/ a beta of 1.1.

- We have assumed that the group's EBIT margin should be close to 30-35% over a long period thanks to the rising momentum of Elocta and Alprolix (for which we estimate a net gross margin at almost 80%e).

- Given SOBI's status as a growth stock and the various factors set to underpin the development of its various target markets, we have assumed a growth rate to infinity of 3%.

Fig. 8: SOBI – DCF valuation

(in USDm)	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025
Revenues	5,065	5,962	7,237	8,427	9,149	9,558	9,639	9,462	9,169	8,914
% chg yoy		17.7%	21.4%	16.4%	8.6%	4.5%	0.8%	-1.8%	-3.1%	-2.8%
(+) Current EBIT	**860**	**1,289**	**1,994**	**2,509**	**3,005**	**3,150**	**3,178**	**3,115**	**3,009**	**2,916**
in % of sales	17.0%	21.6%	27.5%	29.8%	32.8%	33.0%	33.0%	32.9%	32.8%	32.7%
% chg yoy		50.0%	54.6%	25.9%	19.7%	4.8%	0.9%	-2.0%	-3.4%	-3.1%
(-) Taxes	189	284	439	552	661	693	699	685	662	642
(+) D&A	334	376	398	421	421	411	395	378	367	357
= Net operating income after tax	**1,005**	**1,381**	**1,953**	**2,379**	**2,765**	**2,868**	**2,874**	**2,808**	**2,714**	**2,631**
(-) CAPEX	203	238	289	337	366	382	386	378	367	357
(-) Change in WCR	289	21	276	617	144	82	16	-35	-59	-51
= Free Cash Flows	**513**	**1,122**	**1,388**	**1,425**	**2,254**	**2,404**	**2,473**	**2,465**	**2,406**	**2,326**

= Enterprise Value (EURm)	**29,005**
(-) Minority interests	0
(-) Net debt	1,651
= Equity value (SEKm)	**27,354**
Number of diluted shares	270.4
= Fair Value per share (SEK)	**101**

Source: Bryan, Garnier & Co ests.

2.4. A FV of SEK150 in a more optimistic scenario

The main risk to our recommendation would clearly be higher than expected growth in the haemophilia franchise. Forthcoming quarterly publications should obviously help assess this aspect, but we would nevertheless highlight the fact that a **re-rating on our part could also stem from the confirmation of Elocta's ability to rapidly induce immune tolerance in haemophilia A patients with inhibitors** (which would really help the product stand out from all the other long-acting drugs on the market).

SOBI and BIIB have not yet decided whether to launch trials aimed at validating this assumption and for this reason, we have only factored in low upside potential associated with this development (especially since the data we have stems from a fairly small sample of patients). However, if a trial is indeed launched, 1/ we understand that results could be obtained during 2018 and 2019, if it is

initiated in the next few months, and 2/ we estimate that this data would be a key part of the process to differentiate the product and its growth.

For all useful purposes, **note that our FV would stand at SEK150 if we were to integrate this prospect without adding any probability of success ratio.** Note also that if this scenario were to materialise it would have a clear impact on Grifols' EPS and valuation.

Fig. 9: BG valuation – Best-case scenario

(in USDm)	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025
Revenues	5,065	5,962	7,724	9,412	11,031	12,356	13,369	14,033	13,786	13,577
% chg yoy		17.7%	29.6%	21.8%	17.2%	12.0%	8.2%	5.0%	-1.8%	-1.5%
(+) Current EBIT	**860**	**1,289**	**2,136**	**2,817**	**3,656**	**4,123**	**4,477**	**4,718**	**4,628**	**4,551**
in % of sales	17.0%	21.6%	27.7%	29.9%	33.1%	33.4%	33.5%	33.6%	33.6%	33.5%
% chg yoy		50.0%	65.7%	31.9%	29.8%	12.8%	8.6%	5.4%	-1.9%	-1.7%
(-) Taxes	189	284	470	620	804	907	985	1,038	1,018	1,001
(+) D&A	334	376	425	471	507	531	548	561	551	543
= Net operating income after tax	**1,005**	**1,381**	**2,091**	**2,668**	**3,359**	**3,747**	**4,040**	**4,242**	**4,161**	**4,093**
(-) CAPEX	203	238	309	376	441	494	535	561	551	543
(-) Change in WCR	289	21	373	716	324	265	203	133	-49	-42
= Free Cash Flows	**513**	**1,122**	**1,409**	**1,575**	**2,594**	**2,988**	**3,303**	**3,547**	**3,659**	**3,592**

= Enterprise Value (EURm)	**41,442**
(-) Minority interests	0
(-) Net debt	1,651
= Equity value (SEKm)	**39,791**
Number of diluted shares	270.4
= Fair Value per share (SEK)	**147**

Source: Bryan, Garnier & Co ests.

3. Haemophilia A: the need to stand out from the crowd

3.1. Eloctate slowing in the US…

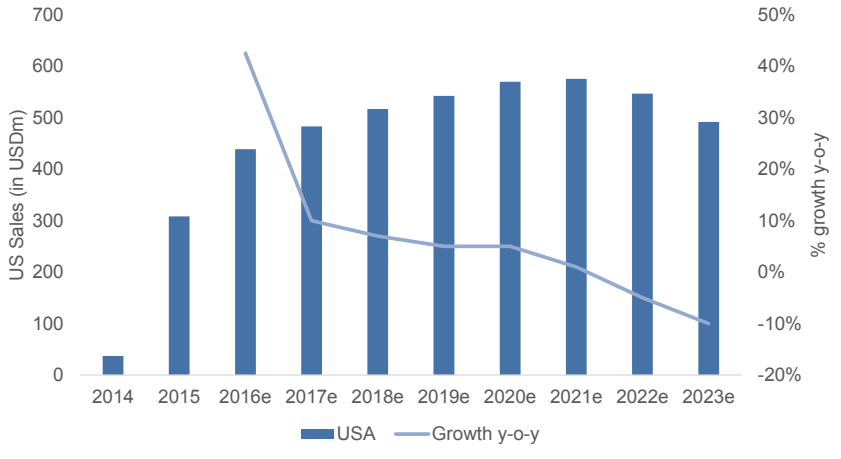
Eloctate has undeniably benefited from its status as the first entrant in the much-coveted segment of long-acting FVIIIs. Proof of this is the fact that it should generate more than USD400m in revenues in the US this year (just two years after its approval by the FDA).

That said, we would note that **recent quarterly publications have shown a clear slowdown in growth from one quarter to the next** and this has also had an impact on SOBI which is paid 12% in royalties on these sales. Contrary to the consensus on BIIB/Bioverativ, which is still forecasting growth of 20-30% in 2017e, we believe the trend is unlikely to improve for a large number of reasons:

- **Three other long-acting rFVIIIs have come onto the US market in recent months** (Adynovate, Kovaltry, Afstyla). While the data obtained from pivotal studies show no major differences in terms of efficacy and toxicity (at least in haemophilia A patients without inhibitors), we nevertheless consider that these new therapies could provide leverage to the patient bases created by the companies that have developed them (Shire, Bayer and CSL).

- **The reduction in the number of weekly injections is actually fairly low and we believe that this puts a significant brake on the prospect of a mass switchover by patients undergoing prophylactic treatment** to this first generation of long-acting solutions. In addition, a portion of these patients (also difficult to quantify) fear the possibility of developing inhibitors due to a possible change in product or brand.

Fig. 10: Eloctate –BG sales estimates for the US



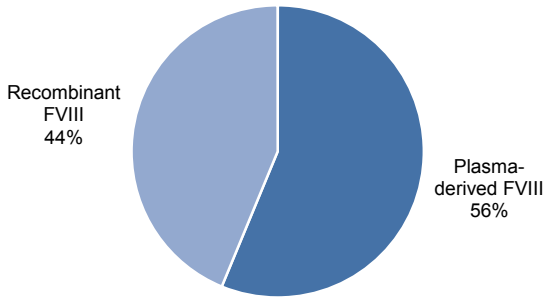
Source: Bryan, Garnier & Co. ests

3.2. … and the risk of disappointment in Europe is far from zero

We are also fairly reserved about the ramp-up of Elocta in Europe. The fact that it is the first entrant is obviously positive, but this does not mask the fact that a **second product (Kovaltry by Bayer) was launched a few months after its approval by the watchdog,** and more precisely in March of this year.

We should also bear in mind that **Europe as a whole is far less keen on recombinant approaches** and this is probably due to the additional costs involved compared with pdFVIIIs, which are nevertheless 20-30% less expensive. We believe this situation is unlikely to change radically, especially in a backdrop whereby the SIPPET study showed that the risk of developing inhibitors is far less important 1/ with plasma derivatives containing vWF, and 2/ in treatment-naive patients.

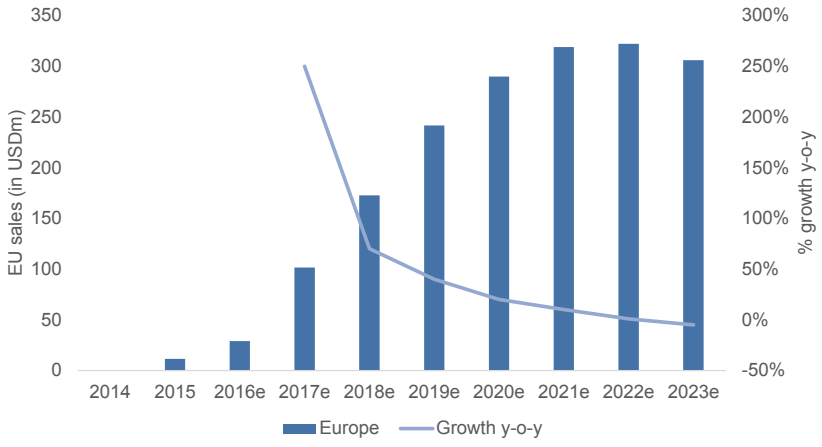
Fig. 11: FVIII - Volumes depending on the factor's origins (Europe)



Source: MRBI; Bryan, Garnier & Co. ests

Under these conditions, we estimate that Elocta's European sales should be closer to USD300-350m at the start of the next decade, rather than the USD700m that the low end of the consensus is currently pointing to.

Fig. 12: Eloctate –BG sales estimates for Europe



Source: Bryan, Garnier & Co. ests

3.3. An opportunity in ITI… to be confirmed!

It is fairly difficult to find exact figures concerning the market's forecasts for Elocta out to 2020, although our interactions with BIIB and SOBI nevertheless suggest that we are at the low-end of the consensus range, and it is highly likely that this difference stems especially from our cautious position on the advent of the project.

However, nothing is set in stone and we admit that we could revise our figures upwards if Eloctate were to confirm the first clinical results generated as a "desensitisation treatment" for haemophilia A patients with inhibitors. For the moment, data here is very few and far between, and neither BIIB nor SOBI have confirmed their intention to launch a confirmatory clinico-marketing trial. All of this therefore remains very theoretical, although the likelihood of this type of development being initiated is high in our view, since without it, we do not see how the product could genuinely stand out from other rival products.

■ What proof is there?

A few months ago, retrospective data implied the use of Eloctate and Elocta in three young children having developed high levels of inhibiting antibodies. The results were admittedly very promising, especially in terms of efficacy.

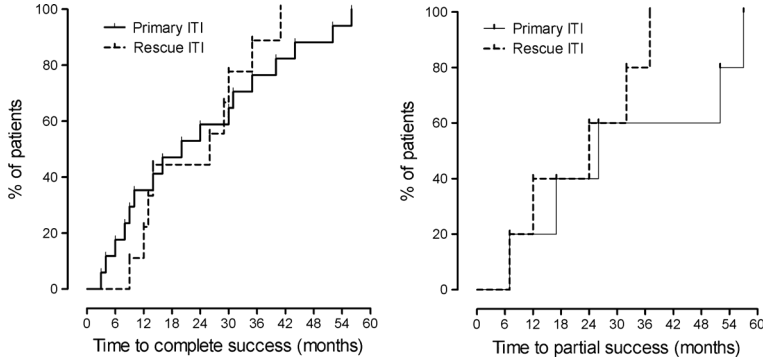
These three patients were able to be desensitised in less than three months (and even within four weeks for the patient that was refractory to a previous ITI based on rFVIII), whereas the duration of the treatment before a complete or even partial response is generally far higher than 12 months with pdVIIIs containing vWF (Oldenburg et al, 2014).

Fig. 13: Eloctate - Immune tolerance induction (ITI) – preliminary results

Patient	1	2	3
Haemophilia severity	< 0.01 IU/ml	< 0.01 IU/ml	< 0.01 IU/ml
F8 gene mutation	Intron 22 inversion	Nonsense	Not available
Age at anti-FVIII detection	13 months	9 months	10 years
Peak anti-FVIII titer	32 BU	422 BU	16 BU
Prior ITI	No	Yes	No
Initial ITI dose	200 IU/kg QOD	200 IU/kg 3x / week	100 IU/kg QOD
Time to anti-FVIII = 0	**12 weeks**	**4 weeks**	**11 weeks**
Current anti-FVIII	0 BU	0 BU	0 BU

Source: Biogen; Bryan, Garnier & Co ests.

Fig. 14: ITI with vWF/pdFVIII - time to complete/partial success



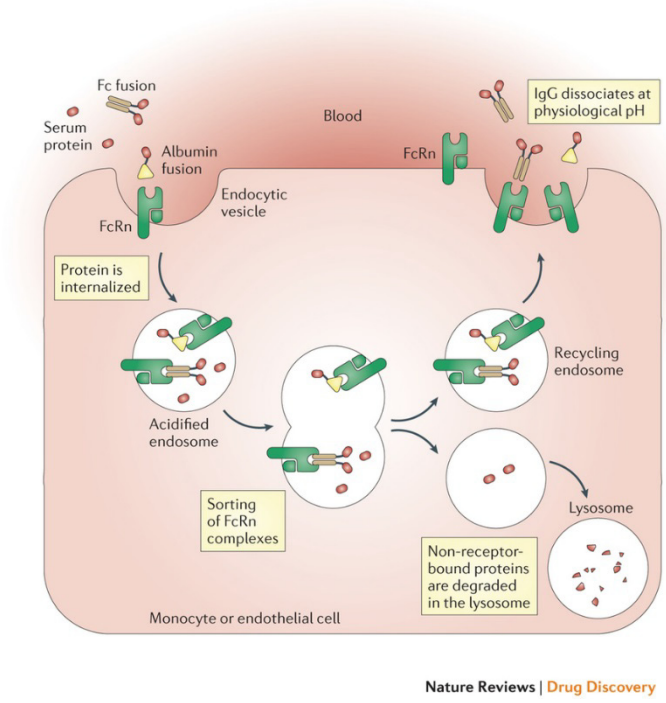
Source: Oldenburg et al (2014)

■ **The possibility of differentiation thanks to a unique action mechanism**

The fact that Eloctate is potentially more efficient from a desensitisation stance could stem from its very construction (fusion protein associating an rFVIII with an Fc fragment from a recombinant human IgG1 immunoglobulin), which enables not only a reduction in lysosomal deterioration in the coagulation factor, but also an induction in regulatory T-cells.

For those that would like to go into further detail on the mechanism, note that Fc is the constant part of an antibody and plays a key role in 1/ initiating effector functions (such as ADCC after joining up with its receptor, or activation of the complement after joining up with the antigen), and 2/ transport/intra-cellular survival, by protecting from an enzymatic deterioration and enabling their recycling (and this is what helps explain the extension in the half-life).

Fig. 15: Fc fusion or how to reduce intra-cellular deterioration



Source: Nature; Bryan, Garnier & Co. ests

In addition, the fact that Eloctate/Elocta is an Fc fusion protein also seems to have immuno-modulating/tolerogenic virtues given its ability to induce Tregs (De Groot et al, 2008; Lei et al, 2005). This is what could explain Eloctate's ability to induce a desensitisation more quickly than a native FVIII, especially since the formation of inhibiting antibodies is the result of an immune response mediated by T-cells.

■ **What impact on our figures and the rest of the sector in an optimistic scenario?**

However, caution is the mother of safety, especially since prospective data on a sufficiently large number of patients is missing. For this reason, we have decided not to factor the opportunity into our forecasts, or at least until conclusive results are presented.

For all useful purposes, we have nevertheless factored in the impact that the success of a large multi-centric study focused on patients with inhibitors could have (ideally the study would be randomised with several arms including Eloctate and other types of FVIIIs). The result is that our sales forecasts for SOBI territories could be increased by around USD400m by 2023e if the results were to be published in 2018 or 2019 (although this would depend on the trial design) and on the basis of the following assumptions:

Fig. 16: Eloctate – additional sales potential in ITI

	2016e	2017e	2018e	2019e	2020e	2021e	2022e	2023e
Congenital haemophilia A - Prevalence	**30,000**	**30,300**	**30,603**	**30,909**	**31,218**	**31,530**	**31,846**	**32,164**
- US	15,000	15,150	15,302	15,455	15,609	15,765	15,923	16,082
- Europe (SOBI territory)	15,000	15,150	15,302	15,455	15,609	15,765	15,923	16,082
- RoW	9,000	9,090	9,181	9,273	9,365	9,459	9,554	9,649
% Severe haemophilia A (FVIII levels < 1%)	70%	70%	70%	70%	70%	70%	70%	70%
% Diagnosed & treated	65%	65%	65%	65%	65%	65%	65%	65%
% Incidence of inhibitors	30%	30%	30%	30%	30%	30%	30%	30%
% Market penetration - US	0%	0%	10%	20%	30%	40%	50%	50%
% Market penetration - Europe	0%	0%	5%	10%	20%	30%	40%	50%
% Market penetration - RoW	0%	0%	5%	10%	20%	30%	40%	50%
Pricing per patient - US (in USD)	500,000							
Pricing per patient - Europe (in USD)	400,000							
Eloctate - Non-risk adjusted sales (in USDm)	**0**	**0**	**171**	**346**	**592**	**844**	**1,100**	**1,251**
% var y-o-y		n/s	n/s	102%	71%	42%	30%	14%
- US	0	0	104	211	320	430	543	549
- Europe	0	0	42	84	170	258	348	439
- ROW	0	0	25	51	102	155	209	263

Source: Bryan, Garnier & Co. ests

- We base ourselves on the principle that the time-to-complete/partial response is around 15 weeks and that during this time-lapse, Eloctate would be administered five times a week (rather than every four days) at a dose of 100 IU/kg (vs 50 IU/kg under a prophylactic treatment and without inhibitors). This more or less points to an overall cost of USD400-500,000 per patient.

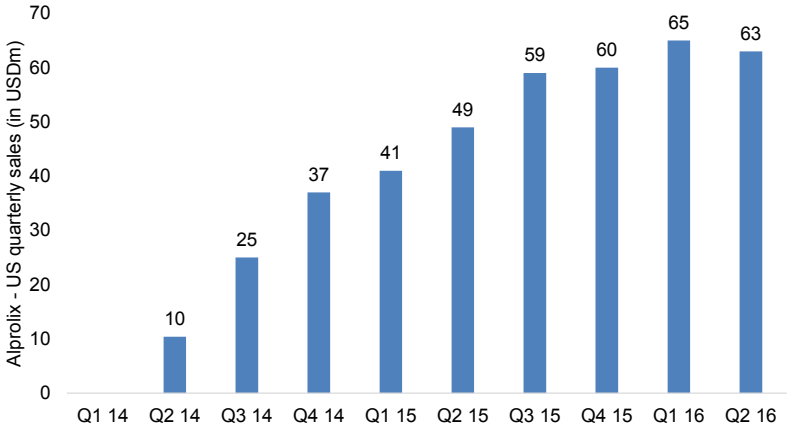
- Given the time gain provided, and for a potentially lower cost than current alternatives, it seems likely that 40% of patients developing inhibitors (whatever their title count) would switch to Eloctate as a first intention therapy as of 2022e.

- As we said in the part of our study dedicated to Grifols, it is highly likely that this would impact sales of pdFVIIIs, but also those of ACE910, Feiba and NovoSeven in view of their second intention positioning.

4. Idelvion set to weigh on Alprolix ramp-up

Alprolix is the counterpart to Eloctate in haemophilia B in that it is a long-acting recombinant FIX with an Fc fusion protein enabling the extension of its half-life. Here again, its ramp-up has been more encouraging in the US thanks to its position as a first-entrant and the lack of direct competition for two years.

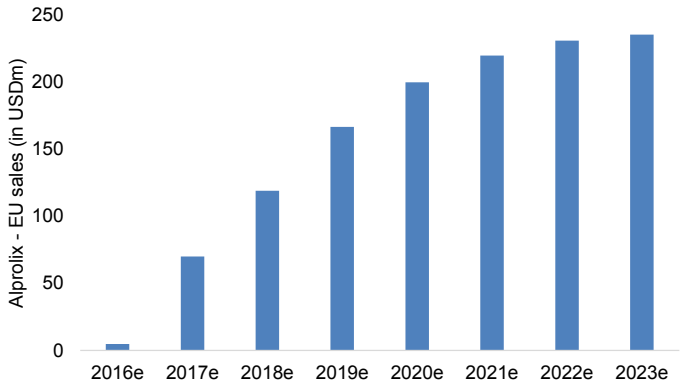
Fig. 17: Alprolix – Quarterly sales in the US



Source: Biogen; Bryan, Garnier & Co. ests.

However, as for Elocta, we believe that growth in Europe is unlikely to be as high as in the US given the simultaneous launch of rival alternatives. As it happens, the risk is even greater given that 1/ the said rival is actually a best-in-class, whether in terms of efficacy or administration schedule (every 10-14 days or 21 in certain cases, vs. every 7-10 days for Alprolix), 2/ development of inhibitors is far less significant in haemophilia B patients (< 5%e) and the eventual increase in sales associated with a positioning in ITI would only be very limited.

Fig. 18: Alprolix –BG sales estimates for Europe



Source: Bryan, Garnier & Co. ests.

5. Appendix

Fig. 19: Product sales estimates (2015-2021e)

Fig. 20: (in SEKm)	2015	2016	2017	2018	2019	2020	2021
Product sales	**1,841**	**3,748**	**4,653**	**5,932**	**7,125**	**7,847**	**8,254**
% var y-o-y	41%	104%	24%	27%	20%	10%	5%
- Elocta - Hemophilia A	96	244	854	1,451	2,032	2,438	2,682
% var y-o-y		154%	250%	70%	40%	20%	10%
- Alprolix - Hemophilia B	0	40	589	1,001	1,401	1,682	1,850
% var y-o-y	n/s	n/s	1370%	70%	40%	20%	10%
- Hemophilia - Royalty and one-off payment		1,477	973	1,062	1,126	1,185	1,211
% var y-o-y			-34%	9%	6%	5%	2%
- Kineret - Inflammation (RA & others)	805	1,047	1,203	1,312	1,404	1,333	1,267
% var y-o-y	32%	30%	15%	9%	7%	-5%	-5%
- Orfadin - Hereditary Tyrosinemia Type 1	796	796	876	937	984	1,023	1,054
% var y-o-y	45%	0%	10%	7%	5%	4%	3%
- Others	144	144	158	169	178	185	191
% var y-o-y	21%	0%	10%	7%	5%	4%	3%

Source: Bryan, Garnier & Co ests.

Fig. 21: Eloctate & Alprolix sales estimates (2014-2021e)

(in USDm)	2014	2015	2016e	2017e	2018e	2019e	2020e	2021e
Eloctate/Elocta	**37**	**331**	**528**	**662**	**783**	**887**	**970**	**1,010**
% var y-o-y			59%	25%	18%	13%	9%	4%
- US	37	308	439	483	517	543	570	575
% var y-o-y			43%	10%	7%	5%	5%	1%
- Europe	0	11	29	102	173	242	290	319
% var y-o-y				250%	70%	40%	20%	10%
- ROW	0	12	60	78	94	103	110	116
% var y-o-y		n/s	n/s	30%	20%	10%	7%	5%
Alprolix	**80**	**234**	**325**	**434**	**515**	**587**	**641**	**673**
% var y-o-y		n/s	39%	34%	19%	14%	9%	5%
- US	76	209	260	286	306	321	337	348
% var y-o-y		175%	24%	10%	7%	5%	5%	3%
- Europe	0	0	5	70	119	167	200	220
% var y-o-y		n/s	n/s	n/s	70%	40%	20%	10%
- ROW	4	25	60	78	90	99	104	106
% var y-o-y		n/s	n/s	30%	15%	10%	5%	2%

Source: Bryan, Garnier & Co ests.

Page left blank intentionally

Page left blank intentionally

Bryan Garnier stock rating system

For the purposes of this Report, the Bryan Garnier stock rating system is defined as follows:

Stock rating

BUY — Positive opinion for a stock where we expect a favourable performance in absolute terms over a period of 6 months from the publication of a recommendation. This opinion is based not only on the FV (the potential upside based on valuation), but also takes into account a number of elements that could include a SWOT analysis, momentum, technical aspects or the sector backdrop. Every subsequent published update on the stock will feature an introduction outlining the key reasons behind the opinion.

NEUTRAL — Opinion recommending not to trade in a stock short-term, neither as a BUYER or a SELLER, due to a specific set of factors. This view is intended to be temporary. It may reflect different situations, but in particular those where a fair value shows no significant potential or where an upcoming binary event constitutes a high-risk that is difficult to quantify. Every subsequent published update on the stock will feature an introduction outlining the key reasons behind the opinion.

SELL — Negative opinion for a stock where we expect an unfavourable performance in absolute terms over a period of 6 months from the publication of a recommendation. This opinion is based not only on the FV (the potential downside based on valuation), but also takes into account a number of elements that could include a SWOT analysis, momentum, technical aspects or the sector backdrop. Every subsequent published update on the stock will feature an introduction outlining the key reasons behind the opinion.

Distribution of stock ratings

BUY ratings 57,4% NEUTRAL ratings 31% SELL ratings 11,6%

Research Disclosure Legend

1	Bryan Garnier shareholding in Issuer	Bryan Garnier & Co Limited or another company in its group (together, the "Bryan Garnier Group") has a shareholding that, individually or combined, exceeds 5% of the paid up and issued share capital of a company that is the subject of this Report (the "Issuer").	No
2	Issuer shareholding in Bryan Garnier	The Issuer has a shareholding that exceeds 5% of the paid up and issued share capital of one or more members of the Bryan Garnier Group.	No
3	Financial interest	A member of the Bryan Garnier Group holds one or more financial interests in relation to the Issuer which are significant in relation to this report	No
4	Market maker or liquidity provider	A member of the Bryan Garnier Group is a market maker or liquidity provider in the securities of the Issuer or in any related derivatives.	No
5	Lead/co-lead manager	In the past twelve months, a member of the Bryan Garnier Group has been lead manager or co-lead manager of one or more publicly disclosed offers of securities of the Issuer or in any related derivatives.	No
6	Investment banking agreement	A member of the Bryan Garnier Group is or has in the past twelve months been party to an agreement with the Issuer relating to the provision of investment banking services, or has in that period received payment or been promised payment in respect of such services.	No
7	Research agreement	A member of the Bryan Garnier Group is party to an agreement with the Issuer relating to the production of this Report.	No
8	Analyst receipt or purchase of shares in Issuer	The investment analyst or another person involved in the preparation of this Report has received or purchased shares of the Issuer prior to a public offering of those shares.	No
9	Remuneration of analyst	The remuneration of the investment analyst or other persons involved in the preparation of this Report is tied to investment banking transactions performed by the Bryan Garnier Group.	No
10	Corporate finance client	In the past twelve months a member of the Bryan Garnier Group has been remunerated for providing corporate finance services to the issuer or may expect to receive or intend to seek remuneration for corporate finance services from the Issuer in the next six months.	No
11	Analyst has short position	The investment analyst or another person involved in the preparation of this Report has a short position in the securities or derivatives of the Issuer.	No
12	Analyst has long position	The investment analyst or another person involved in the preparation of this Report has a long position in the securities or derivatives of the Issuer.	No
13	Bryan Garnier executive is an officer	A partner, director, officer, employee or agent of the Bryan Garnier Group, or a member of such person's household, is a partner, director, officer or an employee of, or adviser to, the Issuer or one of its parents or subsidiaries. The name of such person or persons is disclosed above.	No
14	Analyst disclosure	The analyst hereby certifies that neither the views expressed in the research, nor the timing of the publication of the research has been influenced by any knowledge of clients positions and that the views expressed in the report accurately reflect his/her personal views about the investment and issuer to which the report relates and that no part of his/her remuneration was, is or will be, directly or indirectly, related to the specific recommendations or views expressed in the report.	Yes
15	Other disclosures	Other specific disclosures: Report sent to Issuer to verify factual accuracy (with the recommendation/rating, price target/spread and summary of conclusions removed).	No

A copy of the Bryan Garnier & Co Limited conflicts policy in relation to the production of research is available at www.bryangarnier.com

Please see the section headed "Important information" on the back page of this report.

BRYAN, GARNIER & CO

London
Beaufort House
15 St. Botolph Street
London EC3A 7BB
Tel: +44 (0) 207 332 2500
Fax: +44 (0) 207 332 2559
Authorised and regulated by the Financial Conduct Authority (FCA)

Paris
26 Avenue des Champs Elysées
75008 Paris
Tel: +33 (0) 1 56 68 75 00
Fax: +33 (0) 1 56 68 75 01
Regulated by the Financial Conduct Authority (FCA) and the Autorité de Contrôle prudential et de resolution (ACPR)

New York
750 Lexington Avenue
New York, NY 10022
Tel: +1 (0) 212 337 7000
Fax: +1 (0) 212 337 7002
FINRA and SIPC member

Munich
Widenmayerstrasse 29
80538 Munich
Germany
+49 89 2422 62 11