PRESS RELEASE

ASCO 2022: New Cabometyx® data show encouraging results in monotherapy and in combination across different tumor types including metastatic non-small cell lung cancer

- COSMIC-021 Phase Ib study is evaluating Cabometyx® (cabozantinib) in combination with atezolizumab in advanced solid tumors, including non-small cell lung cancer
- New analyses from pivotal Phase III Checkmate -9ER trial further support the superior efficacy of Cabometyx and nivolumab over sunitinib in advanced renal cell carcinoma
- Two new analyses from pivotal Phase III COSMIC-311 trial further support the potential of Cabometyx in radioactive iodine-refractory differentiated thyroid cancer

PARIS, FRANCE, 26 May 2022 – Ipsen (Euronext: IPN; ADR: IPSEY) today announced encouraging data to be presented for the multi-targeted tyrosine kinase inhibitor (TKI), Cabometyx® (cabozantinib), across a range of cancer types at this year's American Society of Clinical Oncology Annual Meeting (ASCO 2022) to be held on 3-7 June. Data presentations will include findings in metastatic non-small cell lung cancer (NSCLC), as well as established indications of advanced renal cell carcinoma and radioactive iodine-refractory differentiated thyroid cancer (RAI-R DTC). These data show that the therapeutic potential of Cabometyx as a key treatment option in a broad range of tumors is continuing to be realized.

Updated outcomes from the multicenter Phase Ib COSMIC-021 trial evaluating the combination of Cabometyx plus atezolizumab in an expanded patient population in metastatic NSCLC demonstrate encouraging clinical activity with manageable toxicity in people previously treated with an immune checkpoint inhibitor (ICI).[1] These data lay the foundations for the potential of Cabometyx in metastatic NSCLC which is being further examined in the ongoing Phase III CONTACT-01 trial. This trial is evaluating the combination of Cabometyx plus atezolizumab vs docetaxel in patients with metastatic NSCLC previously treated with an ICI and platinum-containing chemotherapy, and topline results of the study are expected to be announced in the second half of 2022.

"Currently, first-line immunotherapy with or without chemotherapy is the standard of care for patients with metastatic NSCLC but there is a real need for additional effective treatment options for those patients who progress after a prior immunotherapy," said Santiago Ponce-Aix, M.D., Head of Drug Development Department, Institute Gustave Roussy, France, and an investigator in the COSMIC-021 trial. "These new data are encouraging as they show the potential role of Cabometyx in creating an environment which may enhance atezolizumab's activity in NSCLC. We look forward to further data evaluating this combination for this patient population where there remains such a high unmet medical need."

"The therapeutic potential of Cabometyx as a treatment option against a broad range of tumors including NSCLC is continuing to be evaluated and these data demonstrate our ambition to bring meaningful new treatments to patients. These latest data support the potential role of Cabometyx to positively impact treatment when paired with immunotherapy, and we will continue to evaluate Cabometyx as both a monotherapy and in combination with other innovative therapies for the most difficult-to-treat cancers," said Dr. Howard Mayer, Executive Vice President and Head of Research and Development at Ipsen.

An exploratory analysis will also be presented investigating the relationship between depth of response (DepOR) and clinical outcomes in CheckMate -9ER, evaluating Cabometyx in combination with nivolumab vs sunitinib in previously untreated advanced renal cell carcinoma.[2] DepOR was defined as the best percent reduction from baseline in sum of diameters of target lesions. Overall, greater proportions of patients receiving Cabometyx plus nivolumab demonstrated deeper responses vs sunitinib. Regardless of treatment, deeper responses were generally associated with improved progression-free survival (PFS) and overall survival.[2]

Additionally, two new data analyses from the pivotal Phase III trial COSMIC-311 evaluating Cabometyx in RAI-R DTC will be presented. One analysis relates to outcomes for prespecified subgroups based on the baseline histology subtypes of papillary and follicular thyroid cancers, with results showing Cabometyx maintained superior efficacy vs placebo irrespective of histology subtype.[3] Median PFS was 9.2 months for Cabometyx vs 1.9 months for placebo in the papillary thyroid cancer (PTC) subgroup (HR 0.27 95% CI, 0.17-0.43) and 11.2 months vs 2.5 months in the follicular thyroid cancer (FTC) subgroup (HR 0.18 95% CI, 0.10-0.31). The overall response rate (ORR) was 15% for Cabometyx vs 0% for placebo in the PTC subgroup and 8% vs 0% in the FTC subgroup.[3]

Another analysis will be presented related to outcomes for prespecified subgroups who received prior lenvatinib and/or sorafenib treatment. The data from this analysis showed Cabometyx maintained its PFS vs placebo irrespective of prior lenvatinib and/or sorafenib treatment.[4] Median PFS across the different groups included 16.6 months for Cabometyx vs 3.2 months for placebo in prior sorafenib (no lenvatinib) (HR 0.13, 95% CI 0.06–0.26), 5.8 months vs 1.9 months in prior lenvatinib (no sorafenib) (HR 0.28, 95% CI 0.16-0.48), and 7.6 months vs 1.9 months in prior sorafenib and lenvatinib (HR 0.27, 95% CI 0.13–0.54).[4]

The safety profile identified in COSMIC-021, CheckMate -9ER and COSMIC-311 was consistent with that previously observed for Cabometyx in monotherapy and in combination.

Ipsen thanks the patients and investigators involved in the COSMIC-021, CheckMate -9ER and COSMIC-311 clinical trials.

ENDS

More information can be found during the presentation sessions outlined below:

Lead author	**Indication**	**Abstract title**	**Presentation number/timing (CDT)**
Neal	NSCLC	Cabozantinib (C) Plus Atezolizumab (A) or C Alone in Patients (Pts) With Advanced Non-Small Cell Lung Cancer (aNSCLC) Previously Treated With an Immune Checkpoint Inhibitor (ICI): Results From Cohorts 7 and 20 of the COSMIC-021 Study	**Oral** *Abstract 9005* Fri 3 Jun 2:24- 2:36 PM Lung Cancer – Non-Small Cell Metastatic
Suárez	RCC	Association between depth of response and clinical outcomes: exploratory analysis in patients with previously untreated advanced renal cell carcinoma (aRCC) in CheckMate 9ER	**Oral** *Abstract 4501* Fri 3 Jun 2:57- 3:09 PM GU Cancer - Kidney and Bladder
Pal	Urothelial Carcinoma	Cabozantinib (C) in Combination With Atezolizumab (A) in Urothelial Carcinoma (UC): Results From Cohorts 3, 4, 5 of the COSMIC-021 Study[5]	**Oral** *Abstract 4504* Fri 3 Jun 3:57 PM – 4:09 PM GU Cancer - Kidney and Bladder
Capdevila	RAI-R DTC	Cabozantinib versus placebo in patients (pts) with radioiodine-refractory (RAIR) differentiated thyroid cancer (DTC) who have progressed after prior VEGFR-targeted therapy: outcomes in prespecified subgroups based on histology subtypes	**Poster** *Abstract 6081* Mon Jun 6 1:15-4:15 PM Head & Neck Cancer

Hernando	RAI-R DTC	Cabozantinib (C) versus placebo (P) in patients (pts) with radioiodine-refractory (RAIR) differentiated thyroid cancer (DTC) who have progressed after prior VEGFR-targeted therapy: outcomes in prespecified subgroups based on prior VEGFR-targeted therapy	**Poster** *Abstract 6083* Mon Jun 6 1:15-4:15 PM Head & Neck Cancer

About non-small cell lung cancer (NSCLC)
Lung cancer is one of the leading causes of cancer death globally.[6] There are broadly two different groups of lung cancer - NSCLC and SCLC (small cell lung cancer). NSCLC accounts for around 80-85% of all cases.[7] The main subtypes of NSCLC are adenocarcinoma, squamous cell carcinoma, and large cell carcinoma. These subtypes, which start from different types of lung cells are grouped together as NSCLC because their treatment and prognoses are often similar.[7]

About renal cell carcinoma (RCC)
There were over 430,000 new cases of kidney cancer diagnosed worldwide in 2020.[8] Of these, RCC is the most common type of kidney cancer, accounting for approximately 90% of cases.[9,10] It is almost twice as common in men, and male patients account for over two thirds of deaths.[9] If detected in the early stages, the five-year survival rate is high, but for patients with or late-stage metastatic RCC the survival rate is much lower, around 12%, with no identified cure for this disease.[11,12]

About radioactive iodine-refractory differentiated thyroid cancer (RAI-R DTC)
In 2020, over 580,000 new cases of thyroid cancer were diagnosed worldwide.[13] Thyroid cancer is the ninth most commonly occurring cancer globally and incidence is three times higher in women than in men, with the disease representing one in every 20 cancers diagnosed among women.[13] While cancerous thyroid tumors include differentiated, medullary and anaplastic forms, differentiated thyroid cancer (DTC) makes up about 90 to 95% of cases.[14,15] DTC is typically treated with surgery, followed by ablation of the remaining thyroid tissue with radioactive iodine (RAI), but approximately 5 to 15% of cases are resistant to RAI treatment.[16] Patients who develop RAI-R DTC have a poor prognosis with an average estimated survival of three to five years.[17]

About the COSMIC-021 trial[18]
COSMIC-021 is a multicenter, Phase Ib, open-label study that was divided into two parts: a dose-escalation phase and an expansion cohort phase. In the expansion phase, the trial enrolled 23 cohorts in 12 tumor types: NSCLC, RCC, UC, castration-resistant prostate cancer, hepatocellular carcinoma, triple-negative breast cancer, epithelial ovarian cancer, endometrial cancer, gastric or gastroesophageal junction adenocarcinoma, colorectal adenocarcinoma, head and neck cancer, and DTC. Exelixis is the study sponsor of COSMIC-021. Both Ipsen and Takeda Pharmaceutical Company Limited (Takeda) have opted in to participate in the trial and are contributing to the funding for this study under the terms of the companies' respective collaboration agreements with Exelixis. Roche is providing atezolizumab for the trial.

About the CheckMate -9ER trial[19]
CheckMate -9ER was an open-label, randomized, multi-national Phase III trial evaluating people living with previously untreated advanced or metastatic RCC. A total of 651 patients (23% favorable risk, 58% intermediate risk, 20% poor risk; 25% PD-L1 ≥1%) were randomized to Cabometyx plus nivolumab (n= 323) versus sunitinib (n=328). The primary endpoint was progression-free survival (PFS). The secondary endpoints included overall survival (OS) and objective response rate (ORR). The primary efficacy analysis compared the doublet combination versus sunitinib in all randomized patients. The trial was sponsored by Bristol Myers Squibb and Ono Pharmaceutical Co and co-funded by Exelixis, Ipsen and Takeda.

About the COSMIC-311 trial[20]
COSMIC-311 was a multicenter, randomized, double-blind, placebo-controlled Phase III trial that enrolled 258 patients at 164 sites globally. Patients were randomized in a 2:1 ratio to receive either Cabometyx 60 mg or placebo once-daily. The primary endpoints were progression-free survival in the intention-to-treat population as well as objective response rate in the first 100 randomly assigned patients (objective response rate intention-to-treat [OITT] population), both evaluated by a blinded independent radiology

committee. Additional endpoints included safety, overall survival and quality of life. Exelixis is the sponsor, and Ipsen is co-funding the COSMIC-311 trial.

About Cabometyx (cabozantinib)
Outside the United States and Japan, Cabometyx is currently approved in 60 countries, including in the European Union (E.U.), Great Britain, Norway, Iceland, Australia, New Zealand, Switzerland, South Korea, Canada, Brazil, Taiwan, Hong Kong, Singapore, Macau, Jordan, Lebanon, the Russian Federation, Ukraine, Turkey, the United Arabic Emirates (U.A.E.), Saudi Arabia, Serbia, Israel, Mexico, Chile, Peru, Panama, Guatemala, the Dominican Republic, Ecuador, Thailand, Malaysia, Colombia, Egypt and Kazakhstan for the treatment of advanced renal cell carcinoma (RCC) in adults who have received prior vascular endothelial growth factor (VEGF)-targeted therapy; in the E.U., Great Britain, Norway, Iceland, Canada, Australia, New Zealand, Brazil, Taiwan, Hong Kong, Singapore, Lebanon, Jordan, the Russian Federation, Ukraine, Turkey, the U.A.E., Saudi Arabia, Israel, Serbia, Mexico, Chile, Peru, Panama, Guatemala, the Dominican Republic, Ecuador, Thailand, Egypt, Malaysia and Kazakhstan for previously untreated intermediate- or poor-risk advanced RCC; and in the E.U., Great Britain, Norway, Iceland, Canada, Australia, Switzerland, Saudi Arabia, Serbia, Israel, Taiwan, Hong Kong, South Korea, Singapore, Jordan, the Russian Federation, Ukraine, Turkey, Lebanon, the U.A.E., Peru, Panama, Guatemala, Chile, the Dominican Republic, Ecuador, Thailand, Brazil, New Zealand, Egypt, Malaysia and Kazakhstan for hepatocellular carcinoma (HCC) in adults who have previously been treated with sorafenib. Cabometyx is approved in combination with nivolumab as first-line treatment for people living with advanced RCC, in the E.U., Great Britain, Norway, Iceland, Switzerland, Canada, Taiwan, Singapore, the U.A.E., Australia, Chile, Israel, Thailand, Malaysia, South Korea, Saudi Arabia, the Russian Federation, Brazil and Kazakhstan. Cabometyx is also approved in the E.U., Great Britain and Canada as a monotherapy for the treatment of adult patients with locally advanced or metastatic differentiated thyroid carcinoma (DTC), refractory or not eligible to radioactive iodine who have progressed during or after prior systemic therapy. In the U.S., Cabometyx tablets are approved for the treatment of people living with advanced RCC; for the treatment of people living with HCC who have been previously treated with sorafenib; for patients with advanced RCC as a first-line treatment in combination with nivolumab; and for adults and pediatric patients 12 years of age and older with locally advanced or metastatic DTC.

The detailed recommendations for the use of Cabometyx are described in the Summary of Product Characteristics (EU SmPC)* and in the U.S. Prescribing Information (USPI).

Ipsen has exclusive rights for the commercialization of Cabometyx outside the U.S. and Japan. Cabometyx is marketed by Exelixis in the U.S. and by Takeda in Japan. Cabometyx is a registered trademark of Exelixis.

**This SmPC does not include details of the approval of Cabometyx on 3 May 2022 for use in the E.U. in the treatment of adult patients with locally advanced or metastatic DTC, refractory or not eligible to radioactive iodine who have progressed during or after prior systemic therapy. More information can be found on the European Commission's website.*

About Ipsen
Ipsen is a global, mid-sized biopharmaceutical company focused on transformative medicines in Oncology, Rare Disease and Neuroscience. With Specialty Care sales of €2.6bn in FY 2021, Ipsen sells medicines in over 100 countries. Alongside its external-innovation strategy, the Company's research and development efforts are focused on its innovative and differentiated technological platforms located in the heart of leading biotechnological and life-science hubs: Paris-Saclay, France; Oxford, U.K.; Cambridge, U.S.; Shanghai, China. Ipsen, excluding its Consumer HealthCare business, has around 4,500 colleagues worldwide and is listed in Paris (Euronext: IPN) and in the U.S. through a Sponsored Level I American Depositary Receipt program (ADR: IPSEY). For more information, visit ipsen.com

Ipsen's Forward-Looking Statements
The forward-looking statements, objectives and targets contained herein are based on Ipsen'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 Ipsen'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 Ipsen'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 Ipsen. 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 medicine 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. Ipsen must face or might face competition from generic medicine 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 Ipsen may fail to achieve its objectives and be forced to abandon its efforts with regards to a medicine in which it has invested significant sums. Therefore, Ipsen 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 medicine concerned. There can be no guarantees a medicine will receive the necessary regulatory approvals or that the medicine 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 healthcare legislation; global trends toward healthcare cost containment; technological advances, new medicine and patents attained by competitors; challenges inherent in new-medicine development, including obtaining regulatory approval; Ipsen'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 Ipsen's patents and other protections for innovative medicines; and the exposure to litigation, including patent litigation, and/or regulatory actions. Ipsen also depends on third parties to develop and market some of its medicines which could potentially generate substantial royalties; these partners could behave in such ways which could cause damage to Ipsen's activities and financial results. Ipsen 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 Ipsen's partners could generate lower revenues than expected. Such situations could have a negative impact on Ipsen's business, financial position or performance. Ipsen 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. Ipsen'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 Ipsen's 2021 Universal Registration Document, available on ipsen.com

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