

# Oncology and rare diseases

Ipsen's patient-focused approach to oncology and rare diseases delivers for some conditions benefits along every step of the treatment pathway and uses targeted therapies to address conditions with high unmet needs. —

In the fields of oncology and rare diseases, Ipsen takes a patient-focused approach to improving the lives of people affected by cancers and rare disorders, and develops high-quality, innovative treatments that address unmet needs. Our goal is to support patients with drugs, services and solutions across the entire continuum of care, from diagnosis to treatment follow-up.

## An increased focus to oncology

— Ipsen has been active in oncology since 1986, and over the years has grown its reputation and portfolio, branching out from a solid base in prostate, neuroendocrine tumors (NETs), bladder, kidney, pancreatic and breast cancers. Somatuline® is key to Ipsen's leadership in the treatment of NETs. New indications were launched in 2015 in the United States and in 2016 in Europe, as Somatuline® was shown by the CLARINET® study to reduce the risk of disease progression or death by 53% in gastroenteropancreatic NETs patients whose disease is unresectable or metastasized. In addition, the efficacy of Somatuline® in patients with lung NETs is being assessed in the multinational SPINET® study. Ipsen is the first

and only company assessing the efficacy and safety of a somatostatin analog (SSA) in a prospective phase 3 trial in these patients. Somatuline® is marketed in over 55 countries, 27 of them in Europe.

Effective treatments to improve the health and lives of patients whose carcinoid syndrome is not adequately controlled with SSA therapy are needed. Ipsen and Lexicon Pharmaceuticals entered into an exclusive licensing agreement for Ipsen to commercialize telotristat outside of the United States and Japan in October 2014. Lexicon received FDA approval for Xermelo® in the USA at the end of February 2017 and outside the USA telotristat is still subject to the evaluation of the benefits and risks by regulatory authorities before being made available.

Ipsen's leadership in NETs was further supported by the 2015 acquisition of OctreoPharm Sciences, and is expected to be enhanced by the potential approval of telotristat in carcinoid syndrome in EU.

## A reinforced oncology pipeline

Ipsen's oncology pipeline was reinforced in March 2016 with the in-licensing of

cabozantinib from Exelixis. In September 2016, the European Medicines Agency approved Cabometyx® (cabozantinib tablets) for the treatment of second-line advanced renal cell cancer based on the results of the METEOR phase 3 trial. In September 2016 also, Ipsen and Exelixis announced positive results from the phase 2 CABOSUN trial of cabozantinib versus sunitinib in previously untreated advanced RCC. This treatment offers an opportunity to extend survival for patients suffering from RCC, responsible for nine out of ten cases of kidney cancers.

A major strategic step forward in bolstering Ipsen's growing oncology presence and leveraging its oncology infrastructure in the United States was taken in early 2017 with the acquisition of oncology assets of Merrimack Pharmaceuticals. The highlight of the transaction is the acquisition of commercialization rights for Onivyde® (irinotecan liposome injection), a landmark, FDA-approved treatment for metastatic pancreatic cancer (see box p. 16).

# Boosting our portfolio

Ipsen offers a broad range of high-quality, innovative treatments to help improve the lives of patients with cancer and rare diseases.

**ACROMEGALY**  
69,000 patients worldwide  
**LANREOTIDE**  
Early and sustained long-term biochemical control as well as improvement in symptoms, tumor size, and quality of life

**MEDULLARY THYROID CANCER**  
5% of thyroid cancers  
**CABOZANTINIB (capsules)**  
Significant difference in the duration of progression-free survival with cabozantinib (11.2 months) versus placebo (4.0 months)<sup>(3)</sup>

**PANCREATIC CANCER**  
3<sup>rd</sup> leading cause of cancer-related death in the US  
**IRINOTECAN LIPOSOME INJECTION<sup>(4)</sup>**  
Significant improvement of overall survival in adult patients with metastatic adenocarcinoma of the pancreas

**BREAST CANCER**  
20% of invasive breast cancer in premenopausal patients  
**TRIPTORELIN**  
86.6% disease-free survival at 5 years when added to tamoxifen  
22% risk reduction in distant recurrence when added to exemestane

**NEUROENDOCRINE TUMORS**  
112,000 people living with NETs in the US and 178,000 people in Europe  
**LANREOTIDE**  
Reduction of risk of disease progression or death by 53%

**CARCINOID SYNDROME**  
Occurs in about 20% of all neuroendocrine tumors  
**LANREOTIDE**  
Reduction by 50% in bowel movement and flushing episodes in more than 50% of lanreotide treated patients

**RENAL CELL CARCINOMA**  
More than 250,000 new cases per year worldwide  
**CABOZANTINIB (tablets)**  
1<sup>st</sup> and only multi-targeted therapy to prolong survival, slow disease progression, and shrink tumors

**PROSTATE CANCER**  
2<sup>nd</sup> most common type of cancer in men<sup>(1)</sup>  
**TRIPTORELIN**  
Over 90% of patients achieve and maintain medical castration below the most stringent threshold levels (< 20 ng/dl)<sup>(2)</sup>

**BLADDER CANCER**  
2<sup>nd</sup> most frequent urological cancer, after prostate cancer  
**HEXAMINOLEVULINATE**  
Improved treatment and improved detection and resection of non-invasive bladder cancer

(1) Globocan 2015.  
(2) Future Oncol. 2013;9(1): 93-102 – Prog Urol. 2007;17(2): 235-9 – Adv. Ther. 2016;33:1072-1093.  
(3) Stratified Hazard Ratio [HR] = 0.28; 95% CI: 0.19, 0.40; p<0.0001 J Clin Oncol. 2013 Oct 10;31(29):3639-46.  
(4) Liposome injection with fluorouracil and folinic acid.

## Fighting pancreatic cancer

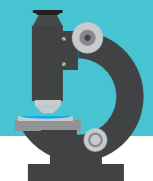
• Pancreatic cancer, a rapidly progressive disease with high unmet treatment needs, is the third leading cause of cancer-related death in adults in the United States (surpassing breast cancer). Ipsen now owns US commercialization rights for Onivyde®, an FDA-approved treatment for metastatic pancreatic cancer. Additional indications are being studied including first-line, previously untreated metastatic pancreatic cancer, relapsed small-cell lung cancer and breast cancer. —



Patients inspire our strategy and our innovations —



**In 2016, Oncology** represents more than 57% of sales.



Decapeptyl® (triptorelin) is a synthetic hormone therapy primarily indicated for the hormonal treatment of locally advanced metastatic prostate cancer, that can be now injected subcutaneously too. In early March 2017, the MHRA in the UK, in coordination with 14 other European regulatory agencies, has approved a new indication for Decapeptyl® as adjuvant treatment in combination with tamoxifen or an aromatase inhibitor, for women at high-risk of breast cancer recurrence. Hexvix® (hexaminolevulinate), a significant improvement for urologists and their patients, is a photosensitizing agent that improves detection and resection of non-invasive bladder cancer.

## Becoming a key player in rare diseases

— Ipsen has been an active actor in the rare

disease field and intends to bringing new solutions to these patients, notably for children. Somatuline® is also used for the long-term treatment of acromegaly – a rare disease caused by excess growth hormone production as a result of a tumor in the pituitary gland – in patients who cannot be treated with surgery or radiation. We are currently developing extended-release formulations of Somatuline® so that fewer injections would be required. NutropinAq® is a liquid formulation of recombinant human growth hormone administered with the NutropinAq® Pen. Available in more than 20 countries, notably in Europe and Australia, it is indicated for the treatment of growth failure stemming from various origins. Increlex® is a recombinant insulin-like growth factor (IGF-1) that treats growth delay in children who lack it in their bodies. If IGF-1 is not present in sufficient quantities, the patient will not reach normal stature, despite having

normal or high growth-hormone levels. As a result, these children do not respond adequately to growth hormone treatment. Increlex® has obtained orphan drug status based on the low incidence of the disease, which affects fewer than 5 people per 10,000. Besides, Ipsen offers a number of other important solutions for patients with other debilitating or life-threatening conditions. For instance, Decapeptyl® (triptorelin) is also approved for the treatment of central precocious puberty (CPP) endometriosis, uterine fibroma, and *in vitro* fertilization.

## Partnerships with patients and healthcare providers

— To ensure that NETs patients are fully informed, Ipsen launched the website [www.livingwithnets.com](http://www.livingwithnets.com) at the end of 2016. Designed by and with patients for the use

of patients, the site provides the full picture of the condition and offers all the information and support patients need to help them on their journey.

Ipsen's support for acromegaly patients also goes beyond treatments. The Acromunity.com website, to be launched in 2017, will offer them a platform, developed in conjunction with patients and healthcare professionals, that delivers content, tools and services to match their needs, from the time the first symptoms are noticed to years after diagnosis.

In the United States, Ipsen supports IPSEN CARES™ (Coverage, Access, Reimbursement and Education Support), a program that assists patients in overcoming obstacles to start or continue treatment with Somatuline® for gastroenteropancreatic NETs and acromegaly, as well as Increlex® and Dysport®, including coverage access, distribution and financial concerns.

In Europe, the Group has set up INKEP (Ipsen Network of Knowledge Exchange Program) for small groups of physicians specializing in pediatric endocrinology. It combines scientific presentations, case discussions and interactive sit-in clinic visits.

Other initiatives in pediatric endocrinology include APPRI in France, a personalized training program for patients that helps increase their autonomy at home during treatment with the recombinant growth hormone NutropinAq® and the NutropinAq® injection pen, and improves treatment compliance.

Furthermore, Ipsen is committed to promoting transparent and evidence-based discussions between stakeholders on policies concerning the management of conditions on which it focuses – including NETs, rare diseases and urological cancers. ●