*Press release*

# Ipsen grants Menarini exclusive European licence rights to Adenuric® (febuxostat), its novel treatment for chronic hyperuricaemia in gout

- **Ipsen to co-promote in France**
- **Launch expected early 2010**

**Paris (France), 20 October 2009** - Ipsen (Euronext: FR0010259150; IPN), an innovation-driven global specialty pharmaceutical group, today announced an agreement whereby Ipsen grants the Menarini Group the exclusive licence rights to Adenuric® (febuxostat) in 41 countries. Ipsen retains co-promotion rights for Adenuric® in France. With its significant pan-European presence, Menarini ranks fourth largest pharmaceutical team for delivering medical information to physicians. Adenuric® received marketing authorisation in the European Union on 21st April 2008. Its 80 mg and 120 mg tablets are indicated for the treatment of chronic hyperuricaemia for conditions in which urate deposition has already occurred (including a history, or presence of, tophus and/or gouty arthritis). In 2003, Teijin Pharma Limited, Tokyo who discovered febuxostat had granted Ipsen the exclusive development and marketing rights to Adenuric® in Europe.

**Dr. Alberto Aleotti**, Chairman and Chief Executive Officer of the Menarini Group said *"Research in new treatments for gout has been absent for nearly forty years, making it an orphan disease in some respects. We are therefore extremely proud that Ipsen has chosen Menarini as the ideal partner to substantially contribute to European patients' health with an innovative drug in this therapeutic area."*

**Jean-Luc Bélingard**, Chairman and Chief Executive Officer of Ipsen said : *"We are proud to bring to the medical community the first treatment alternative in decades in the treatment of hyperuricaemia in gout. It addresses a high unmet medical need in an environment where less than half the patients have been receiving appropriate lifestyle advice and / or urate lowering treatment[1]."* Jean-Luc Bélingard added: *"Adenuric® is the first product launch coming from our fruitful two-way collaboration with our long-standing and valuable partner, Teijin, across Europe and Japan. We are delighted to enter into this agreement with the Menarini Group, an excellent partner in terms of geographical coverage and quality of medical information. Adenuric® will also strengthen our primary care franchise in France through our co-promotion agreement."*

In its evaluation[2], the French *Haute Autorité de Santé* indicates that Adenuric® has demonstrated, in three clinical studies at 80 mg or at both 80 mg and 120 mg dosage, superiority over fixed allopurinol doses (300, 200 or 100 mg/day) in decreasing and maintaining uricaemia below the therapeutic objective of 360 µmol/l (6 mg/dl). Additionally, Adenuric® can be prescribed without dose adjustment to patients suffering from mild to moderate renal impairment and might be an alternative option for patients that are intolerant to allopurinol.

[1] Michael Doherty, Professor of Rheumatology at the University of Nottingham (UK) and Co-chair of the 2006 EULAR Task Force for the Recommendations on Diagnosis and Management of Gout

[2] Avis de la commission de transparence M04AA03 - ADENURIC - CT-6315

**About the agreement**
Under the terms of the agreement announced today, Ipsen grants Menarini exclusive licence rights to Adenuric® in the European Union, Russia and countries west of Russia for a total of 41 countries. In return, Ipsen will receive progressive payments of up to €132 million starting at the signature of the transaction and upon the achievement of certain launch and commercial milestones. Ipsen will also receive low-teens royalties on Menarini's net sales. In France, Adenuric® will be co-promoted by Menarini and Ipsen. Menarini expects the first European launches in early 2010. The product will be directly supplied to Menarini by Teijin. The agreement shall remain in force for the longer of a minimum of ten years or the expiry of last valid patent claim in all geographies (up to 2023).

**About gout**
Gout, a particularly painful type of arthritis, is the most frequent arthritis in men. It is caused by elevated levels of uric acid in the body : hyperuricaemia. In this condition, crystals of monosodium urate (MSU) are deposited on the articular cartilage of joints, tendons, and surrounding tissues. It is marked by transient painful attacks of acute arthritis initiated by crystallization of urates within and about the joints and can eventually lead to chronic gouty arthritis and the deposition of masses of urates in joints and other sites, sometimes creating tophi. In the absence of treatment, symptomatic chronic hyperuricemia may lead to a handicap and / or a noticeable degradation of quality of life, linked to articular and/or renal (lithiasis, nephropathy) impairment[1].

In 2006, European League Against Rheumatism (EULAR)[2] established the following principles:
- Optimal management requires both non-pharmacological and pharmacological treatment and needs to be tailored to the individual
- Urate lowering therapy to promote crystal dissolution and prevent crystal formation is achieved by maintaining the serum uric acid below the saturation point for monosodium urate (360 µmol/l or 6 mg/dl)

Epidemiology data on gout is scarce[3]. However, a 1999 study[4] estimated that prevalence of gout in the U.K. reached 1.4% with rates approaching 7% in men over the age of 65. This prevalence was confirmed by a another study[5] conducted from 2000 to 2005, in the U.K. and Germany. An observational study[6] took place in France in 1981 on 4,663 men employed by a Parisian public organisation, showed prevalence of 1.2% (0.4% in men aged 20-34; 1.1% on men aged 35-39; 2% on men aged 40-44).

**About Adenuric® (febuxostat)**

Febuxostat, an oral, once-daily medication, is a novel non-purine, selective inhibitor of xanthine oxidase studied for its effects on lowering levels of serum uric acid (sUA) in patients with gout.

In the APEX study[7] (n=1,072), the proportion of subjects whose last 3 serum urate levels were <6.0 mg/dl (357 µmol/l) (primary endpoint) was 0%, 48%, 65%, 69%, and 22% in the placebo, febuxostat 80 mg QD, febuxostat 120 mg QD, febuxostat 240 mg QD, and allopurinol 300/100 mg QD groups, respectively. Both,

[1] Avis de la commission de transparence M04AA03 - ADENURIC - CT-6315
[2] W. Zhang et al. EULAR evidence-based recommendations for gout. Part II: management. Report of a task force of the Eular Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). Ann of Rheum Dis 2006: 65:1312-1324
[3] Avis de la commission de transparence M04AA03 - ADENURIC - CT-6315
[4] Mikuls TR, Farrar JT, Bilker WB, et al. Gout epidemiology: results from the UK General Practice Research Database, 1990-1999. Ann Rheum Dis 2005;64:267-72.
[5] Annemans L et al. Gout in the UK and Germany: prevalence, comorbidities and management in clinical practice. Ann Rheum Dis 2008;67:960-966
[6] Zalokar J, Lellouch J, Claude JR. Goutte et uricémie dans une population de 4663 hommes jeunes actifs. Sem. Hôp. 1981 ;57 : 664-670
[7] CHMP ASSESSMENT REPORT FOR Adenuric Doc Ref : EMEA/258531/2008

febuxostat 80 mg QD and febuxostat 120 mg QD were statistically superior compared to the fixed dose of allopurinol 300 mg QD. (p<0.001 febuxostat 80mg and 120mg vs allopurinol 300/100mg).

In the FACT study[1] (n=762), the proportions of subjects whose last 3 serum urate levels were <6.0 mg/dl (primary endpoint) were 53% (febuxostat 80 mg QD), 62% (febuxostat 120 mg QD), and 21% (allopurinol 300 mg QD). The proportion was significantly higher in the febuxostat groups than in the allopurinol group (P<0.001). Both, febuxostat 80 mg QD and febuxostat 120 mg QD were statistically superior compared to the fixed 300 mg QD dose of allopurinol (p<0.001 febuxostat 80mg and 120mg vs allopurinol 300mg)

In the CONFIRMS study[2] (n=2,269 patients), efficacy of febuxostat was evaluated in gouty patients with the same profile as in the APEX and FACT studies, including patients suffering from mild (48% of the group) to moderate (18% of the group) renal impairment. Moderate renal impairment was defined by a creatinine clearance between 30 and 59 ml/mn. Mild renal impairment was defined by a creatinine clearance between 60 ml/mn et 89 ml/mn. In the renal impaired patient sub-group, the proportion of patients reaching the therapeutic objective (uriceamia < 360 µmol/l or < 6 mg/dl) was greater with febuxostat 40 mg (49.7%) and 80 mg (71.6%) than with allopurinol 300/200 mg (42.3%), p<0,05 febuxostat 40mg vs allopurinol, p<0.001 febuxostat 80mg vs allopurinol and febuxostat 40 mg.

The recommended oral dose of Adenuric® is 80 mg once daily. The therapeutic objective is to decrease and maintain serum uric acid below 360µmol/l (6 mg/dl). If serum uric acid is > 360 µmol/l (6 mg/dl) after 2-4 weeks, Adenuric® 120 mg once daily may be considered. Gout flare prophylaxis of at least 6 months is recommended at initiation of treatment with Adenuric®.

The most commonly reported adverse drug reactions[3] (investigator assessment) are liver function abnormalities (3.5%), diarrhoea (2.7%), headache (1.8%), nausea (1.7%), rash (1.5 %).

A numerically greater incidence of investigator-reported cardiovascular events was observed in the febuxostat total group compared to the allopurinol group in the pivotal Phase III (1.3 vs 0.3 events per 100 PYs) and long-term extension studies (1.4 vs 0.7 events per 100 PYs), although no statistically significant differences were found and no causal relationship with febuxostat was established. Identified risk factors among these patients were a medical history of atherosclerotic disease and/or myocardial infarction, or of congestive heart failure.

Febuxostat is licensed to Ipsen for Europe from Teijin Pharma Limited, Tokyo. In 2003, Ipsen entered into a Research and Development partnership with Teijin Pharma Limited, the core company of Teijin Group's pharmaceutical and home healthcare business. The Teijin group is a Japanese industrial conglomerate specialising in the businesses of synthetic fibres, films, plastics, trading and retail and information technology (IT) as well as pharmaceuticals and home healthcare. This partnership covers the development and subsequent commercialisation of four of Ipsen's products by Teijin Pharma in Japan and the development and marketing by Ipsen in Europe (i.e. European Union and Russia) of febuxostat, a product owned by Teijin Pharma and known as TMX-67.

**About Menarini**

Menarini is the first Italian Pharmaceutical Group in the world. Menarini employs nearly 13,000 people, with a strong presence throughout Europe, CIS, Africa and in South and Central America. The company has expertise in successfully developing, registering and delivering medical information for drug products in a broad range of therapeutic areas. including drug products generated by its Research and Development activities located in Florence, Rome, Pisa, Barcelona and Berlin. The Group's total revenue exceeds euro 2.6 billion.

[1] CHMP ASSESSMENT REPORT FOR Adenuric Doc Ref : EMEA/258531/2008

[2] Avis de la commission de transparence M04AA03 - ADENURIC - CT-6315

[3] CHMP ASSESSMENT REPORT FOR Adenuric Doc Ref : EMEA/258531/2008

**About Ipsen**
Ipsen is an innovation-driven global specialty pharmaceutical group with over 20 products on the market and a total worldwide staff of nearly 4,200. Its development strategy is based on a combination of specialty medicine, which is Ipsen's growth driver, in targeted therapeutic areas (oncology, endocrinology, neurology and haematology), and primary care products which contribute significantly to its research financing. The location of its four Research & Development centres (Paris, Boston, Barcelona, London) and its peptide and protein engineering platform give the Group a competitive edge in gaining access to leading university research teams and highly qualified personnel. More than 800 people in R&D are dedicated to the discovery and development of innovative drugs for patient care. This strategy is also supported by an active policy of partnerships. In 2008, Research and Development expenditure was about €183 million, close to 19% of consolidated sales, which amounted to €971 million while total revenues exceeded €1 billion. Ipsen's shares are traded on Segment A of Euronext Paris (stock code: IPN, ISIN code: FR0010259150). Ipsen's shares are eligible to the "Service de Règlement Différé" ("SRD") and the Group is part of the SBF 120 index. For more information on Ipsen, visit our website at www.ipsen.com.

**Ipsen 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. 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. Notably, future currency fluctuations may negatively impact the profitability of the Group and its ability to reach its objectives. Actual results may depart significantly from these targets given the occurrence of certain risks and uncertainties. The Group does not commit nor gives any guarantee that it will meet the targets mentioned above. Furthermore, the Research and Development process involves several stages each of which involve 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 favourable 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. 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 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.

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