BRYAN, GARNIER & CO

INDEPENDENT RESEARCH UPDATE

29th March 2016

Ipsen

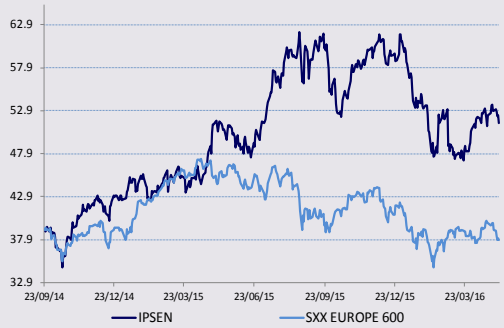
Cabozantinib makes Ipsen a different story

Healthcare

Fair Value EUR60 vs. EUR63 (price EUR48.75) **BUY**

Bloomberg	IPN FP
Reuters	IPN.PA
12-month High / Low (EUR)	62.0 / 43.4
Market capitalisation (EURm)	4,058
Enterprise Value (BG estimates EURm)	4,157
Avg. 6m daily volume ('000 shares)	78.60
Free Float	32.0%
3y EPS CAGR	11.6%
Gearing (12/15)	NM
Dividend yield (12/16e)	1.74%

YE December	12/15	12/16e	12/17e	12/18e
Revenue (€m)	1,444	1,552	1,683	1,823
EBIT (€m)	322.48	332.05	367.16	441.03
Basic EPS (€)	2.31	2.73	2.88	3.54
Diluted EPS (€)	2.78	2.81	3.18	3.86
EV/Sales	2.74x	2.68x	2.42x	2.16x
EV/EBITDA	10.8x	10.5x	9.3x	7.6x
EV/EBIT	12.3x	12.5x	11.1x	8.9x
P/E	17.5x	17.3x	15.3x	12.6x
ROCE	22.6	17.1	18.4	21.4



A combination of full-year results with structuring a deal with Exelixis in early March led us put our rating under review until further analysis. We are now back with the output of this reassessment of perspectives and although the short-term cost base and earnings growth are going to be negatively impacted by the deal, which obviously changes Ipsen's investment case, it makes it different but no less attractive in our view.

- Deal with Exelixis gives ex-US/Japan rights to cabozantinib to Ipsen for USD200m upfront and USD110m regulatory milestones plus royalties. This is a lot of money considering that Ipsen also has to build up a new sales-force in oncology but this asset has two strengths: (i) it is already very advanced in development as it is marketed in a niche indication, filed in a more significant one with strong data (2L RCC) and is ending phase III in a third one (2L HCC); (ii) data collected so far are very encouraging and promising and we see cabozantinib as relatively competitive in RCC and HCC, i.e. on its way to potentially become SoC although the environment is moving very quickly with immuno-oncology drugs as threat number 1.

- Of course, because Ipsen has to invest about EUR50m in a new oncology sales-force to support cabozantinib's launch, some pressure will be put on the cost base in 2016 and 2017 and guidance now implies a 130bp core EBIT margin decline (including currencies). This could nevertheless leave little room for (marginal) core EPS growth in 2016 under a conservative scenario. Now from 2016 to 2020, core EPS would grow even faster at a pace of 15.6% p.a., which is more than attractive considering today's P/E that equals a PEG ratio of 1.1x.

- News flow should remain dense across 2016, including for cabozantinib with OS data in 2L RCC (likely at ASCO), 2L RCC European approval, 2L HCC phase III data and 1L RCC phase II data all expected by year-end. We are hopeful this will increase confidence in the deal and offset short-term pain with long-term value.

Analyst:
Eric Le Berrigaud
33(0) 1 56 68 75 33
eleberrigaud@bryangarnier.com

Sector Analyst Team:
Mickael Chane Du
Hugo Solvet

Company description

Ipsen is a global specialty-driven pharmaceutical company with total sales exceeding €1.2 billion in 2012. Ipsen's ambition is to become a leader in specialty healthcare solutions for targeted debilitating diseases. Its development strategy is supported by 3 franchises: neurology / Dysport®, endocrinology / Somatuline® and uro-oncology / Decapeptyl®. Moreover, the Group has an active policy of partnerships. Ipsen's R&D is focused on its innovative and differentiated technological platforms, peptides and toxins. In 2012, R&D expenditure totaled close to €250 million, representing more than 20% of Group sales. The Group has close to 4,900 employees worldwide. Ipsen's shares are traded on segment A of Euronext Paris (stock code: IPN, ISIN code: FR0010259150) and eligible to the "Service de Règlement Différé" ("SRD"). The Group is part of the SBF 120 index. Ipsen has implemented a Sponsored Level I American Depositary Receipt (ADR) program, which trade on the over-the-counter market in the United States under the symbol IPSEY

Income Statement (EURm)	**2013**	**2014**	**2015**	**2016e**	**2017e**	**2018e**	2019e
Revenues	1,225	1,275	1,444	1,552	1,683	1,823	1,964
Change (%)	*0.5%*	*4.1%*	*13.3%*	*7.5%*	*8.4%*	*8.3%*	*7.7%*
Adjusted EBITDA	236	311	366	398	438	517	596
EBIT	211	261	322	332	367	441	514
Change (%)	*7.4%*	*23.8%*	*23.8%*	*3.0%*	*10.6%*	*20.1%*	*16.6%*
Pre-Tax profits	201	206	237	312	329	405	482
Tax	(59.3)	(53.8)	(49.8)	(87.3)	(92.3)	(113)	(135)
Profits from associates	0.0	1.9	2.5	0.0	0.0	0.0	0.0
Net profit	142	155	190	225	237	291	347
Restated net profit	115	183	228	231	261	317	374
Change (%)	*-25.1%*	*58.3%*	*24.9%*	*1.2%*	*13.1%*	*21.4%*	*17.9%*
Cash Flow Statement (EURm)							
Operating cash flows	209	240	305	260	307	367	428
Change in working capital	(21.1)	5.3	(81.1)	(6.0)	(18.2)	(19.9)	(20.0)
Capex, net	(42.0)	(47.4)	(50.0)	(65.5)	(70.7)	(76.4)	(82.1)
Dividends	0.79	0.77	0.84	1.0	1.2	1.0	1.2
Net debt	(25.4)	(70.5)	(102)	98.4	15.6	(130)	(321)
Free Cash flow	146	198	174	189	218	271	326
Balance Sheet (EURm)							
Tangible fixed assets	508	556	623	841	881	921	961
Intangibles assets	456	485	505	559	559	559	559
Cash & equivalents	131	186	226	(2.9)	79.9	225	416
current assets	602	672	810	663	781	966	1,196
Total assets	1,565	1,713	1,938	2,064	2,222	2,446	2,717
L & ST Debt	374	419	450	447	465	484	503
Shareholders' funds	974	1,068	1,226	1,366	1,507	1,712	1,963
Total Liabilities	592	645	712	697	715	734	753
Capital employed	963	1,042	1,128	1,401	1,441	1,481	1,521
Financial Ratios							
Operating margin	17.19	20.43	22.33	21.39	21.81	24.19	26.18
Tax rate	29.47	26.07	20.97	28.00	28.00	28.00	28.00
Net margin	11.07	11.60	12.51	13.71	13.42	15.26	16.89
ROE (after tax)	14.57	14.47	15.52	16.44	15.74	17.03	17.67
ROCE (after tax)	15.41	18.49	22.59	17.07	18.35	21.45	24.34
Gearing	NM	NM	NM	NM	NM	NM	NM
Pay out ratio	43.25	35.89	30.70	36.00	36.50	27.00	25.40
Number of shares, diluted	84.60	82.22	82.00	82.00	82.00	82.00	82.00
Data per Share (EUR)							
EPS	1.84	1.87	2.31	2.73	2.88	3.54	4.22
Restated EPS	1.85	2.22	2.78	2.81	3.18	3.86	4.56
% change	*5.8%*	*19.9%*	*25.3%*	*1.2%*	*13.1%*	*21.4%*	*17.9%*
BVPS	11.51	12.99	14.95	16.66	18.38	20.88	23.94
Operating cash flows	2.47	2.92	3.72	3.17	3.74	4.48	5.22
FCF	1.73	2.41	2.12	2.30	2.66	3.30	3.97
Net dividend	0.80	0.85	0.85	0.85	1.04	1.16	1.26

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

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

1. Cabozantinib: a structural change

1.1. The in-licensing deal with Exelixis

1.1.1. The terms of the deal

On 1 March 2016, i.e. on the same day Ipsen was presenting its full-year 2015 results, the group announced that it had entered into a licensing agreement for the ex-US/Japan rights of Tk inhibitor cabozantinib in all indications with Exelixis.

The fourth pillar ?

Immediately, Ipsen presented the drug as its fourth pillar within its Specialty Care business which illustrates its bright perspectives, which has also been reflected in peak sales above the EUR200m mark with timing beyond 2020 (see part 1.2 of this note).

Financially-speaking, the deal is structured in such a way that Ipsen should be making a couple of milestone payments, first as an upfront at the signature (USD200m) and second towards the end of 2016 when cabozantinib is expected to be approved by the EMA in the key second-line RCC indication (USD60m). Assuming a more cautious approach towards the HCC indication pending the release of clinical data (i.e. no expectations in terms of sales contribution), Ipsen is also entitled to pay commercial milestones (in five tranches, starting when annual sales reach USD100m in the first calendar year) and royalties on sales, starting at 2% and going up to 22% and ultimately 26% (see Fig.1). It is important to note that for the first three indications included in the deal, Ipsen will not pay for any R&D expenses as it is already factored in the regulatory milestone payments. The incurred costs for the group are of a commercial and marketing nature and mainly consist of an oncology sales-force to be recruited and trained to support cabozantinib, mainly in Europe and to a lesser degree in Australia. We are talking about 100-150 representatives to be hired and the cost will be equally shared between 2016 and 2017 and is expected to represent about EUR20-25m in 2016 and EUR25-30m in 2017 as the drug should be launched in RCC next year.

Fig. 1: Royalties on sales to be paid by Ipsen, by tranches

Up to USD50m	From USD51m to 150m	From USD151m to 500m	Above USD500m
2%	12%	22%	26%

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

1.1.2. The consequences of the deal

Lower-than-expected core operating margin in 2016 as a consequence

This extra investment for Ipsen over this period of time is meaningful and, as a consequence, the company has warned that its core operating margin would be around 21% in 2016, i.e. 130bp below last year's level when the combined negative impact of cabozantinib and foreign exchange rates will be 250bp.

Marc de Garidel has presented 2016 as the trough year in terms of profitability and, although it is not (yet) a formal commitment, it is not expected that the core operating margin will drop any further below 26% beyond 2016. However, it is not yet fully clear how extra investment in marketing and sales and first amortisation of milestones paid will be balanced. Ipsen is talking about prioritisation which mainly relates to R&D as we understand it and suggest at worst limited growth if any with delays in the initiation of new studies. It is our understanding that management is committing to the Board with no decline in operating margin in 2017 compared to 2016.

1.2. What are we talking about?

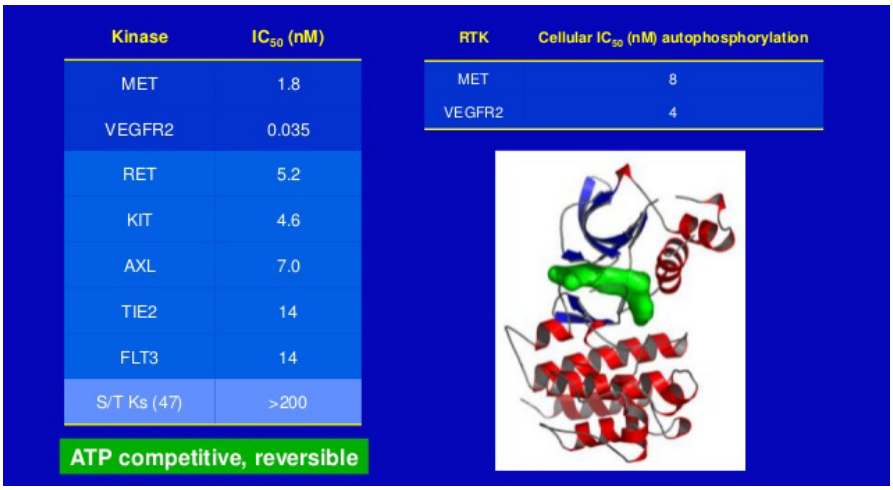
1.2.1. The drug

Obviously, the very first step in evaluating the relevance of this deal is to know more about the drug itself.

Cabozantinib, a multi-tyrosine kinase inhibitor

Cabozantinib is a small molecule that inhibits the activity of various tyrosine kinases but, considering the degree of inhibition of enzymatic reaction measured by Ic50 and reported on Fig.2 below, it is fair to say that this multikinase inhibitor mainly inhibits VEGFR-2 and MET.

Fig. 2: Measurement of the degree of inhibition of kinases by Cabozantinib



Source: Exelixis

MET could be the differentiating factor

Comparing cabozantinib to other members of the same class, it can be highlighted that a slight difference in the final pharmacological effect might come from the MET inhibition which looks very specific to the drug whereas most, if not all, of the others inhibit VEGR-1/2/3 subgroups, PDGFRβ or c-kit but not MET. However, the MET signalling pathway has been shown to be involved in key processes of cancer growth and dissemination and maybe more importantly in resistance to apoptosis.

It is worth noting that cabozantinib is actually already approved in a first indication, although admittedly in a limited one in size called metastatic medullary thyroid cancer (MTC) under the brand name Cometriq, both in Europe and the US. In this rather small indication, Cometriq is mainly competing against Caprelsa, a drug that was bought by Sanofi from AstraZeneca last year for USD165m upfront and potential future payments of USD135m. Our understanding is that Ipsen once competed for these rights as well but was not ready to pay as much as what Sanofi paid in the end. In 2015, Cometriq achieved EUR4m in sales in the MTC indication in Europe and Ipsen will shortly overtake responsibility for the drug in this indication from Sobi and is therefore likely to book sales as early as Q2 2016. However, it is fair to expect sales reported for Cometriq (or under a new name) to be flat vs 2015 and so somewhere between EUR3m and EUR4m.

Second-line RCC is key indication for cabozantinib

Clearly this is not where the interest for cabozantinib lies for Ipsen. The key indication is obviously renal cell carcinoma (RCC) in second-line where clinical data have been available to Ipsen before opting-in (although only interim data have been presented in medical congresses to date) and it is suggested that all endpoints have been reached comfortably, thus making cabozantinib a potential standard of care.

The filing of cabozantinib has already taken place in Europe and feedback from the European Union is expected sometime in the autumn for a global launch starting in Q1 2017.

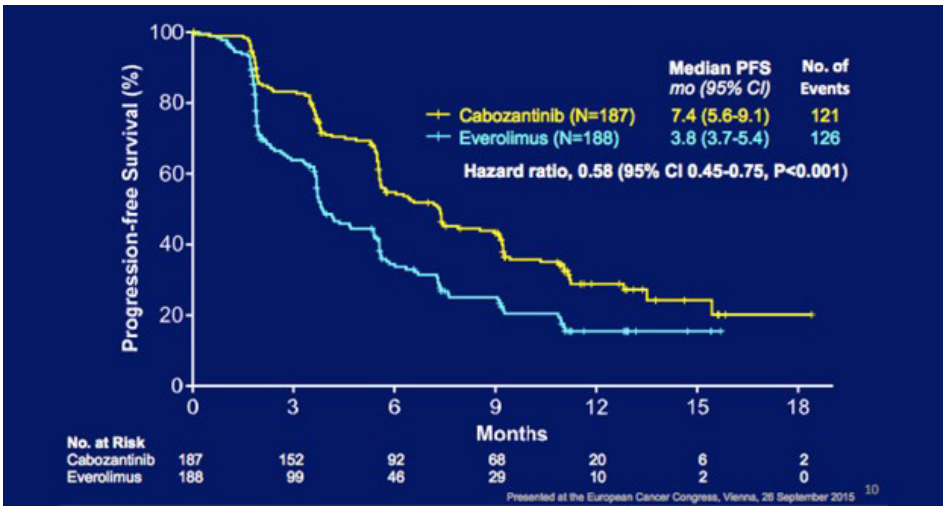
The third indication, and second by order of relevance after RCC, is hepatocellular carcinoma (HCC) where phase III results are expected in 2017 and could add significant potential to the drug.

1.2.2. The key RCC indication

Median PFS meaningfully improved

So RCC is central in Ipsen's decision to buy cabozantinib's rights for ex-US/Japan territories because the comparative trial against everolimus (METEOR) has already delivered robust results that were presented at the ECC/ESMO meeting in Vienna last September with a clear superiority in terms of median PFS which improved from 3.8 to 7.4 months, as illustrated in Fig.3 (HR=0.58).

Fig. 3: PFS measured by ICR review (METEOR trial)



Source: European Cancer Congress (ECC), Vienna, September 2015

Moreover, if the pre-planned analysis showed a strong OS trend in favour of cabozantinib in the trial, statistical significance was not achieved. But a second interim analysis was performed as agreed with regulatory authorities and the results showed "a highly statistically significant and clinical meaningful increase in OS for cabozantinib" according to Ipsen. It has not been determined when the data will be presented but it looks like a fair guess to hypothesise that something might happen at ASCO.

People will compare OS to nivolumab's

Then, cabozantinib is likely to be compared to what nivolumab achieved against the same comparator in the CheckMate 025 study, i.e. 27% reduction in the risk of death with median OS of 25.0 months compared to 19.6 months with everolimus (p=0.002). This data presentation could well be decisive because, depending on how data are received by the medical community vs nivolumab, the scenario could be very different for the drug. In the editorial of the *NEJM* dated November 2015 when the differences were discussed, preference was given to nivolumab based on OS data but also on safety (60% of patients under cabozantinib in METEOR required dose reduction because of side effects, including diarrhoea, palmar-plantar erythrodysesthesia syndrome and fatigue). With a clear OS benefit for cabozantinib too after second analysis and provided there is no question about methodology, and "cabo" therefore being the only drug to show both PFS and OS benefit over Afinitor, what would be the drug of choice?

This is a tough question but we would hypothesise that given the excitement around IO, nivolumab could be a preferred option anyway. That said, can the route of administration make a difference? What about price? At this point, it does not look possible to stratify patients with either of the two drugs to determine higher responders and so physicians are unlikely to make a decision based on epidemiology or based on any tumour testing.

In the end, as the disease progresses, maybe safety and quality of life will be given priority. From that perspective, it remains to be seen which of the two will be preferred as the section of the prescribing information of Opdivo referring to RCC is reporting a discontinuation rate of 16%, a 44% rate of drug delays due to side effects (competitive with the 60% rate of dose reduction with "cabo"?) and a 47% rate of serious adverse reactions in patients receiving Opdivo. So the difference may not be so huge as suggested in the *NEJM*.

What if nivolumab moves in first-line?

There is another unknown factor obviously which is: what happens if the ongoing phase III Checkmate-214 is positive? This one is testing the IO/IO combination of nivolumab with CTLA-4 targeting agent ipilimumab in the first-line setting of RCC in comparison with the current standard of care sunitinib (Sutent). PFS and OS are co-primary endpoints. If positive, despite the very high price, it is likely to become the new standard in first-line RCC. If so, what would happen in second-line? Which VEGFR-based therapy would qualify as standard?

It looks like IO will take an (yet) undefined seat in the RCC market, between first- and second-line. So, cabozantinib, with potential best-in-class survival data, may have to compare with current leaders (i.e. Inlyta, Votrient or Sutent) to increase its legitimacy as a second-to-IO agent in RCC. This could mean extra R&D costs as it is not covered by the existing agreement with Exelixis. Note, however, that a NCI (National Cancer Institute)-sponsored phase II trial (called CABOSUN) is ongoing to test cabo against Sutent in 1L RCC in first-line therapy of intermediate or poor risk patients per standard risk classification. Enrolment of 150 patients was completed in March 2015 and data are anticipated in 2016. Exelixis will finance a phase III trial in 1L and Ipsen will then have the right to opt-in at the beginning or at the end. In any case, we may expect phase II data to impact physicians' decision.

In the end, Ipsen is likely to oppose BMS with nivolumab but also Pfizer (Inlyta, Sutent) and Novartis (Votrient). So the bar is high but we find the data package quite compelling so far in RCC and to say the least quite competitive as well. Moreover, Ipsen suggests that the design of phase III permit several subgroup analysis like patients with bone metastasis or lung metastasis.

EUR200m peak sales looks achievable with conservative assumptions

In spite of these two major unknown factors (i.e. final OS data for "cabo" and outcome for IO/IO study in first-line), we assume "cabo" can reach the EUR200m mark in Europe (+Australia) that Ipsen eluded to during its conference call with the single RCC indication by the middle of the next decade (see Fig.4). The key assumptions when building our sales model have been a mid-range in the estimated addressable market of 15-20% of the 110,000-115,000 patient population, a market share growing up to 25% (Afinitor to which Cabozantinib has been compared holds about 20% currently in Europe), an annual price of EUR60,000 that is factored in only over the period of the median PFS.

The price we opted for looks like a balanced estimate when considering Inlyta (EUR43,800 per annum in France) on one side and Opdivo on the other (around EUR100,000 per year across the various indications in Europe), whereas a premium is likely over the price so far set for Cometriq sold as a capsule formulation for MTC (EUR4,600 per month) when RCC and HCC will be available in a tablet form.

Fig. 4: Cabozantinib – sales model in MTC+RCC

	2016e	2017e	2018e	2019e	2020e	2021e	2022e	2023e	2024e	2025e	2026e	2027e
Prevalence Europe RCC	110,000	111,100	112,211	113,333	114,466	115,611	116,767	117,935	119,114	120,305	121,508	122,723
5% extra prevalence for ROW	5,500	5,555	5,611	5,667	5,723	5,781	5,838	5,897	5,956	6,015	6,075	6,136
Addressable patients (17.5%)	20,213	20,415	20,619	20,825	21,033	21,244	21,456	21,671	21,887	22,106	22,327	22,550
Market share	0	2%	6%	10%	14%	17%	20%	23%	25%	25%	25%	25%
Volume	0	408	1237	2082	2945	3611	4291	4984	5472	5527	5582	5638
PFS median	0,617	0,617	0,617	0,617	0,617	0,617	0,617	0,617	0,617	0,617	0,617	0,617
Annual price	60 000	60 000	60 000	60 000	60 000	60 000	60 000	60 000	60 000	60 000	60 000	60 000
Price x PFS	37 000	37 000	37 000	37 000	37 000	37 000	37 000	37 000	37 000	37 000	37 000	37 000
Sales in MTC	3 000	4 000	4 500	5 000	5 000	5 000	5 000	5 000	5 000	5 000	5 000	5 000
Total Sales MTC+RCC (EURm)	**3 000**	**19 107**	**50 274**	**82 052**	**113 952**	**138 622**	**163 774**	**189 416**	**207 457**	**209 482**	**211 526**	**213 592**

Source: Bryan, Garnier & Co ests.

These are the numbers we are going to factor into our sales model.

Circa 15% royalty rate on sales

This will go together with the calculation of royalties on sales to be paid to Exelixis by Ipsen in various tranches that will represent, when the drug gets mature in the RCC indication, about 15% of sales on average, i.e. EUR30-35m per annum in the middle of the next decade.

Fig. 5: Cabozantinib – royalty model in MTC+RCC

Royalties (USD,000)	2016e	2017e	2018e	2019e	2020e	2021e	2022e	2023e	2024e	2025e	2026e	2027e
2%	67	425	1 117	1 000	1 000	1 000	1 000	1 000	1 000	1 000	1 000	1 000
12%			704	4 941	9 195	18 000	18 000	18 000	18 000	18 000	18 000	18 000
22%						888	7 037	13 305	17 716	18 211	18 711	19 215
26%												
Total royalties (USD, 000)	67	425	1 821	5 941	10 195	19 888	26 037	32 305	36 716	37 211	37 711	38 215
Total royalties (EUR, 000)	**60**	**382**	**1 639**	**5 347**	**9 175**	**17 898**	**23 431**	**29 073**	**33 042**	**33 487**	**33 937**	**34 391**
As a % of sales	2%	2%	3%	7%	8%	13%	14%	15%	16%	16%	16%	16%

Source: Bryan, Garnier & Co ests.

Although the mechanism of commercial milestones is less precise, we have assumed that a first one would be reached when the drug achieves USD100m, which represents about USD25m, i.e. 5% of the total USD545m milestones to be paid to Exelixis contractually if all thresholds are exceeded (the last one would be paid if cabozantinib achieves blockbuster status in Ipsen's territories).

Should Ipsen have to pay Exelixis more commercial milestones, this means we would have to revise our sales estimates upwards.

1.2.3. HCC to be seen as an option

The third indication cabozantinib is very much engaged into is the second-line of treatment of advanced hepatocellular carcinoma (HCC). Although it is far from the first, HCC is however the sixth most common malignancy and the third in terms of mortality worldwide (with predominance in Southern Asia) and one of the poorest if we consider the way it is addressed from a pharmacological perspective. Despite several attempts, very few drugs have proven any efficacy in this disease.

Despite modest efficacy, the current standard in first-line is Bayer's sorafenib (Nexavar) whereas no approved drug is available for more advanced treatment lines.

Interesting early data for nivolumab in HCC

However, the same players as in RCC are currently trying to make inroads into this setting where there is a clear unmet medical need and so a meaningful potential return for healthcare companies: within the small molecules space, it looks like MET inhibition is the most interesting pathway whereas IO can be (once again) disruptive when first (although very early-stage) data are considered. In a first phase I/II trial in 42 evaluable patients presented at ASCO in May 2015, nivolumab (again) showed a 20% response rate with a fairly long duration of response and a 48% stabilisation rate. 12-month survival rate was 62% at the level of the entire population of the study where it is usually about half for those treated with sorafenib in first-line.

A first-line HCC phase III called Checkmate-459, comparable to sorafenib, had already started enrolling in late 2015 with an estimated total number of patients at 726 and a target date for primary outcome measures in July 2017. The co-primary endpoints are TPP and OS whereas the secondary endpoints are ORR and PFS. Obviously, these results will be not only of high significance for sorafenib but also for all drugs currently in development in HCC, be it in first- or second-line. And they will be made available after cabozantinib's phase III results in second-line but before it is approved, so it will potentially impact it before it can get any fruit from this indication.

MET inhibition looks interesting in HCC

That said, let's see how cabozantinib could play out in this disease. First, it looks fair to say that a lot of different approaches have failed to demonstrate any benefit in HCC and even sorafenib's efficacy is considered very modest. So molecules sharing more or less the same targets with sorafenib may not necessarily attract high interest from the medical community. However, what we said for RCC may even apply with more accuracy in HCC, i.e. that the MET component in cabozantinib's TK activity is key. Evidence has emerged and is improving that dysregulation of the HGF-cMET pathway is implicated in HCC carcinogenesis and progression, hence the interest for MET inhibition in this setting.

Two MET tyrosine kinase inhibitors have presented phase II data that are encouraging and deserve further investigation.

First is a highly selective MET inhibitor called tivantinib, developed by ArQule and Daiichi Sankyo which however demonstrated in phase II that its activity was limited to high MET expressers. In this subgroup, median TTP, PFS and OS were all statistically significant and, as a consequence, the sponsors have designed a phase III study with a twice-daily 240mg dose in MET-high HCC patients only (20% to 48% of the total population, depending on the source). Pre-planned sample size is 300-400 patients who have either progressed on or been intolerant to sorafenib. The study is ongoing and the completion date is expected during 2017. OS is the primary endpoint.

Encouraging rate of disease control in phase II

Second is precisely cabozantinib which is a less selective MET inhibitor and has been tested in a wide range of subjects with various advanced solid tumours. Among them, 41 had advanced HCC and Child-Pugh class A (classification that assesses the functional capacity of the liver), with half of them being naïve to any treatment and the other half having received prior sorafenib-based therapy. Over the 36 patients evaluable for tumour assessment at week 12, the overall disease control rate was 68%, including two partial responses (+one that came later).

Ongoing phase III trial with data coming by year-end

Based on these results, Exelixis decided to start a phase III trial (called CELESTIAL) due to enrol about 760 patients with advanced HCC who have received sorafenib in first-line. Unlike tivantinib, participants are not stratified based on MET expression. The suggestion by Exelixis is that MET is involved but may not be the sole pathway to influence response and efficacy. The trial is ongoing at the same daily oral dose as in RCC, i.e. 60mg which by the way is a reduction compared to the 100mg dose tested in phase II. The results are expected to be reported in Q4 2016.

What looks positive for cabozantinib is that it is going to be next to report phase III results and so, if positive, it may well take the lead in second-line HCC. However, considering the history in this field, the limited sample size in phase II, the dose reduction implemented while entering phase III, the absence of patient stratification, we would apply a fairly low PoS to the drug in HCC. Moreover, although they will come later on in 2017, tivantinib and more importantly nivolumab phase III data are very likely to impact the treatment paradigm too. As a consequence, we have decided not to factor any sales in HCC for cabozantinib into our model yet.

Ipsen also refers to 2L HCC as "more challenging" an indication, that would be a "bonus" if successful, worth EUR50-150m in terms of market opportunity.

2. A new investment case?

2.1. Cabozantinib is impactful for Ipsen

We have addressed most of this topic and its consequences in the first part of this note but let's summarise the financial aspects one more time to assess fully the impact the deal has on Ipsen's numbers and on the investment case.

So, for 2016, Ipsen has estimated that the operational cost of the deal, i.e. the pro-forma impact of the cost of a European commercial and marketing infrastructure in oncology, would be EUR20-25m or a negative margin impact of 150bp. Below EBIT, the extra influence will be the financial cost related to the USD200m upfront payment made by Ipsen to Exelixis at the very beginning of the year. On top of this cabozantinib-related impact, Ipsen has also mentioned that currency movements would have an impact of about 200bp on the top-line and 100bp on the EBIT margin. All in all, Ipsen is expecting the core operating income margin to be at around 21% in 2016, which compares to 22.3% in 2015, meaning that, excluding the two above-mentioned negative impacts, it would have grown to about 23.5%, up 120bp, very much in line with expectations.

While referring to 2016 as the "trough year" in terms of margin, Ipsen will in our view support a higher dilutive impact of the deal in 2017 than in 2016, as the full cost of the commercial infrastructure will be charged to the P&L, whereas the revenue contribution will remain modest as the drug will start ramping-up across the year when the full green lights are obtained (including reimbursement prices) on a country basis.

Accretion in 2019 onwards and increased visibility in the next decade

After 2017, the impact of the dilution will progressively reduce and then turn into an accretive effect as of 2019, although core EPS at that time will remain inferior to what we had prior to the full-year results as it also reflects the detrimental influence of currencies for which we adopt – as always – a status quo scenario as we do not make any projection on currency movements. The two influences together make core EPS in reported terms exceed previous levels only in 2020. However, it obviously gives more confidence and visibility on Ipsen's earnings and cash flows into the next decade although cancer is a field where changes are taking place so quickly that other disruptions in RCC or HCC, if only from other agents than nivolumab, can always happen by the start of the next decade.

Fig. 6: Changes to the sequence or our core EPS

EUR	2015	2016e	2017e	2018e	2019e	2020e
EPS old	2.70 (e)	3.10	3.70	4.17	4.66	4.98
EPS new	**2.78 (a)**	**2.82**	**3.27**	**3.86**	**4.45**	**5.00**
Diff.	+3%	-9%	-11%	-6%	-1%	+1%

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

Clearly, this deal is illustrative of a period when a company has to take the opportunity of short-term growth to build a medium- and long-term stronger outlook. Provided the target is the right one and the dilutive impact not too heavy, we fully endorse the decision and support the rationale of this type of strategic move. In this specific case, we tried to be balanced in the way we presented the deal with the pros and cons of cabozantinib in RCC and HCC.

One way or another, IO approaches are likely to impact cabozantinib

In general terms, a cabozantinib-like deal, i.e. the acquisition of rights for a late-stage compound in oncology (including with phase III data available) is carrying limited risks of failure. The field of oncology is the subject of so much innovation nowadays including with disruptive immune-oncologic agents that it is difficult to predict as accurately as historically how a new drug candidate will perform in three, five or ten years. Afinitor or Zelboraf are good recent examples of molecules whose peak sales have been severely cut as a consequence of the emergence of an expectedly severe form of competition. With the increasing number of players in the field of immune-oncology, we would expect this scenario to take place even more often. For cabozantinib, what we suggest is that very good clinical data may not fully prevent a severe and in the end impactful competition from IO agents like nivolumab or others, be it in similar lines of treatment or for earlier ones, then potentially delaying use of cabozantinib to a later stage. However, cabozantinib is also developed in a quite extensive programme of phase II and III trials in comparison with sunitinib and sorafenib in first and second-line of RCC and HCC and may well prove superior to these in-market drugs. So our assumptions are very much balanced in our view for RCC (with a 25% market share at peak in 2L) and more than conservative with no sales in HCC. So if anything we see upside to our numbers.

2.2. The rest of the business is healthy

Unexpected support from GI franchise

Because the two pieces of news came out on the same day, it is worth underlying that actually the full-year 2015 results were good and even slightly above expectations. In particular, consensus was relaxed and comfortable with the Somatuline and Dysport figures but was somewhat more anxious about Primary Care, mainly on the back of the slowing-down emerging markets. Not only was Primary Care resilient in Q4 2015 but it actually achieved a spectacular 8.4% ex-currency growth, driven by the GI franchise. This was all the more surprising that it did not come from Smecta and it did, but only marginally, come from Forlax. In fact, a series of smaller products, usually not even disclosed, performed extremely well, as illustrated by Etiasa in China, Fortrans in Russia or Eziclen in various European countries where it is currently ramping-up. As a consequence, the "other" line in the GI franchise has become so significant in size that Ipsen is thinking about disclosing more products on an individual basis. Therefore, it also suggests that what has been noticed in Q4 2015 is not a one-off, although some modest inventory movements might have helped, but looks like a growth driver for 2016 and is a key component in the guidance for "slight Primary Care growth".

So we were cautious about 2016 in emerging markets and also about the reflection an inflection could have had on Primary Care sales but this guidance is reassuring. Dysport is actually helping a lot in Russia and in Brazil whereas Decapeptyl and swith-to-OTC strategy are supporting China.

With Primary Care being neutral to slightly positive to sales, we can refocus on Speciality Care, which of course is the heart of the investment case at Ipsen.

Not a lot to say frankly if we don't want to re-do the whole story behind Somatuline and Dysport which is not the purpose of this note:

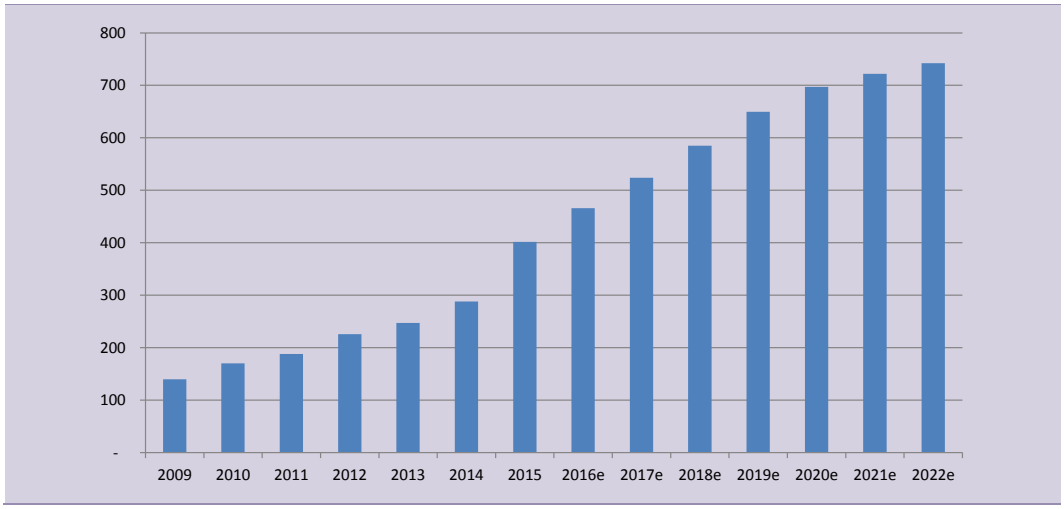
Somatuline is delivering

- Somatuline has delivered another spectacular quarter in Q4 2015 with a local currency growth of 44.4% to EUR110m which reflects continuing market share gains in the NET indication both in the US (doubling in one year from about 6% to close to 13%) and in Europe (to exceed 44%, up 22pp over the previous year). What is really good news is that Ipsen is not only capturing the majority of new patients but is also increasing the pace of patient switches from Novartis's Sandostatin which could significantly help to achieve peak sales earlier than expected if not exceed original targets.

With annual sales jumping from EUR287m in 2014 to EUR402m in 2015 (up 34%), it is reasonable to expect Somatuline to approach the half-billion mark in 2016 (see Fig. 7) and to remain the main growth and mix driver.

Encouraged by this strong trend and the fact that the market itself is expanding (less "watch-and-wait" strategies), Ipsen has decided to target clinics and not only large hospitals, which should support growth going forward.

Fig. 7: Somatuline sales growth profile (EURm)



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

Dysport on a different track in aesthetic vs medical indications so far

- Dysport had been less spectacular over the first nine months of 2015 but it was expected to rebound during the last quarter if only because billings to Galderma were expected to reflect better the underlying good growth of the drug in the aesthetic indications for which Galderma has responsibility. The underlying market is growing at an annual rate of about 10% and Dysport is gaining share which is then reflected not only in the sales of the drug as it is manufactured by Ipsen and sold to Galderma but also in other revenues where the royalties received are booked. Ipsen looks very happy with the job done by Galderma since they recovered the US rights of the drug from Valeant less than a couple of years ago. During this time, Dysport has gained about 7pp market share in the US, almost entirely at the expense of Botox. Now the performance was also very good in several ex-US markets like Brazil (despite a tough macro environment), Mexico or Australia.

  Where it is still tough to make meaningful inroads is in the medical setting with Dysport, despite the addition of the AUL (adult upper-limb) indication and although reimbursement is not an issue here and this is still because the long history of practice and the use of Botox by doctors and nurses make a change difficult to implement. During the conference call of the annual results, Marc de Garidel illustrated this by the example of AUL where eight different muscles can be affected each of which requiring a specific and precise injection with a different dose of toxin. And so Ipsen is moving on investing behind Dysport to train physicians and nurses about how to use it because there is evidence otherwise that it is a superior product when considering onset of action, duration of use and ease of use. Therefore it will take more time than initially thought but Ipsen suggested that something was maybe moving in the right direction with big accounts and said it would have an update on this with the first-half results.

To sustain double-digit growth, Dysport clearly needs the US to perform strongly because some other countries are facing some form of competition like in Germany and so the next 12 to 18 months will be crucial to see whether, with a reasonably competitive label and scope of indications, Dysport can now grab some market share from Botox in the medical indications in the US and narrow the gap, or if the bar is too high. So far, Dysport in the US is estimated to be only about USD15m in sales for Ipsen. With AUL added to the label (that led to the addition of new reps from 8 to 22) and soon-to-come PLL (first-to-file), Dysport is expected to show some signs of speed up.

2.3. New guidance looks conservative

With a negative 150bp impact from cabozantinib and 100bp from currencies and a target operating margin of 21% for 2016, Ipsen suggests that stripping out these two elements, core EBIT margin would have grown by 120bp from 22.3% in 2015 to 23.5%.

21% core EBIT margin in 2016 looks conservative

First of all, when it comes to the pro-forma cost of the cabozantinib's sales-force that will start being built up in 2016, Ipsen guides towards a EUR20m impact on the P&L which would then represent 130bp rather than 150bp. 150bp would be EUR23m. So there is a first layer of conservatism here. It is less easy to assess how the 100bp impact from currencies stands, i.e. what it is exactly dependent on and what the underlying assumptions are but we would assume, as long as currencies are concerned in this volatile environment, that the company has been cautious on this matter too.

The second element to assess the conservatism of the guidance is top-line growth and mix effect. Ipsen said that it was expecting Speciality Care to grow double-digit in 2016 and Primary Care to be marginally up compared to 2015. The difference in profitability between the two businesses is not big enough to drive a major shift in margin *per se* (42.8% vs 38.2%) but Specialty Care has endorsed full cost of commercial infrastructure's expansion in the US supporting the NET indication of Somatuline (the gap should enlarge in the coming years with PC going down into the 30's and SC going up towards the 50's). It is important to report the mention by Ipsen of first-time profitability being achieved by the US subsidiary not only in Q4 2015 but also in 2015. As North American sales were EUR157.9m in 2015, we assume that the break-even is circa EUR150m. Hence, with EUR48.7m achieved in Q4 2015, it is fair to expect North American sales to exceed EUR200m in 2016 with limited to no extra costs incurred. So profitability will significantly expand as increment will come from Somatuline and Dysport which are highly profitable drugs. This is where we see a major upside for the group's profitability and this will exclusively favour Specialty Care. To illustrate what it could have been, let's assume that the incremental EUR65m in sales anticipated on Somatuline in 2016 vs 2015 carry 70% profitability and the impact on the group's margin of this sole item would be 120bp.

As we speak about mix effects, we usually cover COGS and S&M costs and so this leaves us with three basic operating lines: other revenues, R&D and G&A costs that are not covered. We would make the following comments on each of them:

Other revenues should show good growth in 2016

- "Other revenues" obviously is the more interesting one because we see growth in excess of top-line growth, thus translating into a positive margin impact. This should come from the sequence of milestone recognition as the 2015 annual report says that deferred income in n+1 will be EUR29.8m where it was EUR24.9m in 2015. The difference will more than offset the non-recurring upfront payment of EUR3.4m received for the Ginkor Fort rights.

Moreover, about two-thirds of these revenues actually come from royalties on sales and about two-thirds of the two-thirds relate to Dysport in the aesthetic indications. As the drug is gaining market share out of a market that is growing at about 10% p.a., we see also a positive impact here. Most of the rest comes from Menarini with 100% of the royalties received (including in France, where a co-promotion agreement is in place) going to "other revenues";

R&D expenses will be kept under tight control

- R&D expenses have come down significantly in 2015 as a percentage of sales mainly as the result of the decision to discontinue the development of tasquinimod in prostate cancer. With cabozantinib's phase III development costs in the short term included in the milestones paid to Exelixis (i.e. no impact on R&D costs), Ipsen said it would re-prioritise its investments and it looks fair to anticipate the R&D ratio as a percentage of sales to remain roughly flat over the coming 2-3 years and therefore to be neutral on margins;

- Lastly, administrative and general costs grew 10.4% in 2015 but the first two reasons behind the growth had been an increase in support functions in the US (in connection with the rapid expansion of the business there) and extra IT spending which are unlikely to be repeated in 2016. That said, being here or in the marketing expense line, comments from Ipsen about China suggest the need for incremental resources to adjust for structural changes in the Chinese market.

So we are reasonably confident that Ipsen will reach its 2016 guidance quite easily if not slightly exceed them which, in the end, means that the current year should result in residual – although admittedly very symbolic – growth at the core EBIT and core EPS levels. Thereafter, we see resumption of double-digit earnings growth as of 2017 and from 2016 to 2020, this would result into an attractive sales, core EBIT and core EPS growth of 7.6%, 14.2% and 15.7% respectively.

A very attractive PEG ratio

With a P/E of 17x around for 2015 and 2016, the point of growth over [2016-2020] is without doubt one of the cheapest in our coverage. The PEG ratio 2016 would be 1.1x.

2.4. Are management changes a worry?

Before we close, and although it was not a focus within this note, we would like to say a word about the management changes that were announced shortly before the annual results were presented.

We commented on the management changes when they occurred in mid-February but would like to summarise our thoughts here as we believe it could have a meaningful in the medium-term future if one scenario materialises.

The future of Marc de Garidel within Ipsen looks uncertain to us

It did not come as a surprise to learn that Christel Bories would leave the company with immediate effect as it was our understanding that relations with Marc de Garidel were not very good. Moreover, at a time when the functions of CEO and Chairman are separated and the CEO's one left free, and when the deputy-CEO is not the elected person, there is no option for him/her but to leave.

The point is more about Marc de Garidel's future because the focus on "leading and animating the Board of Directors" does not look like the promotion a Chairman and CEO can dream about when the time to retire has not yet come. And so to make it simple, our question is the following: has the new job, as described, been mutually accepted by the parties or is it a transitioning period in preparation for another departure in a few months' time? Companies of this size are heavily dependent on people and the idea is not to suggest that Ipsen would not survive Marc de Garidel but he has been the architect of the turn-around and he is perceived as such by the investment community.

So we have to admit that the scenario of his departure is a limitation to the investment case. Now, because in any case we see it as unlikely to happen by the very end of 2016, we believe we can first focus on the underlying story and the under-appreciated growth perspectives.

2.5. Valuation

Our valuation derived from a DCF model shows limited change compared to our previous calculation because the FY results and short-term trends partially offset the negative immediate impact of the cabozantinib deal with Exelixis. Moreover, the deal itself is pretty much balanced in terms of cash-flow generation over time although it is dilutive over the first three years based on the cautious estimates we have factored into our sales model. All in all, 2016 and 2017 have a greater negative influence on our FV than the positive ones coming from post-2020 upside from cabazantinib as discount rates obviously differ.

Now, the share price has adjusted significantly more than what we see in our DCF model as a result of the change in perception from various investors about the investment case of Ipsen. So far, it was a short-term strong performer that was benefiting from the success of Somatuline in the US to improve its mix and boost its earnings growth, with a resulting CAGR in the double-digit territory over the next three years. The deal with Exelixis is obviously changing the story as 2016 will show limited to no growth while the success of cabozantinib remains hypothetical, introducing a risk factor to the case that was relatively risk-free so far (although visibility beyond 2018-19 was low).

In financial terms, beyond the introduction of revenues and expenses related to cabozantinib into our model, it is important to note that, cash-flow-wise, the deal with Exelixis will have a dual impact in 2016 with upfront payment of USD200m (already done at the time the deal was inked) and another USD60m upon the approval of the drug in second-line RCC in Europe which is expected sometime in September (based on accelerated approval process). In the following table, we have reported this double cash payment under the capex line. Accounting-wise, both payments will be amortised in the P&L over a 10-year period (maybe more, pending ongoing discussions), starting in 2017. Ipsen has said it would not restate the circa EUR23m p.a. amortisation in its core numbers, although it is non-cash, but we will do, hence the difference materialising between Ipsen's reporting and BG's estimates but favouring apple to apple comparisons in the sector. This represents about 100bp on the core operating margin, hence our projection of 27% in 2020 that compares with the "above 26%" guided by Ipsen.

Note also that royalties paid to Exelixis will be reported in COGS while we will first report them under a separate line just above operating income.

Fig. 8: Cash flow estimates

EURm	2015	2016e	2017e	2018e	2019e	2020e	2021e	2022e
Revenues	1 520.2	1 636.4	1 765.9	1 907.7	2 049.7	2 168.0	2 293.2	2 321.9
Growth	*14.1%*	*7.6%*	*7.9%*	*8.0%*	*7.4%*	*5.8%*	*5.8%*	*1.3%*
Recurring EBIT	322.5	331.0	365.6	439.4	512.0	560.1	607.7	623.6
%sales	21.2%	20.2%	20.7%	23.0%	25.0%	25.8%	26.5%	26.9%
Taxes	(83.1)	(80.8)	(91.4)	(110.9)	(130.8)	(144.3)	(156.6)	(162.9)
Tax rate	*(25.8%)*	*(24.4%)*	*(25.0%)*	*(25.2%)*	*(25.5%)*	*(25.8%)*	*(25.8%)*	*(26.1%)*
D&A	43.7	65.5	70.6	76.3	82.0	86.7	91.7	92.9
%sales	2.9%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%
Change in working capital	(81.1)	(5.8)	(18.1)	(19.9)	(19.9)	(16.6)	(23.5)	(10.6)
Operational cash-flows	202.0	309.8	326.8	384.9	443.3	485.9	519.3	542.9
Capex (incl. intangibles & milestones)	(50.0)	(337.3)	(110.6)	(116.3)	(122.0)	(148.2)	(128.8)	(130.9)
%sales	3.3%	20.6%	6.3%	6.3%	6.3%	6.3%	6.3%	6.3%
Free cash-flows	152.0	(27.5)	216.1	268.6	321.3	337.7	390.4	412.0
% croissance		ns	ns	24.3%	19.6%	5.1%	15.6%	5.5%

Source: Bryan, Garnier & Co ests.

New BG valuation metrics factored in

As long as the main assumptions for the WACC calculation remain more or less unchanged (BG today moves risk-free rate for all covered stocks from 2% to 1.6% and equity risk premium from 6.4% to 7%), although we could, we have decided not to make any changes. Cabozantinib may have improved the long-term growth rate but at least until it is a product, it is premature to impact our DCF model. Similarly, 2016 payments to Exelixis will create leverage and net debt at the end of 2016 but for one year with net debt and the following ones in a cash positive territory, we have opted for status quo and a WACC based on pure cost of equity, i.e. 8.6% (vs 8.4% previously).

A new FV of EUR60

With all this in mind, we derive an enterprise value (EV) of EUR5.0bn and an equity value of EUR4.9bn or EUR60 per share, marginally lower than the FV we had so far, i.e. EUR63.

The new FV of EUR60 represents about 25% upside potential compared to the current share price. Because of the absence of growth in 2016 is well understood and offset in our view by the rich news flow related to cabozantinib (OS phase III data in 2L RCC likely at ASCO, approval in Europe in 2L RCC in September, phase III data in 2L HCC in Q4, phase II data in 1L RCC in Q4), this could/should increase the degree of confidence in what Ipsen already described as its future fourth pillar.

Although we may have a wait-and-see scenario prevailing in some institutions until more data become available (at least until ASCO), we believe we have been cautious enough with the hypothesis we made in our DCF model to support a BUY rating based on the circa 25% upside we currently have.

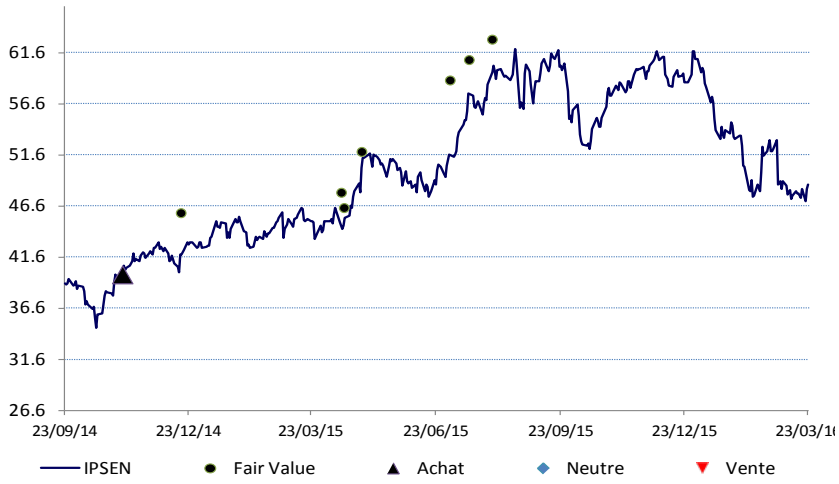
Appendix

	2012	2013	2014	2015	2016e	2017e	2018e	2019e	2020e	2021e	2022e
Specialty Care	**863**	**871**	**947**	**1 114.2**	**1 212.1**	**1 335.7**	**1 472.5**	**1 610.2**	**1 727.4**	**1 804.1**	**1 877.4**
Reported growth	13.6%	1.0%	8.7%	17.7%	8.8%	10.2%	10.2%	9.4%	7.3%	4.4%	4.1%
Decapeptyl (prostate cancer)	306	299	317	334.0	337.7	337.4	330.6	324.0	317.5	311.2	305.0
Reported growth	8.0%	(2.5%)	6.0%	5.5%	1.1%	(0.1%)	(2.0%)	(2.0%)	(2.0%)	(2.0%)	(2.0%)
CER		(1.9%)	6.5%	1.3%	2.0%	-	(2.0%)	(2.0%)	(2.0%)	(2.0%)	(2.0%)
Hexvix	12	14	16	17.2	18.9	20.8	21.8	22.9	24.1	25.3	26.5
Reported growth		17.1%	11.1%	7.3%	10.0%	10.0%	5.0%	5.0%	5.0%	5.0%	5.0%
CER		16.7%	11.1%	6.6%	10.0%	10.0%	5.0%	5.0%	5.0%	5.0%	5.0%
Cabozantinib					3.0	19.1	50.3	82.1	114.0	138.6	163.8
Somatuline (acromegaly)	226	247	288	401.6	465.9	524.0	585.1	650.0	696.9	721.9	741.9
Reported growth	19.8%	9.4%	16.4%	39.7%	16.0%	12.5%	11.7%	11.1%	7.2%	3.6%	2.8%
CER		11.1%	16.8%	34.2%							
Telotristat					-	7.0	22.0	35.0	50.0	60.0	70.0
Reported growth						NS	214.3%	59.1%	42.9%	20.0%	16.7%
CER											
Increlex (IGF-1)	28	13	13	20.4	24.3	26.7	29.3	30.8	32.3	33.9	35.6
Reported growth	12.3%	(55.1%)	(15.0%)	58.1%	19.2%	9.6%	10.0%	5.0%	5.0%	5.0%	5.0%
CER		(53.9%)	1.3%	42.2%	20.0%	10.0%	10.0%	5.0%	5.0%	5.0%	5.0%
Dysport	236	242	255	279.5	301.8	342.1	376.3	410.2	438.9	460.9	483.9
Reported growth	15.7%	2.6%	4.0%	9.8%	8.0%	13.4%	10.0%	9.0%	7.0%	5.0%	5.0%
CER		7.0%	8.6%	9.7%	12.0%	13.0%	10.0%	9.0%	7.0%	5.0%	5.0%
Primary Care	**325**	**320**	**312**	**305.3**	**314.2**	**321.0**	**323.5**	**326.5**	**325.3**	**324.9**	**325.1**
Reported growth	(5.7%)	(1.3%)	(2.6%)	(2.1%)	2.9%	2.2%	0.8%	0.9%	(0.4%)	(0.1%)	0.1%
Smecta (diarrhoea)	114	121	121.3	114.8	113.4	119.5	125.5	131.8	138.4	145.3	152.6
Reported growth	10.9%	6.7%	0.2%	(5.4%)	(1.2%)	5.4%	5.0%	5.0%	5.0%	5.0%	5.0%
CER		8.1%		(10.2%)	5.0%	5.0%	5.0%	5.0%	5.0%	5.0%	5.0%
Forlax (constipation)	39	39	39	39.7	39.2	39.3	39.3	39.3	39.3	39.3	39.3
Reported growth	(6.5%)	-	(0.5%)	3.1%	(1.3%)	0.3%	0.0%	0.0%	0.0%	0.0%	0.0%
CER		0.3%		1.4%	1.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Tanakan (age-related cognitive disorders)	79	67	63	52.0	49.8	47.6	45.2	42.9	40.8	38.7	36.8
Reported growth	(18.0%)	(14.9%)	(6.8%)	(16.9%)	(4.3%)	(4.4%)	(5.0%)	(5.0%)	(5.0%)	(5.0%)	(5.0%)
CER		(13.3%)	(0.6%)	(11.2%)	0.0%	(5.0%)	(5.0%)	(5.0%)	(5.0%)	(5.0%)	(5.0%)
Group sales	**1 219**	**1 225**	**1 275**	**1 443.8**	**1 550.6**	**1 681.0**	**1 820.3**	**1 961.0**	**2 077.0**	**2 153.3**	**2 226.9**

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

Price Chart and Rating History

Ipsen



Ratings		
Date	**Ratings**	**Price**
01/03/16	Under review	EUR53.02
04/11/14	BUY	EUR29.01
02/09/13	NEUTRAL	EUR28

Target Price	
Date	**Target price**
03/08/15	EUR63
17/07/15	EUR61
03/07/15	EUR59
29/04/15	EUR52
16/04/15	EUR46.5
14/04/15	EUR48
17/12/14	EUR46
01/09/14	EUR41
11/04/14	EUR36
07/01/14	EUR33
02/09/13	EUR29.5
14/06/13	EUR30.5
17/01/13	EUR29

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 72% NEUTRAL ratings 0% SELL ratings 28%

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

Summary of Investment Research Conflict Management Policy is available www.bryangarnier.com

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

BRYAN, GARNIER & CO

London	Paris	New York	Geneva	New Delhi
Beaufort House	26 Avenue des Champs Elysées	750 Lexington Avenue	rue de Grenus 7	The Imperial Hotel
15 St. Botolph Street	75008 Paris	New York, NY 10022	CP 2113	Janpath
London EC3A 7BB	Tel: +33 (0) 1 56 68 75 00	Tel: +1 (0) 212 337 7000	Genève 1, CH 1211	New Delhi 110 001
Tel: +44 (0) 207 332 2500	Fax: +33 (0) 1 56 68 75 01	Fax: +1 (0) 212 337 7002	Tel +4122 731 3263	Tel +91 11 4132 6062
Fax: +44 (0) 207 332 2559	Regulated by the	FINRA and SIPC member	Fax+4122731 3243	+91 98 1111 5119
Authorised and regulated by	Financial Conduct Authority (FCA)		Regulated by the	Fax +91 11 2621 9062
the Financial Conduct	and the Autorité de Contrôle		FINMA	
Authority (FCA)	prudential et de resolution (ACPR)			