

Press release

## **Ipsen's partner Roche confirms the promising efficacy profile of Taspoglutide**

- **Taspoglutide, when used alone or added to metformin significantly reduced HbA1c and body weight with low risk of hypoglycemia**
- **Taspoglutide shows comparable or greater reduction in HbA1c levels with a low risk of hypoglycemia versus exenatide, sitagliptin and insulin glargine**

**Paris (France), 26 June 2010** - Ipsen (Euronext: IPN; ADR: IPSEY) a global biopharmaceutical group, today announced that its partner Roche disclosed results of five Phase III 24-week studies for taspoglutide for type 2 diabetes at the American Diabetes Association's (ADA) 70<sup>th</sup> Annual Scientific Sessions. Taspoglutide, the first once weekly glucagon-like peptide-1 (GLP-1) analogue based on a human sequence, originating from Ipsen's research is developed by Roche. This compound is similar to the natural hormone GLP-1 which has a key role in blood sugar regulation.

Three head-to-head comparisons against exenatide, sitagliptin and insulin glargine found that treatment with taspoglutide showed comparable or greater reductions in HbA1c levels with a low risk of hypoglycemia, resulted in more patients reaching the ADA target for HbA1c of <7.0%, and produced clinically meaningful weight loss.

Two additional Phase III studies showed that taspoglutide, when used alone or added to metformin (the most common first-line treatment for type 2 diabetes), significantly reduced HbA1c and body weight with low risk of hypoglycemia. Further studies suggest that taspoglutide may help restore a normal insulin response as well as potentially preserving insulin-producing beta cells and subsequently protect them from cell death.

In the studies, taspoglutide was administered once a week with a pre-filled, disposable syringe with a small-gauge needle.

The most common adverse events seen with taspoglutide based on the 24-week data are related to gastrointestinal tolerability and injection site reactions. Nausea and vomiting were of mild to moderate intensity, generally occurred early in treatment on the day of injection and predominantly as a single episode. Roche also recently announced the implementation of a risk mitigation plan in the Phase III programme designed to identify patients at potential risk of hypersensitivity reactions. While the occurrence of hypersensitivity reactions reported as related to taspoglutide is higher than expected for the study population in the Phase III trials, the incidence remains uncommon (< 1%).

**Jean-Luc Bélingard, Chairman and Chief Executive Officer of the Ipsen Group**, stated: *"These 5 phase III clinical trials have clearly demonstrated the marked and reproducible efficacy profile of taspoglutide in blood glucose control and body weight loss. The T-emerge programme provides the medical community with extensive data on the competitive positioning of this promising compound in the treatment of type 2 diabetes. We are confident that the ongoing clinical programme will further establish taspoglutide as a potential best-in-class with the added convenience of a once-a-week injection."*

### About the T-emerge Programme

The T-emerge Phase III clinical trial programme is designed as multicenter, multi-country, randomized, controlled (active or placebo), double-blind and open studies. Over 6,000 patients have been enrolled in the eight studies that comprise the T-emerge programme. Studies include two parallel taspoglutide arms including 10 mg once weekly and 10 mg once weekly titrated up to 20 mg once weekly after four weeks. Four of the eight studies have active comparators, including exenatide, sitagliptin, insulin glargine and pioglitazone.

Unless noted in the tables below, the T-emerge studies presented at ADA included two parallel taspoglutide arms with 10 mg and 20 mg doses (starting at 10 mg and titrated up after four weeks). Pre-specified analyses were conducted after 24 weeks of treatment. Measures refer to changes from baseline. All T-emerge Phase III studies continue for at least 52 weeks and some for up to three years.

### Results of five Phase III 24-week T-Emerge studies presented at ADA

#### T-emerge 1

Number: **399-PP**: "Taspoglutide, a Once-Weekly Human GLP-1 Analog, as Monotherapy Significantly Lowers A1c and Body Weight in Patients with Type 2 Diabetes (T2D)"

This study evaluated the efficacy and safety profile of once-weekly taspoglutide used alone in treatment-naïve patients whose diabetes was uncontrolled after diet and exercise. 373 patients with HbA1c  $\geq 6.5$  and  $\leq 10.0\%$  were randomized into three groups and given either taspoglutide 10 mg, taspoglutide 20 mg, or placebo.

<b>Efficacy summary at 24-weeks</b>	<b>Taspoglutide 10 mg (N=112)</b>	<b>Taspoglutide 20 mg (N=127)</b>	<b>Placebo (N=115)</b>
Baseline HbA1c	7.5%	7.7%	7.6%
Primary endpoint: Average HbA1c change from baseline (p<0.001)	-1.01%	-1.18%	-0.09%
% of patients who met target HbA1c of <7%*	65%	71%	20%
Baseline weight (kg)	88 kg	85 kg	87 kg
Average body weight change from baseline (p<0.05)	-1.5 kg	-2.3 kg	-1.2 kg

<b>Most common adverse events at 24-weeks</b>	<b>Taspoglutide 10 mg (N=116)</b>	<b>Taspoglutide 20 mg (N=129)</b>	<b>Placebo (N=123)</b>
Nausea	25.9% (30)	31% (40)	4.1% (5)
Vomiting	17.2% (20)	17.8% (23)	-
Injection site reactions	28.5% (33)	27.1% (35)	1.6% (2)
Hypoglycemia Reported	5.2% (6)	3.9% (5)	0.8% (1)

Most common adverse events at 24-weeks	Taspoglutide 10 mg (N=116)	Taspoglutide 20 mg (N=129)	Placebo (N=123)
Confirmed (<55 mg/dL)	-	0.8% (1)	-
% discontinuation due to GI adverse events	3.4% (4)	4.7% (6)	-

\*excluding patients who entered the study with HbA1c <7.0% at baseline

### **T-emerge 2**

Number: **62-OR**: “Superior Glycemic Control with Taspoglutide, a Once-Weekly Human GLP-1 Analog, Compared With Twice Daily Exenatide in Type 2 Diabetes (T2DM) Inadequately Controlled on Oral Agents: The T-emerge 2 Trial” Saturday, June 26, 8:00 am EST

The study compared the efficacy and safety profile of once-weekly taspoglutide to twice-daily exenatide (10 mcg) in patients inadequately controlled on metformin +/- thiazolidinedione. 1,189 patients with HbA1c ≥ 7.0% and ≤10% were randomized into three groups and given taspoglutide 10 mg, taspoglutide 20 mg, or exenatide, in addition to their current regimens.

Efficacy summary at 24-weeks	Taspoglutide 10 mg + metformin +/- thiazolidinedione (N=399)	Taspoglutide 20 mg + metformin +/- thiazolidinedione (N=398)	Exenatide 10 mcg + metformin +/- thiazolidinedione (N=392)
Baseline HbA1c	8.1%	8.1%	8.1%
Primary endpoint: Average HbA1c change from baseline (p<0.001)	-1.24%	-1.31%	-0.98%
% of patients who met target HbA1c of <7%*	62%	63%	46%
Baseline weight (kg)	95 kg	93 kg	95 kg
Average body weight change from baseline (p<0.05)	-1.6 kg	-2.3 kg	-2.3 kg

Most common adverse events at 24-weeks	Taspoglutide 10 mg (N=394)	Taspoglutide 20 mg (N=394)	Exenatide 10 mcg (N=385)
Nausea	40.1% (158)	47.2% (186)	29.9% (115)
Vomiting	20.8% (82)	23.6% (93)	10.9% (42)
Injection site reactions	24.7% (97)	31.7% (125)	1.4% (5)
Hypoglycemia Reported Confirmed (<55 mg/dL)	8.6% (34) 0.5% (3)	9.9% (39) 2.3% (5)	9.9% (38) 1.8% (3)
% discontinuation due to GI adverse events (p<0.001)	4.1% (16)	7.6% (30)	6.5% (25)

T-emerge 2 subset analysis, number: **719-P**: A meal tolerance test was conducted in a subset of 148 patients, randomized into three groups and given either taspoglutide 10 mg, taspoglutide 20 mg or exenatide. Post-meal glucagon and post-meal glucose were measured at baseline and week 24. Patients in all three groups experienced a similar average reduction in post-meal glucagon (-4.5 for taspoglutide 10 mg, -5.0 for taspoglutide 20 mg, -4.3 for exenatide) and similar improvement in post-meal glucose (-32.1, -35.3, -31.7, respectively). Significantly increased insulin was observed in patients who received taspoglutide 10 mg (23.1) and taspoglutide 20 mg (7.3), while increase in insulin was not significant for exenatide (-10.1). Results reflect 95% confidence interval.

**T-emerge 2: 52 week data**

Data from the 52-weeks trials from T-emerge 2 and other T-emerge studies are expected soon and will be published at a future scientific congress. Roche believes that these 52-week data will help us better inform the safety and efficacy profile of taspoglutide in diabetes.

**T-emerge 4**

Number: **58-OR**: “Once-weekly Taspoglutide, a Human GLP-1 Analog, is Superior to Sitagliptin in Improving Glycemic Control and Weight Loss in Patients with Type 2 Diabetes (T2D): Results from the T-emerge 4 Trial,” Saturday, June 26, 8:00 am EST

This study compared the efficacy and safety profile of once-weekly taspoglutide to daily oral sitagliptin in patients whose diabetes was inadequately controlled on metformin. 666 patients with HbA1c  $\geq 7.0\%$  and  $\leq 10\%$  were randomized into four groups and given either taspoglutide 10mg, taspoglutide 20mg, sitagliptin, or placebo, in addition to their current regimens.

<b>Efficacy summary at 24-weeks</b>	<b>Taspoglutide 10 mg + metformin (N=182)</b>	<b>Taspoglutide 20 mg + metformin (N=187)</b>	<b>Sitagliptin 100 mg + metformin (N=177)</b>	<b>Placebo (N=90)</b>
Baseline HbA1c	8.0%	8.0%	7.9%	8.0%
Primary endpoint: Average HbA1c change from baseline (p<0.001)	-1.23%	-1.30%	-0.89%	-0.10%
% of patients who met target HbA1c < 7% (p<.001)	64%	65%	50%	14%
Baseline weight (kg)	94 kg	92 kg	93 kg	91 kg
Average body weight change from baseline	-1.8 kg (p<0.01 vs. placebo) (p<0.05 vs. sitagliptin)	-2.6 kg (p<0.001 vs. placebo and vs. sitagliptin)	-0.9 kg	-0.5 kg

<b>Most common adverse events at 24-weeks</b>	<b>Taspoglutide 10 mg (N=187)</b>	<b>Taspoglutide 20 mg (N=192)</b>	<b>Sitagliptin 100 mg (N=184)</b>	<b>Placebo (N=93)</b>
Nausea	43.9% (82)	42.2% (81)	10.3% (19)	8.6% (8)

Most common adverse events at 24-weeks	Taspoglutide 10 mg (N=187)	Taspoglutide 20 mg (N=192)	Sitagliptin 100 mg (N=184)	Placebo (N=93)
Vomiting	21.4% (40)	28.1% (54)	4.3% (8)	1.1% (1)
Injection site reactions	21.9% (41)	50.4% (77)	9.2% (17)	7.7% (7)
Hypoglycemia Reported Confirmed ( $<55$ mg/dL)	7% (13) -	4.7% (9) 0.5% (1)	5.4% (10) 1.1% (2)	1.1% (1) -
% discontinuation due to GI adverse events ( $p<0.001$ )	12.3% (23)	8.3% (16)	0.5% (1)	-

### **T-emerge 5**

Number: **60-OR**: “Taspoglutide, a Once-Weekly Human GLP-1 Analog, Provides Comparable Glycemic Control to Insulin Glargine, with Superior Weight Loss and Less Hypoglycemia in Type 2 Diabetes (T2D): A Phase III, Open-Label Trial,” Saturday, June 26, 8:00 am EST

The study compared the efficacy and safety profile of once-weekly taspoglutide to daily insulin glargine in patients whose diabetes was inadequately controlled on metformin + sulfonylurea. 1,049 patients with HbA1c  $\geq 7.0\%$  and  $\leq 10.0\%$  were randomized into three groups and given either taspoglutide 10 mg, taspoglutide 20 mg, or insulin glargine in addition to their current regimens. Sulfonylurea was withdrawn five days prior to randomization.

Efficacy summary at 24-weeks	Taspoglutide 10 mg + metformin (N=361)	Taspoglutide 20 mg + metformin (N=348)	Insulin glargine + metformin (N=319)
Baseline HbA1c	8.2%	8.3%	8.3%
Primary endpoint: Average HbA1c change from baseline ( $p<0.001$ )	-0.77%	-0.98%	-0.84%
% of patients who met target HbA1c of $< 7\%$	34%	41%	28%
Baseline weight (kg)	90 kg	91 kg	91 kg
Average body weight change from baseline ( $p<0.001$ )	-3.3 kg	-4.1 kg	-0.4 kg

Most common adverse events at 24-weeks	Taspoglutide 10 mg (N=364)	Taspoglutide 20 mg (N=351)	Insulin glargine (N=322)
Nausea	39.3% (143)	45.3% (159)	1.9% (6)
Vomiting	19.8% (72)	22.8% (80)	1.2% (4)
Injection site reactions	17.8% (65)	20.5% (72)	0.3% (1)
Hypoglycemia Reported Confirmed	4.9% (18) 0.3% (1)	6.0% (21) 0.9% (3)	17.4% (56) 3.1% (10)

Most common adverse events at 24-weeks	Taspoglutide 10 mg (N=364)	Taspoglutide 20 mg (N=351)	Insulin glargine (N=322)
(<55 mg/dL)			
% discontinuation due to GI adverse events	4.4% (16)	6.6% (23)	-

### **T-emerge 7**

Number: **585-P**: “Once-Weekly Taspoglutide, a Human GLP-1 Analog, is Superior to Placebo in Improving Glycemic Control and Body Weight Loss in Obese Patients with Type 2 Diabetes (T2D) Inadequately Controlled with Metformin Monotherapy”

This study evaluated efficacy and safety profile of once-weekly 20 mg taspoglutide used alone in obese patients whose diabetes was uncontrolled on metformin alone. 305 obese patients with HbA1c  $\geq$  6.5% and  $\leq$  9.5% were randomized into two groups and given taspoglutide 20 mg or placebo in addition to their current regimens.

Efficacy summary at 24-weeks	Taspoglutide 20mg + metformin (N=149)	Placebo + metformin (N=143)
Baseline HbA1c	7.5%	7.5%
Primary endpoint: Average HbA1c change from baseline (p<0.001)	-0.81%	-0.09%
% of patients who met target HbA1c of < 7% *	53%	21%
Baseline weight (kg)	104 kg	101 kg
Average body weight change from baseline (p <0.01)	-3.2 kg	-1.9 kg

Most common adverse events at 24-weeks	Taspoglutide 20mg + metformin (N=154)	Placebo + metformin (N=150)
Nausea	35.1% (54)	5.3% (8)
Vomiting	24% (37)	3.3% (5)
Injection site AEs	50.6% (78)	8.1% (12)
Hypoglycemia Confirmed ( $\leq$ 55 mg/dL)	9.7% (15)	2.7% (4)
% discontinuation due to GI adverse events	3.9% (6)	-

\*excluding patients who entered the study with HbA1c <7.0% at baseline

Full efficacy and safety data for each study will be presented at ADA.

### **Additional taspoglutide posters to be presented at the meeting:**

“Effect of Taspoglutide, a Human GLP-1 Analog, on Insulin Secretion in Patients with Type 2 Diabetes (T2D),” Poster, Monday, June 28 12 noon, number: **588-P**

“Taspoglutide, a Novel Human Once-Weekly GLP-1 Analog, Improves B-Cell Survival In ZDF Rats,” Poster, Monday, June 28 12 noon, number **544-P**

### **About Taspoglutide (R1583)**

Taspoglutide was selected from a family of human once-weekly long-acting glucagon-like peptide-1 (GLP-1) analogues with structural modifications which confer intrinsic controlled release properties. Ipsen is the originator of the concept of matrix free sustained release formulation applied to therapeutic peptides and proteins. Taspoglutide is being developed, by Roche, as a novel and innovative treatment for patients with type 2 diabetes mellitus, the fourth leading cause of death in most developed countries. The structure of the molecule is similar to that of the natural human hormone GLP-1, and has the potential for intervals of up to two weeks in between administration without the use of a matrix.

#### **About the agreement**

Roche exercised its licensing option for taspoglutide from Ipsen in 2006 and acquired exclusive worldwide rights to develop and market taspoglutide, except in Japan where these rights are shared with Teijin and in France where Ipsen has elected to retain co-marketing rights.

#### **About Ipsen**

Ipsen is a global biopharmaceutical group with total sales in excess of 1 billion euros in 2009, and total worldwide staff of more than 4,400. Its strategy is based on fast growing specialty care drugs in oncology, endocrinology, neurology and hematology, and primary care drugs, which significantly contribute to research financing. This strategy is also supported by an active policy of partnerships. Ipsen's specific Research & Development (R&D) centers and peptide & protein engineering platform give the Group a competitive edge. Nearly 900 people are dedicated to the discovery and development of innovative drugs for patient care. Nearly 900 people are dedicated to the discovery and development of innovative drugs for patient care. In 2009, R&D spend reached close to €200 million, representing more than 19% of total Group sales. 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. Ipsen has implemented a Sponsored Level I American Depositary Receipt (ADR) program, which trade on the over-the-counter market in the United States under the symbol IPSEY. For more information on Ipsen, visit our website at [www.ipsen.com](http://www.ipsen.com).

#### **Ipsen's 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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