

Ipsen and Exelixis announce results from Phase 2 CABOSUN trial of cabozantinib versus sunitinib in previously untreated advanced renal cell carcinoma at ESMO 2017

- **Independent Radiology Review Committee confirms primary endpoint analysis per investigator: cabozantinib provided statistically significant improvement of progression-free survival, with a 52 percent reduction in the rate of progression or death compared to sunitinib**
- **Exelixis and Ipsen will host an investor and media webcast from Madrid to discuss the data on Sunday, September 10 starting at 18h45 CEST**

Paris (France), September 10, 2017 – Ipsen (Euronext: IPN; ADR: IPSEY) and Exelixis, Inc. (NASDAQ:EXEL) today announced updated results from the CABOSUN randomized phase 2 trial of cabozantinib in patients with previously untreated advanced renal cell carcinoma (RCC) with intermediate- or poor-risk disease per the International Metastatic Renal Cell Carcinoma Database Consortium (IMDC). Principal investigator Toni K. Choueiri, M.D., will present detailed data from late-breaking CABOSUN abstract [#LBA38_PD] today in the Genitourinary Tumors, Non-Prostate poster discussion session, starting at 2:45 p.m. CEST (local Madrid time) / 8:45 a.m. EDT / 5:45 a.m. PDT at the European Society for Medical Oncology (ESMO) 2017 congress, which is being held September 8-12, 2017 in Madrid, Spain.

CABOSUN is being conducted by The Alliance for Clinical Trials in Oncology as part of Exelixis' collaboration with the National Cancer Institute's Cancer Therapy Evaluation Program (NCI-CTEP). The data presented at ESMO 2017 included the analysis from a blinded independent radiology review committee (IRC), which confirmed the primary efficacy endpoint results of investigator-assessed progression-free survival (PFS), as well as an updated investigator-assessed analysis. Per the IRC analysis, cabozantinib demonstrated a clinically meaningful and statistically significant 52 percent reduction in the rate of disease progression or death (HR 0.48, 95% CI 0.31-0.74, two-sided P=0.0008). The median PFS for cabozantinib was 8.6 months versus 5.3 months for sunitinib, corresponding to a 3.3 month (62 percent) improvement favoring cabozantinib over sunitinib.

"These updated analyses from CABOSUN consistently show that cabozantinib provided a statistically significant decrease in the rate of disease progression or death compared to sunitinib, a current standard of care – potentially offering a new treatment option for physicians to treat patients in the first-line advanced renal cell carcinoma setting," said Toni K. Choueiri, M.D., Director, Lank Center for Genitourinary Oncology, Dana-Farber Cancer Institute. "The CABOSUN trial included patients with intermediate or poor prognostic factors per the IMDC criteria; in addition, patients had a notable number of other independent adverse prognostic risk factors. These included a high rate of bone metastases, two or more sites of metastatic disease, ECOG 2 performance status, and lack of prior nephrectomy. This patient population fares poorly and is in need of new therapies to better control their disease."

The following chart outlines data from the CABOSUN trial presented today at ESMO 2017, as compared to the data previously published in the *Journal of Clinical Oncology* (JCO) in October 2016:

	JCO Investigator-assessed (April 11, 2016 Cut-off)		ESMO 2017 Investigator-assessed (Sept 15, 2016 Cut-off)		ESMO 2017 IRC Review (Sept 15, 2016 Cut-off)	
	Cabozantinib N = 79	Sunitinib N = 78	Cabozantinib N = 79	Sunitinib N = 78	Cabozantinib N = 79	Sunitinib N = 78
Progression-free survival						
Median PFS, months	8.2	5.6	8.3	5.4	8.6	5.3
Stratified HR (95% CI)	0.66 (0.46-0.95)		0.56 (0.37-0.83)		0.48 (0.31-0.74)	
P value	0.012 (1-sided)		0.0042 (2-sided)		0.0008 (2-sided)	
Tumor Response						
Objective response rate (95% CI),^a %	46 (34-57)	18 (10-28)	33 (23-44)	12 (5-21)	20 (12-31)	9 (4-18)
Disease control rate,^b %	78	54	76	49	75	47
Progressive disease,^c %	18	26	18	24	18	29
Not evaluable or missing, %	4	21	6	27	8	23
Any reduction in target lesions, %	87	44	85	38	80	50

^a One complete response was observed with cabozantinib for both investigator assessments, and one complete response was observed with sunitinib for the original investigator assessment, all other responses were partial responses; ^b Complete response + partial response + stable disease; ^c Progressive disease as best overall response.

The updated 2017 data sets and methods differ from the initial investigator analyses presented in 2016. The comprehensive image collection for IRC review used a later cut-off point (5 months) than the initial investigator analysis and followed a rigorous IRC review process. The analysis of IRC data applied U.S. Food and Drug Administration (FDA) guidance for PFS analyses in oncology studies, including recommended censoring rules (i.e., censoring at the last adequate tumor assessment prior to initiation of subsequent anti-cancer therapy, and censoring for events that occur after two or more missing adequate tumor assessments).¹ Both the updated investigator assessment and IRC analysis demonstrated consistent and statistically significant improvement of PFS with cabozantinib as compared to sunitinib.

The updated overall survival (OS) analysis had a data cut-off of July 1, 2017, and showed a favorable trend for patients randomized to cabozantinib compared to sunitinib that was not statistically significant. Median overall survival was 26.6 months for patients receiving cabozantinib versus 21.2 months for those receiving sunitinib (HR= 0.80, 95% CI 0.53-1.21, two-sided P=0.29).



“We are very encouraged by the clinically meaningful and statistically significant efficacy results on the primary endpoint of progression-free survival, which formed the basis of the recent supplemental New Drug Application submitted to the U.S. Food and Drug Administration for cabozantinib in first-line advanced renal cell carcinoma,” said **Michael M. Morrissey, Ph.D., President and Chief Executive Officer of Exelixis.** *“The latest CABOSUN data continue to underscore the value that cabozantinib may offer patients with previously untreated renal cell carcinoma, and we are working tirelessly in our efforts to bring this option to patients and their physicians as quickly as possible.”*

David Meek, Chief Executive Officer of Ipsen stated *“Following the recent European approval of cabozantinib for second-line treatment of patients with advanced renal cell carcinoma following prior VEGF-targeted therapy, the latest data from the CABOSUN study being presented this year at ESMO extends the clinical benefit of cabozantinib in first-line therapy setting of patients with advanced RCC. With our partner Exelixis, we are committed to strengthening the medical value of cabozantinib and to continuing to bring innovative therapeutic solutions for the treatment of patients with RCC. ”*

The most common all-causality grade 3 or 4 adverse events in more than 5 percent of patients for cabozantinib (N=78) and sunitinib (N=72), respectively, were diarrhea (10 vs. 11 percent), hypertension (28 vs. 21 percent), fatigue (6 vs. 17 percent), increased alanine aminotransferase (ALT; 5 vs. 0 percent), decreased appetite (5 vs. 1 percent), palmar-plantar erythrodysesthesia syndrome (PPES; 8 vs. 4 percent), decreased platelet count (1 vs. 11 percent) and stomatitis (5 vs. 6 percent). Twenty-one percent of patients in the cabozantinib arm and 22 percent of patients in the sunitinib arm discontinued treatment due to adverse events.

Exelixis filed a supplemental New Drug Application based on the CABOSUN data with the FDA for cabozantinib as a treatment for previously untreated advanced RCC on August 16, 2017. Ipsen also submitted to EMA the regulatory dossier for cabozantinib as a treatment for first-line advanced RCC in the European Union on August 28, 2017; on September 8, 2017, Ipsen announced that the EMA validated the application.

About the CABOSUN Study

On May 23, 2016, Exelixis announced that CABOSUN met its primary endpoint, demonstrating a statistically significant and clinically meaningful improvement in PFS compared with sunitinib in patients with advanced intermediate- or poor-risk RCC as determined by investigator assessment. The CABOSUN trial is being conducted by The Alliance for Clinical Trials in Oncology as part of Exelixis' collaboration with the NCI-CTEP. These results were first presented in a plenary session by Dr. Toni Choueiri at the ESMO 2016 Congress, and published in the *JCO*.² In June 2017, a blinded IRC confirmed that cabozantinib provided a clinically meaningful and statistically significant improvement in the primary efficacy endpoint of investigator-assessed PFS.

CABOSUN is a randomized, open-label, active-controlled phase 2 trial that enrolled 157 patients with advanced RCC determined to be intermediate- or poor-risk by the IMDC criteria. Patients were randomized 1:1 to receive cabozantinib (60 mg once daily) or sunitinib (50 mg once daily, 4 weeks on followed by 2 weeks off). The primary endpoint was PFS. Secondary endpoints included OS and objective response rate.



Eligible patients were required to have locally advanced or metastatic clear-cell RCC, ECOG performance status 0-2 and had to be intermediate or poor risk per the IMDC criteria (Heng, JCO, 2009).³ Prior systemic treatment for RCC was not permitted. Baseline characteristics included:

Characteristic	Cabozantinib (N=79)	Sunitinib (N=78)
ECOG performance status, %		
0	46	46
1	42	41
2	13	13
IMDC risk group, %		
Intermediate	81	81
Poor	19	19
Bone metastasis per IxRS,^a %		
Yes	37	36
No	63	64
Prior nephrectomy, %		
Yes	72	77
No	28	23
Number of metastatic sites per investigator, %		
1	22	33
2	47	26
≥3	32	41

^a interactive voice/web response system

CABOMETYX is approved in the EU for the treatment of advanced renal cell carcinoma in adults following prior vascular endothelial growth factor (VEGF)-targeted therapy. Please see full EU prescribing information at: <https://cabometyx.eu/eu/>

Webcast for the Financial Community and Media

Exelixis and its partner Ipsen will jointly host a live webcast later today, Sunday, September 10. The webcast will begin at 18:45 CEST (local Madrid time) / 12:45 p.m. EDT / 9:45 a.m. PDT. During the webcast, Exelixis and Ipsen management and invited guest speakers will review results from the CABOSUN trial, along with the other relevant data sets presented at the conference.

To access the webcast link, log onto www.exelixis.com and proceed to the News & Event Calendar page under the Investors & Media heading. Please connect to the company's website at least 15 minutes prior to the webcast to ensure adequate time for any software download that may be required to view the program. To listen to an audio-only version of the program by phone, please dial (855) 793-2457 (domestic) or (631) 485-4921 (international/toll dial) and use passcode 68961937. A telephone replay



will be available until 11:59 p.m. EDT on September 17, 2017. Access numbers for the telephone replay are: 855-859-2056 (domestic) and 404-537-3406 (international); the passcode is 68961937. A webcast replay will also be available archived on www.exelixis.com for one year.

About Advanced Renal Cell Carcinoma

The American Cancer Society's 2017 statistics cite kidney cancer as among the top ten most commonly diagnosed forms of cancer among both men and women in the U.S.⁴ Clear cell RCC is the most common type of kidney cancer in adults.⁵ If detected in its early stages, the five-year survival rate for RCC is high; for patients with advanced or late-stage metastatic RCC, however, the five-year survival rate is only 12 percent, with no identified cure for the disease.⁶ Approximately 30,000 patients in the U.S. and 68,000 globally require treatment, and an estimated 14,000 patients in the U.S. each year are in need of a first-line treatment for advanced kidney cancer.⁷

The majority of clear cell RCC tumors have lower than normal levels of a protein called von Hippel-Lindau, which leads to higher levels of MET, AXL and VEGF.^{8,9} These proteins promote tumor angiogenesis (blood vessel growth), growth, invasiveness and metastasis.¹⁰⁻¹³ MET and AXL may provide escape pathways that drive resistance to VEGF receptor inhibitors.^{8,9}

About CABOMETYX® (cabozantinib)

CABOMETYX is the tablet formulation of cabozantinib. Its targets include MET, AXL and VEGFR-1, -2 and -3. In preclinical models, cabozantinib has been shown to inhibit the activity of these receptors, which are involved in normal cellular function and pathologic processes such as tumor angiogenesis, invasiveness, metastasis and drug resistance. CABOMETYX is available in 20 mg, 40 mg or 60 mg doses. The recommended dose is 60 mg orally, once daily.

On April 25, 2016, the FDA approved CABOMETYX tablets for the treatment of patients with advanced RCC who have received prior anti-angiogenic therapy. In February of 2016, Exelixis and Ipsen jointly announced an exclusive licensing agreement for the commercialization and further development of cabozantinib indications outside of the United States, Canada and Japan. This agreement was amended in December of 2016 to include commercialization rights for Ipsen in Canada. On September 9, 2016, the European Commission approved CABOMETYX tablets for the treatment of advanced RCC in adults who have received prior vascular endothelial growth factor (VEGF)-targeted therapy in the European Union, Norway and Iceland.

On January 30, 2017, Exelixis and Takeda Pharmaceutical Company Limited announced an exclusive licensing agreement for the commercialization and further clinical development of cabozantinib for all future indications in Japan, including RCC.

CABOMETYX is not indicated for the treatment of previously untreated advanced RCC.

Indications: CABOMETYX® is indicated for the treatment of advanced renal cell carcinoma (RCC) in adults following prior vascular endothelial growth factor (VEGF)-targeted therapy.

Dosage and Administration: The recommended dose of CABOMETYX® is 60 mg once daily. Treatment should continue until the patient is no longer clinically benefiting from therapy or until unacceptable toxicity occurs. Management of suspected adverse drug reactions may require temporary interruption and/or dose reduction of CABOMETYX® therapy. For dose modification, please refer to full SmPC. CABOMETYX® is for oral use. The tablets should be swallowed whole and not crushed. Patients should be instructed to not eat anything for at least 2 hours before through 1 hour after taking CABOMETYX®.

Contraindications: Hypersensitivity to the active substance or to any of the excipients listed in the SmPC.

Special warnings and precautions for use: As most events can occur early in the course of treatment, the physician should evaluate the patient closely during the first eight weeks of treatment to determine if dose modifications are warranted. Events that generally have early onset include hypocalcaemia, hypokalaemia, thrombocytopenia, hypertension, palmarplantar erythrodysesthesia syndrome (PPES), proteinuria, and gastrointestinal (GI) events (abdominal pain, mucosal inflammation, constipation, diarrhoea, vomiting). Dose reductions and dose interruptions due to an AE occurred in 59.8% and 70%, respectively, of cabozantinib-treated patients in the pivotal clinical trial. Two dose reductions were required in 19.3% of patients. The median time to first dose reduction was 55 days, and to first dose interruption was 38 days. Perforations and fistulas: Serious gastrointestinal perforations and fistulas, sometimes fatal, have been observed with cabozantinib. Patients who have inflammatory bowel disease (e.g., Crohn's disease, ulcerative colitis, peritonitis, diverticulitis, or appendicitis), have tumour infiltration in the GI tract, or have complications from prior GI surgery (particularly when associated with delayed or incomplete healing) should be carefully evaluated before initiating cabozantinib therapy and subsequently they should be monitored closely for symptoms of perforations and fistulas including abscesses. Persistent or recurring diarrhoea while on treatment may be a risk factor for the development of anal fistula. Cabozantinib should be discontinued in patients who experience a GI perforation or a fistula that cannot be adequately managed.

Thromboembolic events: Events of venous thromboembolism, including pulmonary embolism, and events of arterial thromboembolism have been observed with cabozantinib. Cabozantinib should be used with caution in patients who are at risk for, or who have a history of, these events. Cabozantinib should be discontinued in patients who develop an acute myocardial infarction or any other clinically significant arterial thromboembolic complication.

Haemorrhage: Severe haemorrhage has been observed with cabozantinib. Patients who have a history of severe bleeding prior to treatment initiation should be carefully evaluated before initiating cabozantinib therapy. Cabozantinib should not be administered to patients that have or are at risk for severe haemorrhage.

Wound complications: Wound complications have been observed with cabozantinib. Cabozantinib treatment should be stopped at least 28 days prior to scheduled surgery, including dental surgery, if possible. The decision to resume cabozantinib therapy after surgery should be based on clinical judgment of adequate wound healing. Cabozantinib should be discontinued in patients with wound healing complications requiring medical intervention.

Hypertension: Hypertension has been observed with cabozantinib. Blood pressure should be well-controlled prior to initiating cabozantinib. During treatment with cabozantinib, all patients should be monitored for hypertension and treated as needed with standard anti-hypertensive therapy. In the case of persistent hypertension despite use of anti-hypertensives, the cabozantinib dose should be reduced. Cabozantinib should be discontinued if hypertension is severe and persistent despite anti-hypertensive therapy and dose reduction of cabozantinib. In case of hypertensive crisis, cabozantinib should be discontinued.

Palmar-plantar erythrodysesthesia syndrome: Palmar-plantar erythrodysesthesia syndrome (PPES) has been observed with cabozantinib. When PPES is severe, interruption of treatment with cabozantinib should be considered. Cabozantinib should be restarted with a lower dose when PPES has been resolved to grade 1.

Proteinuria: Proteinuria has been observed with cabozantinib. Urine protein should be monitored regularly during cabozantinib treatment. Cabozantinib should be discontinued in patients who develop nephrotic syndrome.

Reversible posterior leukoencephalopathy syndrome: Reversible Posterior Leukoencephalopathy Syndrome (RPLS), also known as Posterior Reversible Encephalopathy Syndrome (PRES), has been observed with cabozantinib. This syndrome should be considered in any patient presenting with multiple symptoms, including seizures, headache, visual disturbances, confusion or altered mental function. Cabozantinib treatment should be discontinued in patients with RPLS.

Prolongation of QT interval

Cabozantinib should be used with caution in patients with a history of QT interval prolongation, patients who are taking antiarrhythmics, or patients with relevant pre-existing cardiac disease, bradycardia, or electrolyte disturbances. When using cabozantinib, periodic monitoring with on-treatment ECGs and electrolytes (serum calcium, potassium, and magnesium) should be considered.

Interactions: CYP3A4 inducers and inhibitors: cabozantinib is a CYP3A4 substrate. Concurrent administration of cabozantinib with the strong CYP3A4 inhibitor ketoconazole resulted in an increase in cabozantinib plasma exposure. Caution is required when administering cabozantinib with agents that are strong CYP3A4 inhibitors. Concurrent administration of cabozantinib with the strong CYP3A4 inducer rifampicin resulted in a decrease in cabozantinib plasma exposure. Therefore, chronic administration of agents that are strong CYP3A4 inducers with cabozantinib should be avoided. P-glycoprotein substrates: Cabozantinib was an inhibitor but not a substrate, of P-glycoprotein (P-gp) transport activities in a bi-directional assay system using MDCK-MDR1 cells. Therefore, cabozantinib may have the potential to increase plasma concentrations of co-administered substrates of P-gp. Subjects should be cautioned regarding taking a P-gp substrate while receiving cabozantinib. MRP2 inhibitors: Administration of MRP2 inhibitors may result in increases in cabozantinib plasma concentrations. Therefore, concomitant use of MRP2 inhibitors should be approached with caution. Bile salt-sequestering agents: Bile salt-sequestering agents may interact with cabozantinib and may impact absorption (or reabsorption) resulting in potentially decreased exposure. The clinical significance of these potential interactions is unknown. Excipient related warnings: Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Pregnancy and lactation: Avoid pregnancy, use effective methods of contraception and discontinue breast-feeding during treatment with cabozantinib, and for at least 4 months after completing therapy.

Drive and use machines: Caution is recommended

Undesirable effects:

The most common serious adverse reactions associated with cabozantinib are abdominal pain (3%), pleural effusion (3%), diarrhoea (2%), and nausea (2%). The most frequent adverse reactions of any grade (experienced by at least 25% of patients) included diarrhoea (74%), fatigue (56%), nausea (50%), decreased appetite (46%), palmar-plantar erythrodysesthesia syndrome (PPES) (42%), hypertension (37%), vomiting (32%), weight decreased (31%), and constipation (25%). Other very common adverse reactions: anemia, hypophosphataemia, hypoalbuminaemia, hypomagnesaemia, hyponatraemia, hypokalaemia, hyperkalaemia, hypocalcaemia, hyperbilirubinemia, dysgeusia, headache, dizziness, dysphonia, dyspnea, cough, stomatitis, abdominal pain, dyspepsia, rash, dry skin, muscle spasms, arthralgia, proteinuria, mucosal inflammation, serum ALT, AST, and ALP



increased, creatinine increased, triglycerides increased, hyperglycaemia, hypoglycaemia, lymphopenia, neutropenia, thrombocytopenia, GGT increased, amylase increased, blood cholesterol increased, lipase increased

For all common and uncommon adverse reactions, please refer to full SmPC. For more information, see the regularly updated registered product information on the European Medicine Agency <https://cabometyx.eu/eu/>

About Exelixis

Founded in 1994, Exelixis, Inc. (Nasdaq: EXEL) is a commercially successful, oncology-focused biotechnology company that strives to accelerate the discovery, development and commercialization of new medicines for difficult-to-treat cancers. Following early work in model genetic systems, we established a broad drug discovery and development platform that has served as the foundation for our continued efforts to bring new cancer therapies to patients in need. We discovered our lead compounds, cabozantinib and cobimetinib, and advanced them into clinical development before entering into partnerships with leading biopharmaceutical companies in our efforts to bring them to patients globally. With growing revenues from the three resulting commercialized products – CABOMETYX[®], COMETRIQ[®], and COTELLIC[®] – we are reinvesting in our business to maximize the potential of our pipeline, which we intend to supplement with targeted business development activities and internal drug discovery, all to deliver the next generation of Exelixis medicines and help patients recover stronger and live longer. For more information about Exelixis, please visit www.exelixis.com or follow @ExelixisInc on Twitter.

About Ipsen

Ipsen is a global specialty-driven biopharmaceutical group focused on innovation and specialty care. The group develops and commercializes innovative medicines in three key therapeutic areas - Oncology, Neurosciences and Rare Diseases. Its commitment to oncology is exemplified through its growing portfolio of key therapies for prostate cancer, neuroendocrine tumors, renal cell carcinoma and pancreatic cancer. Ipsen also has a well-established Consumer Healthcare business. With total sales close to €1.6 billion in 2016, Ipsen sells more than 20 drugs in over 115 countries, with a direct commercial presence in more than 30 countries. Ipsen's R&D is focused on its innovative and differentiated technological platforms located in the heart of the leading biotechnological and life sciences hubs (Paris-Saclay, France; Oxford, UK; Cambridge, US). The Group has about 5,100 employees worldwide. Ipsen is listed in Paris (Euronext: IPN) and in the United States through a Sponsored Level I American Depositary Receipt program (ADR: IPSEY). For more information on Ipsen, visit www.ipсен.com.

Forward-Looking Statement Disclaimer

The forward-looking statements, objectives and targets contained herein are based on the Group's management strategy, current views and assumptions. Such statements involve known and unknown risks and uncertainties that may cause actual results, performance or events to differ materially from those anticipated herein. All of the above risks could affect the Group's future ability to achieve its financial targets, which were set assuming reasonable macroeconomic conditions based on the information available today. Use of the words "believes," "anticipates" and "expects" and similar expressions are intended to identify forward-looking statements, including the Group's expectations regarding future events, including regulatory filings and determinations. Moreover, the targets described in this document were prepared without taking into account external growth assumptions and potential future acquisitions, which may alter these parameters. These objectives are based on data and assumptions regarded as reasonable by the Group. These targets depend on conditions or facts likely to happen in the future,

and not exclusively on historical data. Actual results may depart significantly from these targets given the occurrence of certain risks and uncertainties, notably the fact that a promising product in early development phase or clinical trial may end up never being launched on the market or reaching its commercial targets, notably for regulatory or competition reasons. The Group must face or might face competition from generic products that might translate into a loss of market share. Furthermore, the Research and Development process involves several stages each of which involves the substantial risk that the Group may fail to achieve its objectives and be forced to abandon its efforts with regards to a product in which it has invested significant sums. Therefore, the Group cannot be certain that favorable results obtained during pre-clinical trials will be confirmed subsequently during clinical trials, or that the results of clinical trials will be sufficient to demonstrate the safe and effective nature of the product concerned. There can be no guarantees a product will receive the necessary regulatory approvals or that the product will prove to be commercially successful. If underlying assumptions prove inaccurate or risks or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements. Other risks and uncertainties include but are not limited to, general industry conditions and competition; general economic factors, including interest rate and currency exchange rate fluctuations; the impact of pharmaceutical industry regulation and health care legislation; global trends toward health care cost containment; technological advances, new products and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approval; the Group's ability to accurately predict future market conditions; manufacturing difficulties or delays; financial instability of international economies and sovereign risk; dependence on the effectiveness of the Group's patents and other protections for innovative products; and the exposure to litigation, including patent litigation, and/or regulatory actions. The Group also depends on third parties to develop and market some of its products which could potentially generate substantial royalties; these partners could behave in such ways which could cause damage to the Group's activities and financial results. The Group cannot be certain that its partners will fulfil their obligations. It might be unable to obtain any benefit from those agreements. A default by any of the Group's partners could generate lower revenues than expected. Such situations could have a negative impact on the Group's business, financial position or performance. The Group expressly disclaims any obligation or undertaking to update or revise any forward looking statements, targets or estimates contained in this press release to reflect any change in events, conditions, assumptions or circumstances on which any such statements are based, unless so required by applicable law. The Group's business is subject to the risk factors outlined in its registration documents filed with the French Autorité des Marchés Financiers. The risks and uncertainties set out are not exhaustive and the reader is advised to refer to the Group's 2016 Registration Document available on its website (www.ipsen.com).

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