

## Cabometyx<sup>®</sup> approved in the EU for previously treated advanced neuroendocrine tumors

- Cabometyx<sup>®</sup> is the first and only systemic therapy to be approved in the European Union for previously treated unresectable or metastatic neuroendocrine tumors, regardless of tumor site, grade or previous non-somatostatin analogue-based systemic therapy<sup>1,2</sup>
- Approval based on pivotal CABINET Phase III trial which demonstrated a 77% and 62% reduction in the risk of disease progression or death versus placebo in advanced pancreatic and extra-pancreatic neuroendocrine tumors, respectively<sup>3,4</sup>

**PARIS, FRANCE, 24 July 2025** – Ipsen announced today that the European Commission has approved Cabometyx<sup>®</sup> (cabozantinib) for adult patients with unresectable or metastatic, well differentiated pancreatic (pNET) and extra-pancreatic (epNET) neuroendocrine tumors who have progressed following at least one prior systemic therapy other than somatostatin analogues.

Most forms of neuroendocrine tumors (NETs) develop slowly, can originate in various parts of the body<sup>5</sup> and require multiple lines of therapy as the disease progresses.<sup>1,2</sup> Treatment options upon progression are often limited depending on primary tumor site and other factors, making it challenging to define optimal sequencing of treatments specific to individual patient needs.<sup>1,2,6</sup> In particular, for the 27% of people diagnosed with lung NETs<sup>7</sup>, there have been no approved treatment options upon progression on a prior therapy.<sup>1,2</sup>

"The complex nature of neuroendocrine tumors and lack of innovation in recent years has resulted in significant physical and emotional strain for patients as their disease progresses," said Sandra Silvestri, MD, PhD, EVP and Chief Medical Officer, Ipsen. "We are pleased that for the first time, this approval offers a unique, simplified and efficacious treatment option upon progression, where few to no other options currently exist. We look forward to working with local health authorities to make Cabometyx<sup>®</sup> available to even more patients, reinforcing our longstanding commitment to delivering transformational therapies in oncology."

NETs can have a significant impact on both individuals' lives and wider society, with 71% of people reporting NETs having a negative effect on their daily life, with 92% reporting that they have to make lifestyle changes to accommodate their disease.<sup>8</sup>

"Sequential use of systemic therapies remains challenging in the different types of neuroendocrine tumor (NET) that may arise from various organ sites. The number of available therapies is limited and not all NET patients may benefit from currently approved therapies," said Professor Marianne Pavel, Endocrinologist and NET expert at the Department of Medicine 1, Friedrich-Alexander University of Erlangen, Germany. "Advancements like those achieved through the CABINET Phase III study, as recognized by the approval for Cabometyx in a wide range of NET, is offering new treatment opportunities to delay disease progression in patients with well differentiated NET irrespective of the type of neuroendocrine tumor."

The EC approval was based on data from the CABINET Phase III trial which investigated Cabometyx versus placebo in people living with advanced pNETs or epNETs whose disease had progressed after

prior systemic therapy. Final results from the trial, as presented at the 2024 European Society for Medical Oncology Congress and simultaneously published in the *New England Journal of Medicine*, demonstrated progression-free survival (PFS) benefits in favor of Cabometyx versus placebo.<sup>3,4</sup>

- In the pNET cohort, at a median follow-up of 13.8 months, median PFS was 13.8 months for Cabometyx versus 4.4 months for placebo (hazard ratio (HR) 0.23 [95% confidence interval (CI) 0.12–0.42]  $p < 0.001$ ).<sup>3,4</sup>
- In the epNET cohort, at a median follow-up of 10.2 months, median PFS based on local radiology review was 8.4 months for Cabometyx versus 3.9 months for placebo (HR 0.38 [95% CI 0.25–0.59]  $p < 0.001$ ).<sup>3,4</sup>
- Overall survival data were not mature at the time of the analyses and potentially confounded by the crossover design of the CABINET trial.<sup>3,4</sup>
- The safety profile of Cabometyx observed in each cohort was consistent with its known safety profile; no new safety signals were identified.<sup>3,4</sup>
- Per presentation at the Annual Society of Clinical Oncology Annual Meeting 2025, health-related quality of life was also found to be maintained or improved versus placebo.<sup>9</sup>

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### About Cabometyx

Cabometyx is a small molecule that inhibits multiple receptor tyrosine kinases, including VEGFRs, MET, RET and the TAM family (TYRO3, MER, AXL).<sup>10</sup> These receptor tyrosine kinases are involved in both normal cellular function and pathological processes such as oncogenesis, metastasis, tumor angiogenesis (the growth of new blood vessels that tumors need to grow), drug resistance, immune modulation, and maintenance of the tumor microenvironment.<sup>10,11,12,13</sup>

Exelixis granted Ipsen exclusive rights for the commercialization and further clinical development of Cabometyx outside of the U.S. and Japan. Exelixis granted exclusive rights to Takeda Pharmaceutical Company Limited (Takeda) for the commercialization and further clinical development of Cabometyx for all future indications in Japan. Exelixis holds the exclusive rights to develop and commercialize Cabometyx in the U.S.

In over 65 countries outside of the United States and Japan, including in the European Union, Cabometyx is currently indicated as:<sup>11</sup>

- Monotherapy for advanced renal cell carcinoma (aRCC).
  - as first-line treatment of adults with intermediate- or poor-risk disease.
  - in adults following prior VEGFR-targeted therapy.
- A combination with nivolumab for the first-line treatment of aRCC in adults.
- Monotherapy for the treatment of adults living with locally advanced or metastatic differentiated thyroid carcinoma, refractory or not eligible to radioactive iodine who have progressed during or after prior systemic therapy.
- Monotherapy for the treatment of hepatocellular carcinoma in adults who have previously been treated with sorafenib.
- Monotherapy for adult patients with unresectable or metastatic, well differentiated pancreatic (pNET) and extra-pancreatic (epNET) neuroendocrine tumors who have progressed following at least one prior systemic therapy other than somatostatin analogues.

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### About CABINET (Alliance A021602)

CABINET (randomized, double-blinded Phase III trial of CABozantinib versus placebo in patients with advanced Neuroendocrine Tumors after progression on prior therapy) is sponsored by the National Cancer Institute (NCI), part of the National Institutes of Health in the U.S., and is being led and conducted by the NCI-funded Alliance for Clinical Trials in Oncology with participation from the NCI-funded National Clinical Trials Network, as part of Exelixis' collaboration through a Cooperative Research and Development Agreement with the NCI's Cancer Therapy Evaluation Program.

The multicenter Phase III CABINET pivotal trial enrolled a total of 298 patients in the U.S. at the time of the analysis. Patients were randomized 2:1 to Cabometyx or placebo in two separately powered cohorts. The epNET cohort included patients with the following primary tumor sites: gastrointestinal tract, lung, unknown primary and other organs. Each cohort was randomized separately and had its own statistical analysis plan. Patients must have had measurable disease per RECIST 1.1 criteria and must have experienced disease progression or intolerance after at least one U.S. Food and Drug Administration-approved line of prior systemic therapy other than somatostatin analogues. The primary endpoint in each cohort was PFS per RECIST 1.1 by retrospective blinded independent central review. Upon confirmation of disease progression, patients were unblinded, and those receiving placebo were permitted to cross over to open-label therapy with Cabometyx. Secondary endpoints included overall survival, objective response rate and safety. More information about this trial is available at [ClinicalTrials.gov](https://ClinicalTrials.gov).

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### About Ipsen

We are a global biopharmaceutical company with a focus on bringing transformative medicines to patients in three therapeutic areas: Oncology, Rare Disease and Neuroscience.

Our pipeline is fueled by external innovation and supported by nearly 100 years of development experience and global hubs in the U.S., France and the U.K. Our teams in more than 40 countries and our partnerships around the world enable us to bring medicines to patients in more than 100 countries.

Ipsen 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 [ipсен.com](https://ipсен.com).

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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 forwardlooking 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 latest Universal Registration Document, available on [ipсен.com](https://www.ipсен.com).

## References

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<sup>1</sup>Pavel M, *et al.* Gastroenteropancreatic neuroendocrine neoplasms: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol.* 2020;31(7):844–860.

<sup>2</sup>Baudin E, *et al.* Lung and thymic carcinoids: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol.* 2021 Nov;32(11):1453–1455.

<sup>3</sup>Chan *et al.* Phase 3 Trial of Cabozantinib in Previously Treated Advanced Neuroendocrine Tumors. 2024 *New England Journal of Medicine*. DOI: 10.1056/NEJMoa2403991

<sup>4</sup>Chan *et al.* Cabozantinib Versus Placebo for Advanced Neuroendocrine Tumors (NET) after Progression on Prior Therapy (CABINET Trial/Alliance A021602): Updated Results Including Progression Free-Survival (PFS) by Blinded Independent Central Review (BICR) and Subgroup Analyses. As presented at ESMO Congress 2024 during the 'Proffered Paper: NETs and Endocrine Tumors at 2:45 p.m. CEST Barcelona, Spain

<sup>5</sup>Neuroendocrine tumor (NET). <https://www.cancer.gov/pediatric-adult-rare-tumor/rare-tumors/rare-endocrine-tumor/carcinoid-tumor>. Accessed July 2025.

<sup>6</sup>McClellan, K., Chen. E.Y, Kardosh A., *et al.* Therapy Resistant Gastroenteropancreatic Neuroendocrine Tumors. *Cancers.* 2022, 14(19), 4769.

<sup>7</sup>Frilling *et al.* Neuroendocrine tumor disease: an evolving landscape. 2012. 19:R163–R185

<sup>8</sup>Singh *et al.* Patient-Reported Burden of a Neuroendocrine Tumor (NET) Diagnosis: Results From the First Global Survey of Patients With NETs. *J Glob Oncol.* 2017 Feb; 3(1): 43–53.

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<sup>9</sup>Dueck *et al.* Health-related quality of life (HRQOL) in the phase 3 trial of cabozantinib vs placebo for advanced neuroendocrine tumors (NET) after progression on prior therapy (CABINET, Alliance A021602). As presented at ASCO Congress 2025.

<sup>10</sup>El-Khoueiry A. *et al.*, Cabozantinib: An evolving therapy for hepatocellular carcinoma. *Cancer Treatment Reviews*. 2021 Jul;98:102221. DOI: 10.1016/j.ctrv.2021.102221.

<sup>11</sup>European Medicines Agency. Cabometyx® (cabozantinib) EU Summary of Product Characteristics. Available from: [https://www.ema.europa.eu/en/documents/product-information/cabometyx-epar-product-information\\_en.pdf](https://www.ema.europa.eu/en/documents/product-information/cabometyx-epar-product-information_en.pdf). Accessed July 2025.

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