

## Ipsen announces MHRA<sup>1</sup> approval of new indication for Decapeptyl<sup>®</sup> for the treatment of pre-menopausal women with early stage breast cancer

**Paris (France), 13 March 2017** – Ipsen (Euronext: IPN; ADR: IPSEY) today announced that the Medicines and Healthcare Products Regulatory Agency (MHRA) in the UK, in coordination with fourteen other European regulatory agencies, has approved a new indication for Decapeptyl<sup>®</sup> as adjuvant treatment in combination with tamoxifen or an aromatase inhibitor, of endocrine-responsive early-stage breast cancer in women at high-risk of recurrence who are confirmed as pre-menopausal after completion of chemotherapy.

**Alexandre Lebeaut, Executive Vice President, R&D, Chief Scientific Officer, Ipsen** stated: *“We are pleased to receive the first European approval which brings a new treatment option offering disease free survival benefit for high-risk pre-menopausal breast cancer patients. This is the result of a longstanding scientific collaboration between Ipsen and the IBCSG, one of the leading international cooperative groups in Breast Cancer which exemplifies Ipsen’s continuous commitment to improving patients care.”*

The approval is based on international trials sponsored by the International Breast Cancer Study Group (IBCSG) and conducted on a total of 5,700 randomized patients in 27 countries. Two randomized Phase 3 trials were conducted, SOFT (Suppression of Ovarian Function Trial) and TEXT (Tamoxifen and Exemestane Trial), which evaluated pre-menopausal women with early-stage hormone-receptor-positive breast cancer.

The IBCSG presented the combined results of the TEXT and SOFT clinical trials at the 2014 American Society of Clinical Oncology (ASCO) Annual Meeting plenary session in Chicago and the 2014 San Antonio Breast Cancer Symposium. Results were published in the New England Journal of Medicine<sup>2,3</sup>.

On the basis of results from SOFT and TEXT studies, the international guidelines of St Gallen, the European Society for Medical Oncology (ESMO), the National Comprehensive Cancer

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<sup>1</sup> Medicines and Healthcare Products Regulatory Agency

<sup>2</sup> Pagani O, Regan MM, Walley BA, et al.: Adjuvant exemestane with ovarian suppression in premenopausal breast cancer N Engl J Med 2014; 371: 107–118.

<sup>3</sup> Francis PA, Regan MM, Fleming GF, et al.: Adjuvant ovarian suppression in premenopausal breast cancer. N Engl J Med 2015; 372: 436–446.



Network (NCCN) and ASCO have been updated to recommend the use of ovarian function suppression with either tamoxifen or exemestane as a new therapeutic option for women at high risk of recurrence.

**Meredith M. Regan, Associate Professor in the Department of Biostatistics and Computational Biology at the Dana-Farber Cancer Institute, Associate Professor of Medicine at Harvard Medical School, IBCSG Group Statistician,** commented: *“IBCSG initiated those 2 prospective studies SOFT and TEXT more than fifteen years ago with the ambitious goal to address a major question on the role of OFS in the adjuvant setting for premenopausal women. We are very happy that these studies have been the foundation for a MHRA approval of triptorelin which will facilitate patient’s access to this new treatment paradigm. We thank Ipsen for their support since the beginning of those studies”.*

#### **About SOFT and TEXT**

The main objectives of the SOFT and TEXT trials were to assess the value of adding Ovarian Function Suppression (OFS) to adjuvant tamoxifen in premenopausal women and whether adjuvant therapy with the aromatase inhibitor (exemestane) improves outcomes compared with tamoxifen in premenopausal women treated with OFS.

The primary endpoint in both studies was Disease Free Survival (DFS) and compared tamoxifen + OFS to tamoxifen alone in SOFT study, tamoxifen + OFS to exemestane + OFS in the TEXT and SOFT studies. The main secondary endpoints were breast cancer free interval (BCFI), distant recurrence free interval (DRFI) and overall survival (OS).

Although the primary end-point (DFS) was not met in SOFT study, (T+OFS versus T alone), the combination of exemestane + OFS with triptorelin has shown to significantly improve DFS when compared to tamoxifen only, with a risk reduction of DFS events of 32% (SOFT: HR=0.68, 95% CI, 0.53 to 0.86). The same combination of exemestane + OFS with triptorelin has demonstrated to significantly improve DFS with a risk reduction of DFS events of 28% (SOFT/TEXT: HR=0.72; 95% CI, 0.60 to 0.86; p=0.0002) when compared to tamoxifen + OFS with triptorelin<sup>4</sup>.

In SOFT, the clinical benefit was higher in patients who received adjuvant chemotherapy with a reduction of the risk of DFS events of 18% (HR=0.82; 95% CI, 0.64 to 1.07) for patients receiving T + OFS with triptorelin versus those with tamoxifen only. In particular, the benefit of adding OFS with triptorelin was apparent for 5 year DFS for the subgroup of patients less than 40 years old an absolute benefit of 4.4% for T+OFS compared to T alone (HR=0.74; 95% CI, 0.53, 1.03)<sup>4</sup>.

Furthermore, adding OFS with triptorelin to exemestane significantly reduce the risk of breast cancer recurrence by 36% (HR=0.64; 95% CI, 0.49 to 0.83) as compared to tamoxifen alone (SOFT) and by 34% (HR=0.66; 95% CI, 0.55 to 0.80; P<0.0001) as compared to tamoxifen + OFS with triptorelin (SOFT/TEXT)<sup>4</sup>.

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<sup>4</sup> Summary of Product Characteristics (Decapeptyl® SmPC 2017)

In both studies, adding triptorelin to tamoxifen or AI resulted in increased AEs, most notably menopausal symptoms, depression and AEs with possible long term health implication such as hypertension, diabetes and osteoporosis. Selected adverse events of grade 3 or 4 were reported for 30.6% of the patients in the exemestane + OFS group and 29.4% of those in the tamoxifen + OFS group.

The QoL data in the overall population suggested that the impairment in symptom-related QoL indicators is transitory and decline significantly over time (SOFT).

The International Breast Cancer Study Group (IBCSG) is a Swiss nonprofit cooperative breast cancer research organization that has conducted clinical research in adjuvant endocrine therapy and chemotherapy, timing and duration of adjuvant therapies, and quality of life for over 35 years.

### **About Breast Cancer**

Breast cancer is the most common cancer worldwide for females, and the second most common cancer overall, with more than 1,676,000 new cases diagnosed in 2012 (25% of female cases and 12% of the total)<sup>[1;2]</sup>. Breast cancer was the leading cancer site in women in all countries of Europe in 2012 with 464,000 cases<sup>[1]</sup>. The incidence is stable since 2000 (due to the decreased use of hormonal substitutive treatment)<sup>[3]</sup>. Prognosis has improved due to adjuvant therapies but breast cancer is the most common cause of cancer deaths worldwide with around 522,000 deaths from breast cancer in 2012<sup>[1;2]</sup>. In Europe, breast cancer is the most common cause of cancer death in Europe for females, and the third most common cause of cancer death overall, with more than 131,000 deaths from breast cancer in 2012 (17% of female deaths and 7% of the total)<sup>[1]</sup>. The majority of breast cancers are diagnosed at a local stage and most of them are invasive<sup>[3]</sup>. These early stage invasive breast cancers are operable and the main risk of these patients is the recurrence (loco-regional or contro-lateral or distant breast recurrence). If the average age of onset of menopause is 50 years old, the percentage of invasive breast cancer in premenopausal patients (less than 50 years) represents approximately 20% of all the total cases<sup>[3]</sup>. The determination of hormone receptor status (oestrogen receptors – ERs and progesterone receptors – PgRs) on the primary breast tumour has to be performed systematically<sup>[4]</sup>. Among this population, a subset of patients express clinico-pathological features (such as young age) that expose them to a higher risk of recurrence<sup>[4]</sup>.

1. Ferlay J, Steliarova-Foucher E, Lortet-Tieulent J et al. Cancer incidence and mortality patterns in Europe: Estimates for 40 countries in 2012. *Eur J Cancer* 2013;49:1374-1403.
2. Globocan Cancer Fact Sheet 2015: Breast Cancer. Available at <http://globocan.iarc.fr/old/FactSheets/cancers/breast-new.asp>; accessed 20 April 2015.
3. Cancer Research UK 2015, Breast cancer incidence statistics. Available at <http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/breast-cancer/incidence-invasive#heading-One>; accessed 16 November 2015.
4. Senkus E, Kyriakides S, Ohno S et al. Primary breast cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2015;26 (Suppl 5) v8-v30.

### **About Decapeptyl® (triptorelin one- month formulation)**

Decapeptyl® is a peptide formulation for injection to be used mainly in the treatment of locally advanced or metastatic prostate cancer. Additional indications developed subsequently include the treatment of uterine fibroids (a benign tumour of muscle tissues in the uterus), endometriosis (proliferation of endometrial tissue, the mucous membrane that lines the uterine wall outside the reproductive tract) after surgery or



when surgery is not deemed appropriate, as well as early onset puberty and female infertility (in vitro fertilization).

The active substance in Decapeptyl® is triptorelin pamoate, a decapeptide analogue of GnRH (Gonadotrophin Releasing Hormone), a hormone secreted by the hypothalamus, which initially stimulates the release of pituitary gonadotrophins (hormones produced by the pituitary gland), which in turn control hormonal secretions by the testicles and ovaries. Administration of triptorelin results in the suppression of the GnRH activity leading to hormonal castration in men and menopausal phase in women.

### **About Ipsen**

Ipsen is a global specialty-driven pharmaceutical group with total sales close to €1.6 billion in 2016. Ipsen sells more than 20 drugs in more than 115 countries, with a direct commercial presence in more than 30 countries. Ipsen's ambition is to become a leader in specialty healthcare solutions for targeted debilitating diseases. Its fields of expertise cover oncology, neurosciences and endocrinology (adult & pediatric). Ipsen's commitment to oncology is exemplified through its growing portfolio of key therapies improving the care of patients suffering from prostate cancer, neuro-endocrine tumors, renal cell carcinoma and pancreatic cancer. Ipsen also has a significant presence in primary care. Moreover, the Group has an active policy of partnerships. Ipsen's R&D is focused on its innovative and differentiated technological platforms, peptides and toxins, located in the heart of the leading biotechnological and life sciences hubs (Les Ulis/Paris-Saclay, France; Slough/Oxford, UK; Cambridge, US). In 2016, R&D expenditures exceeded €200 million. The Group has more than 4,900 employees worldwide. Ipsen's shares are traded on segment A of Euronext Paris (stock code: IPN, ISIN code: FR0010259150) and are eligible to the "Service de Règlement Différé" ("SRD"). The Group is part of the SBF 120 index. Ipsen has implemented a Sponsored Level I American Depositary Receipt (ADR) program, which trades on the over-the-counter market in the United States under the symbol IPSEY. For more information on Ipsen, visit [www.ipsen.com](http://www.ipsen.com).

### **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. 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 pre-clinical 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 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 2015 Registration Document available on its website ([www.ipsen.com](http://www.ipsen.com)).

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