Press release

Intended for international media and investor audiences only

Latest Phase III trial data investigating Cabometyx® in combination with immunotherapy to be presented at ASCO GU 2024

- Detailed top-line results from Phase III CONTACT-02 trial demonstrated statistically significant progression-free survival benefit for combination of Cabometyx® and atezolizumab in metastatic castration-resistant prostate cancer

- Four-year extended follow-up data from landmark Phase III CheckMate -9ER trial reinforce sustained long-term efficacy benefits for the combination of Cabometyx® and nivolumab versus sunitinib in advanced renal cell carcinoma

PARIS, FRANCE, 22 January 2024 - Ipsen (Euronext: IPN; ADR: IPSEY) announced today new data to be presented for Cabometyx® (cabozantinib) in combination with immunotherapy across indications at the upcoming American Society of Clinical Oncology Genitourinary Symposium (ASCO GU) taking place on 25-27 January 2024 in San Francisco, U.S.

Detailed top-line results from the Phase III CONTACT-02 trial of the combination of Cabometyx and atezolizumab versus a second novel hormone therapy (NHT) in people living with metastatic castration-resistant prostate cancer (mCRPC) and measurable extra-pelvic soft tissue disease who have progressed on one prior NHT, are to be presented as an oral presentation (Abstract #18).

With a median follow-up of 14.3 months, data from the primary analysis of progression-free survival (PFS) from the CONTACT-02 trial demonstrated a statistically significant PFS benefit for the combination of Cabometyx and atezolizumab of 6.3 months versus 4.2 months for a second NHT (hazard ratio [HR]: 0.65, 95% confidence interval [CI]: 0.50-0.84; p=0.0007). At an interim analysis for the other primary endpoint of overall survival (OS), the data demonstrated a trend toward improvement for the combination, however, these data were immature, and the trial will continue to the next planned analysis, anticipated in 2024. Safety for the combination appeared to be consistent with the known safety profiles of the individual medicines, and no new safety signals were identified.

Prostate cancer is the second most common cancer in men[1] and for those living with advanced metastatic castration-resistant disease, the prognosis is poor, with an estimated survival of 1-2 years[2].

“At the advanced metastatic castration-resistant stage of disease, the prognosis is poor, with a median survival of two years and limited available treatment options,” said Stéphane Oudard, Professor of Oncology and Chief of the Oncology Clinical and Translational Research Unit at Georges Pompidou Hospital in Paris, France. “These results from the CONTACT-02 trial represent a positive step in the context of the current treatment landscape, contributing the first positive Phase III data of its kind for the benefit of patients, as we await further data from the overall survival analysis.”

Also, four-year extended follow-up data from the landmark Phase III CheckMate -9ER trial investigating the combination of Cabometyx and nivolumab versus sunitinib in people living with previously untreated advanced renal cell carcinoma (aRCC) will be presented (Abstract #362).

With a median follow-up of 55.6 months for OS, the combination of Cabometyx and nivolumab demonstrated a sustained and clinically meaningful OS benefit versus sunitinib, with an absolute median OS gain of 10.5 months (46.5 months for the combination vs 36.0 months for sunitinib, HR 0.77, 95% CI: 0.63-0.95). Additionally, median PFS remained almost double that for the combination versus sunitinib,

at 16.4 vs 8.4 months respectively (HR 0.58, 95% CI: 0.49-0.70). The safety profile was consistent with the known safety profiles of the individual medicines, and no new safety signals were identified.

Renal cell carcinoma is the most common form of kidney cancer[3, 4] and for the 30% of people diagnosed with an advanced form of the disease, the 5-year survival rate is low at 12%, with no identified cure for this disease.[5,6]

"Data from our ongoing trials continue to reinforce the value of Cabometyx for patients across a number of challenging tumor types," said Christelle Huguet, EVP and Head of Research and Development, Ipsen. "In combination with immunotherapy, Cabometyx is delivering long-term survival benefits today for people living with renal cell carcinoma worldwide, while also showcasing future potential in metastatic castration-resistant prostate cancer, an area of significant unmet need where no other trials of this modality have proven successful in recent decades."

Additionally, health-related quality of life (HRQoL) data from a modelling analysis based on the CheckMate 9ER trial explored the link between HRQoL and clinical outcomes at a median follow-up of 32.9 months (Abstract #384). These data provide further patient-focused context to the benefits of the combination of Cabometyx and nivolumab, whilst also reinforcing the association of the combination with an increased chance of tumor shrinkage, survival and progression-free survival, independent of early HRQoL deterioration.

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About Cabometyx

Cabozantinib is a small molecule that inhibits multiple receptor tyrosine kinases (RTKs), including VEGFRs, MET, RET and the TAM family (TYRO3, MER, AXL).[7] These receptor tyrosine kinases are involved in both normal cellular function and pathologic processes such as oncogenesis, metastasis, tumor angiogenesis (the growth of new blood vessels that tumors need to grow), drug resistance, modulation of immune activities and maintenance of the tumor microenvironment.[7,8,9,10]

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 60 countries outside of the United States and Japan, including in the European Union (E.U.), Cabometyx is currently indicated as:[8]

- 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.
    - in 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 (DTC), refractory or not eligible to radioactive iodine (RAI) 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.

The detailed recommendations for the use of Cabometyx are described in the Summary of Product Characteristics (EU SmPC).

About mCRPC

Prostate cancer is the second most common cancer in men and the fourth most common cancer overall globally.[1] In 2020, there were more than 1.4 million new cases of prostate cancer and about 375,300 deaths worldwide.[1] Prostate cancer is considered mCRPC when it has spread beyond the prostate and does not respond to androgen-suppression therapies, a common treatment for prostate cancer.[11] Men diagnosed with mCRPC often have a poor prognosis, with an estimated survival of 1-2 years.[2]

About aRCC

There were over 400,000 new cases of kidney cancer diagnosed worldwide in 2020.[12] Of these, RCC is the most common type of kidney cancer, accounting for approximately 90% of cases.[3,4] It is almost twice as common in men, and male patients account for over two thirds of deaths.[12] At diagnosis, up to 30% of patients present with advanced or metastatic RCC. If detected in the early stages, the five-year survival rate is high, but for people living with advanced or late-stage metastatic RCC, the survival rate is much lower, around 12%, with no identified cure for this disease.[5,6]

About the CONTACT-02 trial

CONTACT-02 is a global, multicenter, randomized, Phase III, open-label study that enrolled 575 patients who were randomized 1:1 to the experimental arm of Cabometyx in combination with atezolizumab and the control arm of a second NHT (either abiraterone and prednisone or enzalutamide). The study included patients with mCRPC who have measurable visceral disease or measurable extra-pelvic adenopathy and who have progressed on one prior NHT. The two primary endpoints of the trial are PFS and OS. The PFS analysis was conducted in the first 400 randomized patients (PFS in the intent-to-treat [ITT] population) and assessed by a blinded independent radiology committee (BIRC) per RECIST 1.1. The OS analysis was conducted in the ITT population (n=507). The secondary endpoint is objective response rate (ORR) per BIRC. The trial is sponsored by Exelixis and co-funded by Ipsen, Roche and Takeda. Takeda is conducting the trial in Japan. More information about CONTACT-02 is available at ClinicalTrials.gov.

About the CheckMate -9ER trial

CheckMate -9ER is 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 is progression-free survival (PFS). The secondary endpoints include OS and ORR. The primary efficacy analysis compared the doublet combination versus sunitinib in all randomized patients. The trial is sponsored by Bristol Myers Squibb and Ono Pharmaceutical Co and co-funded by Exelixis, Ipsen and Takeda Pharmaceutical Company Limited. More information about CheckMate -9ER is available at ClinicalTrials.gov.

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 ipsen.com.

Ipsen contacts

Email: corporate.communications@ipsen.com

Investors

Craig Marks | +44 7584 349 193

Media

Joanna Parish | +44 7840 023 741

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and uncertainties set out are not exhaustive and the reader is advised to refer to Ipsen's latest Universal Registration Document, available on ipsen.com.

References

[1] Prostate cancer statistics. World Cancer Research Fund International. Available at: https://www.wcrf.org/cancer-trends/prostate-cancer-statistics/. Last accessed January 2024.
[2] Moreira, D. M., *et al*. Predicting Time From Metastasis to Overall Survival in Castration-Resistant Prostate Cancer: Results From SEARCH. *Clin Genitourin Cancer*. 2017; 15: 60–66.e2.
[3] Kidney Cancer. Mayo Clinic. Available: https://www.mayoclinic.org/diseases-conditions/kidney-cancer/symptoms-causes/syc-20352664. Accessed: January 2024.
[4] Infographic: Kidney Cancer. Mayo Clinic. Available: https://www.mayoclinic.org/diseases-conditions/kidney-cancer/multimedia/kidney-cancer-infographic/ifg-20441505. Accessed: January 2024.
[5] Survival rates for kidney cancer. American Cancer Society. Available: https://www.cancer.org/cancer/kidney-cancer/detection-diagnosis-staging/survival-rates.html Accessed: January 2024.
[6] Orlin I. *et al*. Renal cell carcinomas epidemiology in the era of widespread imaging. Journal of Clinical Oncology. 2019; 37:15. DOI: https://ascopubs.org/doi/10.1200/JCO.2019.37.15_suppl.e13083.
[7] 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.
[8] 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. Last accessed: January 2024
[9] Yakes M. *et al*., Cabozantinib (XL184), a novel MET and VEGFR2 inhibitor, simultaneously suppresses metastasis, angiogenesis, and tumor growth. *Mol Cancer Ther*. 2011;10:2298–2308. DOI: 10.1158/1535-7163.MCT-11-0264
[10] Hsu *et al*., AXL and MET in Hepatocellular Carcinoma: A Systematic Literature Review. *Liver Cancer* 2021 DOI: 10.1159/000520501
[11] Prostate Cancer: Types of Treatment. Cancer.Net. Available at: https://www.cancer.net/cancer-types/prostate-cancer/types-treatment. Accessed January 2024.
[12] Kidney Cancer Factsheet. GLOBOCAN 2020. Available: https://gco.iarc.fr/today/data/factsheets/cancers/29-Kidney-fact-sheet.pdf. Accessed: January 2024.