PRESS RELEASE

Ipsen joins clinical collaboration to evaluate cabozantinib (CABOMETYX®) plus atezolizumab in metastatic non-small cell lung cancer and metastatic castration-resistant prostate cancer

Clinical collaboration marks an important milestone in partnership with Exelixis to further develop cabozantinib

Participation will provide Ipsen access to the respective study results to support potential future regulatory submissions in its territories

PARIS, FRANCE, 02 July 2020 – Ipsen (Euronext: IPN; ADR: IPSEY), today announced it will join the Exelixis and Roche clinical collaboration and participate in the funding of the recently initiated CONTACT-01 and CONTACT-02 global Phase III pivotal trials. CONTACT-01 is evaluating the safety and efficacy of cabozantinib (CABOMETYX®) in combination with atezolizumab (TECENTRIQ®) in patients with metastatic non-small cell lung cancer (NSCLC) who have been previously treated with an immune checkpoint inhibitor and platinum-containing chemotherapy. CONTACT-02 is evaluating the safety and efficacy of cabozantinib given in combination with atezolizumab versus a second novel hormonal therapy (NHT) in men with metastatic castration-resistant prostate cancer (CRPC) who have previously been treated with one NHT.

“There is a growing body of preclinical and clinical evidence that cabozantinib may positively impact treatment when paired with immunotherapy,” said Dr. Howard Mayer, Executive Vice President and Head of Research and Development at Ipsen. “We are pleased to enter into this collaboration with Exelixis and Roche to build on the promising data from COSMIC-021 and further examine the potential of cabozantinib in combination with atezolizumab to treat metastatic non-small cell lung cancer and for men with metastatic castration-resistant prostate cancer.”

“Ipsen has built its strength in oncology through solid long-term partnerships which are evaluating new approaches to target difficult-to-treat cancers. This marks an important milestone in our partnership with Exelixis to further develop cabozantinib and our shared vision to progress the treatment for cancers and indications with high unmet need, ensuring no patient is left behind,” said Bartek Bednarz, Senior Vice President, Global Product & Portfolio Strategy at Ipsen.

Ipsen has an exclusive collaboration agreement with Exelixis for the further development and commercialization of cabozantinib outside of the United States and Japan. Under this agreement, following its decision to opt-in to pivotal studies exploring cabozantinib’s potential in new potential indications, Ipsen gains access to the results of those studies, which if positive, may support potential future regulatory submissions in its territory.

About CONTACT-01
CONTACT-01 is a global, multicenter, randomized, Phase III, open-label study that aims to enroll approximately 350 patients. Patients will be randomized 1:1 to the experimental arm of cabozantinib in combination with atezolizumab and the control arm of docetaxel. The primary endpoint of the trial is overall survival. Secondary endpoints include progression-free survival, objective response rate and duration of response. The trial was initiated on June 11, 2020 and is sponsored by Roche and co-funded by Exelixis, Ipsen and Takeda Pharmaceutical Company Limited.

About NSCLC
Lung cancer is the most commonly occurring cancer in men and the third most commonly occurring cancer in women.[1] There were over two million new cases in 2018.[2] Non-small-cell lung carcinoma (NSCLC) is any type of epithelial lung cancer other than small cell lung carcinoma (SCLC). NSCLC accounts for about 85% of all lung cancers.[3,4]

About CONTACT-02
CONTACT-02 is a global, multicenter, randomized, Phase III, open-label study that plans to enroll approximately 580 patients at 250 sites. Patients will be randomized 1:1 to the experimental arm of cabozantinib in combination with atezolizumab and the control arm of a second novel hormonal therapy (either abiraterone and prednisone or enzalutamide). The co-primary endpoints of the trial are progression-free survival and overall survival. Additional endpoints include objective response rate, prostate-specific antigen response rate and duration of response. The trial was initiated on June 30, 2020 and is sponsored by Exelixis and co-funded by Roche, Ipsen and Takeda Pharmaceutical Company Limited.

About CRPC
Prostate cancer is the second most commonly occurring cancer in men and the fourth most commonly occurring cancer overall.[5] There were 1.27 million new cases in 2018.[6] Approximately 10-20 percent of prostate cancer cases are castration-resistant, and up to 16% of these patients show no evidence that the cancer has spread at the time of the castration-resistant diagnosis.

Metastatic castration-resistant prostate cancer is when the cancer has spread to parts of the body other than the prostate, and it is able to grow and spread even though drugs or other treatments to lower the amount of male sex hormones are being used to manage the cancer.

About Ipsen products
This press release mentions investigational uses of Ipsen products. Product indications and approvals for use vary by jurisdiction; please see SmPC/PI for full indications and safety information.

About CABOMETYX® (cabozantinib**)**
CABOMETYX® is not marketed by Ipsen in the U.S.

CABOMETYX® 20mg, 40mg and 60mg film-coated unscored tablets

Active ingredient: Cabozantinib (S)-malate 20mg, 40mg and 60mg

Other components: Lactose

Indications: CABOMETYX® is currently approved in 51 countries, including in the European Union, the U.K., Norway, Iceland, Australia, Switzerland, South Korea, Canada, Brazil, Taiwan, Hong-Kong, Singapore, Macau, Jordan, Lebanon, Russian Federation, Ukraine, Turkey, United Arab Emirates, Saudi Arabia, Serbia, Israel, Mexico, Chile and Panama for the treatment of advanced RCC in adults who have received prior VEGF-targeted therapy; in the European Union, the U.K., Norway, Iceland, Canada, Australia, Brazil, Taiwan, Hong Kong, Singapore, Jordan, Russian Federation, Turkey, United Arab Emirates, Saudi Arabia, Servia, Israel, Mexico, Chile and Panama for previously untreated intermediate- or poor-risk advanced RCC; and in the European Union, the U.K., Norway, Iceland, Canada, Australia, Switzerland, Saudi Arabia, Serbia, Israel , Taiwan, Hong Kong, South Korea, Singapore, Jordan, Russian Federation, Turkey, United Arab Emirates, and Panama for HCC in adults who have previously been treated with sorafenib.

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:
Monitor closely for toxicity during first 8 weeks of therapy. Events that generally have early onset include hypocalcemia, hypokalemia, thrombocytopenia, hypertension, palmar-plantar erythrodysaesthesia syndrome (PPES), proteinuria, and gastrointestinal (GI) events.

Perforations and fistulas: serious gastrointestinal perforations and fistulas, sometimes fatal, have been observed with cabozantinib. Patients with inflammatory bowel disease, GI tumor infiltration or complications from prior GI surgery should be evaluated prior to therapy and monitored; if perforation and unmanageable fistula occur, discontinue cabozantinib.

Thromboembolic events: use with caution in patients with a history of or risk factors for thromboembolism;

discontinue if acute myocardial infarction (MI) or other significant arterial thromboembolic complication occurs.

Hemorrhage: not recommended for patients that have or are at risk of severe hemorrhage.

Wound complications: treatment should be stopped at least 28 days prior to scheduled surgery (including dental).

Hypertension: monitor blood pressure (BP); reduce with persistent hypertension and discontinue should uncontrolled hypertension or hypertensive crisis occur.

Palmar-plantar erythrodysesthesia (PPES): interrupt treatment if severe PPES occurs.

Proteinuria: discontinue in patients with nephrotic syndrome.

Reversible posterior leukoencephalopathy syndrome (RPLS): discontinue in patients with RPLS.

QT interval prolongation: use with caution in patients with a history of QT prolongation, those on antiarrhythmics or with pre-existing cardiac disease.

Excipients: do not use in patients with hereditary problems of galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption.

Hepatic encephalopathy: In the HCC study (CELESTIAL), hepatic encephalopathy was reported more frequently in the cabozantinib than the placebo arm.

Hepatic effects: Abnormalities of liver function tests have been frequently observed in patients treated with cabozantinib. liver function tests should be performed before initiation and monitored closely during treatment. If there is worsening of liver function tests with no alternative cause evident, the dose should be modified as per SmPC

Drug interactions: Cabozantinib is a CYP3A4 substrate. Potent CYP3A4 inhibitors may result in an increase in cabozantinib plasma exposure (e.g. ritonavir, itraconazole, erythromycin, clarithromycin, grapefruit juice). Coadministration with CYP3A4 inducers may result in decreased cabozantinib plasma exposure (e.g. rifampicin, phenytoin, carbamazepine, phenobarbital, St John's Wort). Cabozantinib may increase the plasma concentration of P-glycoprotein substrates (e.g. fexofenadine, aliskiren, ambrisentan, dabigatran etexilate, digoxin, colchicine, maraviroc, posaconazole, ranolazine, saxagliptin, sitagliptin, talinolol, tolvaptan). MRP2 inhibitors may increase cabozantinib plasma concentrations (e.g. cyclosporine, efavirenz, emtricitabine). Bile salt sequestering agents may impact absorption or reabsorption resulting in potentially decreased cabozantinib exposure. No dose adjustment when co-administered with gastric pH modifying agents. A plasma protein displacement interaction may be possible with warfarin. INR values should be monitored in such a combination.

Women of childbearing potential/contraception in males and females: Ensure effective measures of contraception (oral contraceptive plus a barrier method) in male and female patients and their partners during therapy and for at least 4 months after treatment.

Pregnancy and lactation: CABOMETYX® should not be used during pregnancy unless the clinical condition of the woman requires treatment. Lactation – discontinue breast-feeding during and for at least 4 months after completing treatment. Drive and use machines: Caution is recommended

Adverse reactions:
The most common serious adverse reactions are hypertension, diarrhea, PPES, pulmonary embolism, fatigue and hypomagnesaemia. Very common (>1/10): anaemia, hypothyroidism, decreased appetite, hypomagnesaemia, hypokalaemia, dysgeusia, headache, dizziness, hypertension, haemorrhage, dysphonia, dyspnoea, cough, diarrhoea, nausea, vomiting, stomatitis, constipation, abdominal pain, dyspepsia, PPES, rash, pain in extremity, fatigue, mucosal inflammation, asthenia, peripheral oedema, weight decreased, serum ALT increased, AST increased. Common (>1/100 to <1/10): abscess, thrombocytopenia, neutropenia, dehydration, hypoalbuminaemia, hypophosphataemia, hyponatraemia, hypocalcaemia, hyperkalaemia, hyperbilirubinaemia, hyperglycaemia, hypoglycaemia, peripheral sensory neuropathy, tinnitus, venous thrombosis, arterial thrombosis, pulmonary embolism, gastrointestinal perforation, fistula, gastroesophageal reflux disease, haemorrhoids, oral pain, dry mouth, hepatic encephalopathy, pruritus, alopecia, dry skin, dermatitis acneiform, hair colour change, muscle spasms, arthralgia, proteinuria, blood ALP increased, GGT increased, blood creatinine increased, amylase increased, lipase increased, blood cholesterol increased, white blood cell count decreased. Uncommon (>1/1000 to <1/100): lymphopenia, convulsion, pancreatitis,

glossodynia, hepatitis cholestatic, osteonecrosis of the jaw, blood triglycerides increased, wound complications. Frequency not known: cerebrovascular accident, myocardial infarction. Aneurysms and artery dissections. Selected adverse reactions: GI perforation, hepatic encephalopathy, diarrhoea, fistulas, haemorrhage, RPLS. Prescribers should consult the SmPC in relation to other adverse reactions.

Selected adverse event (AEs): GI perforation, hepatic encephalopathy, diarrhoea, fistulas, hemorrhage, RPLS.

Prescribers should consult the SPC in relation to other adverse reactions.

For more information, see the regularly updated registered product information on the European Medicine Agency www.ema.europa.eu

CABOMETYX® is marketed by Exelixis, Inc. in the United States. Ipsen has exclusive rights for the commercialization and further clinical development of CABOMETYX® outside of the United States and Japan.

U.S. Indications and Important Safety Information

Indications:

CABOMETYX® (cabozantinib) is indicated for the treatment of patients with advanced renal cell carcinoma (RCC).

CABOMETYX® (cabozantinib) is indicated for the treatment of patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib.

IMPORTANT SAFETY INFORMATION

Warnings and precautions:

Hemorrhage: Severe and fatal hemorrhages occurred with CABOMETYX. The incidence of Grade 3 to 5 hemorrhagic events was 5% in CABOMETYX patients. Discontinue CABOMETYX for Grade 3 or 4 hemorrhage. Do not administer CABOMETYX to patients who have a recent history of hemorrhage, including hemoptysis, hematemesis, or melena.

Perforations and Fistulas: Gastrointestinal (GI) perforations, including fatal cases, occurred in 1% of CABOMETYX patients. Fistulas, including fatal cases, occurred in 1% of CABOMETYX patients. Monitor patients for signs and symptoms of perforations and fistulas, including abscess and sepsis. Discontinue CABOMETYX in patients who experience a fistula that cannot be appropriately managed or a GI perforation.

Thrombotic Events: CABOMETYX increased the risk of thrombotic events. Venous thromboembolism occurred in 7% (including 4% pulmonary embolism) and arterial thromboembolism in 2% of CABOMETYX patients. Fatal thrombotic events occurred in CABOMETYX patients. Discontinue CABOMETYX in patients who develop an acute myocardial infarction or serious arterial or venous thromboembolic event requiring medical intervention.

Hypertension and Hypertensive Crisis: CABOMETYX can cause hypertension, including hypertensive crisis. Hypertension occurred in 36% (17% Grade 3 and <1% Grade 4) of CABOMETYX patients. Do not initiate CABOMETYX in patients with uncontrolled hypertension. Monitor blood pressure regularly during CABOMETYX treatment. Withhold CABOMETYX for hypertension that is not adequately controlled with medical management; when controlled, resume at a reduced dose. Discontinue CABOMETYX for severe hypertension that cannot be controlled with anti-hypertensive therapy or for hypertensive crisis.

Diarrhea: Diarrhea occurred in 63% of CABOMETYX patients. Grade 3 diarrhea occurred in 11% of CABOMETYX patients. Withhold CABOMETYX until improvement to Grade 1 and resume at a reduced dose for intolerable Grade 2 diarrhea, Grade 3 diarrhea that cannot be managed with standard antidiarrheal treatments, or Grade 4 diarrhea.

Palmar-Plantar Erythrodysesthesia (PPE): PPE occurred in 44% of CABOMETYX patients. Grade 3 PPE occurred in 13% of CABOMETYX patients. Withhold CABOMETYX until improvement to Grade 1 and resume at a reduced dose for intolerable Grade 2 PPE or Grade 3 PPE.

Proteinuria: Proteinuria occurred in 7% of CABOMETYX patients. Monitor urine protein regularly during CABOMETYX treatment. Discontinue CABOMETYX in patients who develop nephrotic syndrome.

Osteonecrosis of the Jaw (ONJ): ONJ occurred in <1% of CABOMETYX patients. ONJ can manifest as jaw pain, osteomyelitis, osteitis, bone erosion, tooth or periodontal infection, toothache, gingival ulceration or erosion, persistent jaw pain, or slow healing of the mouth or jaw after dental surgery. Perform an oral examination prior to CABOMETYX initiation and periodically during treatment. Advise patients regarding good oral hygiene practices. Withhold CABOMETYX for at least 28 days prior to scheduled dental surgery or invasive dental procedures. Withhold CABOMETYX for development of ONJ until complete resolution.

Wound Complications: Wound complications were reported with CABOMETYX. Stop CABOMETYX at least 28 days prior to scheduled surgery. Resume CABOMETYX after surgery based on clinical judgment of adequate wound healing. Withhold CABOMETYX in patients with dehiscence or wound healing complications requiring medical intervention.

Reversible Posterior Leukoencephalopathy Syndrome (RPLS): RPLS, a syndrome of subcortical vasogenic edema diagnosed by characteristic finding on MRI, can occur with CABOMETYX. Evaluate for RPLS in patients presenting with seizures, headache, visual disturbances, confusion, or altered mental function. Discontinue CABOMETYX in patients who develop RPLS.
Embryo-Fetal Toxicity: CABOMETYX can cause fetal harm. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Verify the pregnancy status of females of reproductive potential prior to initiating CABOMETYX and advise them to use effective contraception during treatment and for 4 months after the last dose.

Adverse reactions

The most commonly reported (≥25%) adverse reactions are: diarrhea, fatigue, decreased appetite, PPE, nausea, hypertension, and vomiting.

Drug interactions:

Strong CYP3A4 Inhibitors: If coadministration with strong CYP3A4 inhibitors cannot be avoided, reduce the CABOMETYX dosage. Avoid grapefruit or grapefruit juice.
Strong CYP3A4 Inducers: If coadministration with strong CYP3A4 inducers cannot be avoided, increase the CABOMETYX dosage. Avoid St. John's wort.

Use in specific populations:

Lactation: Advise women not to breastfeed during CABOMETYX treatment and for 4 months after the final dose.
Hepatic Impairment: In patients with moderate hepatic impairment, reduce the CABOMETYX dosage. CABOMETYX is not recommended for use in patients with severe hepatic impairment.

Please see full Prescribing Information for more information.

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, Neuroscience 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 over €2.5 billion in 2019, 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 5,800 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.ipsen.com

Ipsen's Forward Looking Statement

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, and the outcome of this study or other studies. 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 preclinical 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 6 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 2019 Universal Registration Document available on its website (www.ipsen.com).

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References

1. World Cancer Research Fund. Lung Cancer Statistics. Accessed: July 2020. Available from: https://www.wcrf.org/dietandcancer/cancer-trends/lung-cancer-statistics.
2. GLOBOCAN 2018. Lung Cancer Factsheet. Accessed: July 2020. Available from: https://gco.iarc.fr/today/data/factsheets/cancers/15-Lung-fact-sheet.pdf.
3. Medscape eMedicine. Non-Small Cell Lung Cancer. Accessed: July 2020. Available from: https://emedicine.medscape.com/article/279960-overview.
4. American Cancer Society. Non-Small Cell Lung Cancer (NSCLC). Accessed: July 2020. Available from: https://www.cancer.org/cancer/lung-cancer/about/what-is.html.
5. World Cancer Research Fund. Prostate Cancer Statistics. Accessed: July 2020. Available from: https://www.wcrf.org/dietandcancer/cancer-trends/prostate-cancer-statistics#:~:text=Prostate%20cancer%20is%20the%20second%20most%20commonly%20occurring%20cancer%20in,given%20in%20the%20table%20below.
6. GLOBOCAN 2018. Prostate Cancer Factsheet. Accessed: July 2020. Available from: https://gco.iarc.fr/today/data/factsheets/cancers/27-Prostate-fact-sheet.pdf.