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# Taspoglutide

Prop INN

*GLP-1 Analogue*
*Treatment of Diabetes*

BIM-51077
ITM-077
R-1583

**L-Histidyl-2-methylalanyl-L-glutamyl-glycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-glutamyl-glycyl-L-glutaminyl-L-alanyl-L-alanyl-L-lysyl-L-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-lysyl-2-methylalanyl-L-argininamide**

InChI=1/C152H232N40O45/c1-20-78(10)119(145(233)168-81(13)125(213)174-105(63-87-66-162-92-39-28-27-38-90(87)92)134(222)-176-101(59-75(4)5)135(223)187-117(76(6)7)143(231)173-95(41-30-32-56-154)142(230)192-152(18,19)148(236)184-93(122(157)210)-42-33-57-161-150(158)159)189-136(224)103(60-84-34-23-21-24-35-84)177-131(219)99(50-54-115(206)207)172-130(218)94(40-29-31-55-153)170-124(212)80(12)166-123(211)79(11)167-129(217)98(47-51-110(156)199)169-111(200)68-163-127(215)96(48-52-113(202)203)171-132(220)100(58-74(2)3)175-133(221)102(62-86-43-45-89(198)46-44-86)178-139(227)107(70-193)181-141(229)109(72-195)182-144(232)118(77(8)9)188-138(226)106(65-116(208)209)179-140(228)108(71-194)183-147(235)121(83(15)197)190-137(225)104(61-85-36-25-22-26-37-85)180-146(234)120(82(14)196)186-112(201)69-164-128(216)97(49-53-114(204)205)185-149(237)151(16,17)191-126-(214)91(155)64-88-67-160-73-165-88/h21-28,34-39,43-46,66-67,73-83,91,93-109,117-121,162,193-198H,20,29-33,40-42,47-65,68-72,153-155H2,1-19H3,(H2,156,199)(H2,157,210)(H,160,165)(H,163,215)(H,164,216)(H,166,211)(H,167,217)(H,168,233)(H,169,200)-(H,170,212)(H,171,220)(H,172,218)(H,173,231)(H,174,213)(H,175,221)(H,176,222)(H,177,219)(H,178,227)(H,179,228)(H,180,234)(H,181,229)(H,182,232)(H,183,235)(H,184,236)(H,185,237)(H,186,201)(H,187,223)(H,188,226)(H,189,224)(H,190,225)(H,191,214)(H,192,230)(H,202,203)(H,204,205)(H,206,207)(H,208,209)(H4,158,159,161)/t78-,79-,80-,81-,82?,83?,91-,93-,94-,95-,96-,97-,98-,99-,100-,101-,102-,103-,104-,105-,106-,107-,108-,109-,117-,118-,119-,120-,121-/m0/s1

$C_{152}H_{232}N_{40}O_{45}$
Mol wt: 3339.7095

CAS: 275371-94-3

EN: 305174

**Abstract**

Incretin agonists and analogues are receiving increasing attention as potential antidiabetic agents due to their ability to stimulate insulin secretion only during hyperglycemic states. Exploitation of the incretin effect reduces the risk of rebound hypoglycemia that accompanies many antidiabetic treatments. Taspoglutide (R-1583, BIM-51077, ITM-077) is a long-acting glucagon-like peptide 1 (GLP-1) analogue that shows promise for the treatment of type 2 diabetes. In addition to having enhanced resistance to enzymatic degradation by the protease dipeptidyl peptidase 4 (DPP4), clinical studies have shown that taspoglutide increases insulin levels and lowers glycemia. Phase II trials have also demonstrated that weekly administration of a slow-release formulation was associated with enhanced glycemic control, reduced body weight and improved β-cell function. Taspoglutide is generally well tolerated, with mild gastrointestinal symptoms being the most commonly reported adverse events. Several phase III clinical trials of this novel GLP-1 analogue are under way.

## Background

Type 2 diabetes is a syndrome characterized by an impairment of the homeostatic control of glucose metabolism leading to hyperglycemia. It is associated with several metabolic abnormalities, including insulin resistance, defects in insulin secretion and action, as well as increased endogenous production of glucose (1). Type 2 diabetes, which accounts for 90-95% of all cases of diabetes, is a rampant epidemic in developed countries. In the United States, the number of people diagnosed with diabetes has more than doubled in the last 15 years, reaching 17.9 million (about 8% of the population) in 2007 (2). The multiple acute and chronic complications that accompany this disease increase enormously its economic burden. Thus, there is great interest in developing new antidiabetic drugs that effectively and safely regulate glucose metabolism, especially during the onset of the disease.

Recent advances in the understanding of the pathogenesis of type 2 diabetes have revealed that metabolic mediators other than insulin have a pivotal role in the

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development of this disorder. Incretins, peptide hormones that are produced postprandially in the gastrointestinal tract and stimulate insulin release (3), have special relevance. Two incretins have been identified: glucagon-like peptide 1 (GLP-1), secreted by L-cells in the ileum, and glucose-dependent insulinotropic peptide (GIP), secreted by enteroendocrine K-cells in the duodenum. Both are released into the circulation as active hormones within minutes in response to food consumption and are rapidly inactivated by the enzyme dipeptidyl peptidase 4 (DPP4), a ubiquitous serine protease (4). Activation of incretin receptors on β-cells acutely enhances glucose-dependent exocytosis of insulin. GLP-1 also lowers glycemia through inhibition of glucagon secretion, deceleration of gastric emptying, inhibition of food intake and enhanced glucose disposal in peripheral tissues. Long-term effects include stimulation of insulin synthesis, enhancement of β-cell proliferation and increased resistance to apoptosis. Studies have demonstrated that the incretin effect accounts for two-thirds of the insulin secretory response in subjects with normal glucose tolerance, but only for less than one-fifth of the insulin response in patients with type 2 diabetes (5). This impaired postprandial incretin effect in patients with type 2 diabetes is caused at least in part by a decreased secretion of GLP-1, but not GIP (6). Therefore, an impairment of the incretin response may contribute to dysregulation of insulin and glucagon secretion, particularly during the postprandial period, leading to hyperglycemia.

Due to insulin's dominant effect on glucose metabolism, insulin secretagogues, insulin sensitizers and insulin itself are effective antidiabetic agents. However, they may be associated with weight gain and/or hypoglycemia, as well as toxicity in the case of sulfonylureas and thiazolidinediones (7). In addition, their efficacy diminishes with the progression of type 2 diabetes. For these reasons, therapies that could amplify insulin secretion without causing hypoglycemia and weight gain are highly desirable.

In accordance with its effects on glucose metabolism, GLP-1 infusion has been proven to normalize glycemic control in patients with type 2 diabetes (8). Intravenous infusion of GLP-1 normalizes β-cell responsiveness to glucose, restores insulin responses in patients with type 2 diabetes and modulates glucagon levels. In addition, continuous infusion of GLP-1 reduces diurnal glycemia to near-normal levels (9). Unfortunately, GLP-1 administration is not a feasible treatment due to its rapid inactivation by DPP4 and the impracticality of continuous infusion. Although the half-life of GLP-1 can be indirectly increased by the use of DPP4 inhibitors, pharmacological strategies have been focusing on modifying native GLP-1 to make it more resistant to proteolysis. Here we review the current data on the pharmacology, metabolism, efficacy and safety of taspoglutide (R-1583, BIM-51077, ITM-077), a long-acting human GLP-1 analogue with increased resistance to proteolytic cleavage.

## Preclinical Pharmacology

The efficacy of taspoglutide as an insulin secretagogue was initially demonstrated in vitro using static glucose incubation assays in cultured rat islets. Taspoglutide (10-100 nM) significantly induced insulin secretion in the presence of 10 mM glucose, with a binding $K_i$ value of 1 nM. In in vitro perfusion assays, taspoglutide stimulated insulin secretion in the presence of 10 mM glucose, but not at lower glucose concentrations. Using an in vivo system of cyclic glucose perfusion in pancreas from Zucker diabetic fatty (ZDF) rats, taspoglutide (100 pM) also significantly increased insulin secretion during the second perfusion cycle with 15 mM glucose (10).

The in vivo insulinotropic action of taspoglutide was confirmed in subsequent animal studies. The GLP-1 analogue produced a dose-dependent reduction in glycemia and body weight gain in ZDF rats. Likely due to its longer circulating half-life, taspoglutide showed greater glucose-dependent secretagogue activity ($ED_{50}$ = 16.0 pmol/kg) than recombinant human GLP-1 ($ED_{50}$ = 121 pmol/kg) (11).

To assess the efficacy of taspoglutide in preventing the development of diabetes, male prediabetic ZDF rats were administered the analogue or saline for 28 days via osmotic minipumps implanted i.p. Rats receiving 15 pmol/kg/min of taspoglutide experienced a significant decrease in food intake relative to controls. In addition, significant reductions in glucose levels, plasma fructosamine (–36.6%), blood glycated hemoglobin (HbA1c; –22.9%) and water consumption (a surrogate marker for glucosuria) were reported. Moreover, at the end of the 28-day period, animals exhibited improved tolerance to oral glucose challenge. No preventive effects were observed with lower doses of taspoglutide (12).

## Pharmacokinetics and Metabolism

A pharmacokinetic study of taspoglutide was carried out in male beagle dogs and compared i.v. bolus administration of the peptide in saline solution (3 mg/kg) with s.c. injection of a slow-release formulation (SRF; liquid form containing Zn chloride) of 15 mg/dog. A total of 6 dogs received both formulations 7 days apart. Blood samples were collected during a period of 3.5 h (i.v. bolus) or after 26 days (SRF). The authors reported that following i.v. bolus, the half-life of taspoglutide was 0.26 ± 0.09 h, plasma clearance was 0.52 ± 0.11 l/kg.h and volume of distribution was 1.52 ± 0.37 l. In contrast, following administration of the SRF formulation, taspoglutide plasma levels were detected from 5 min postadministration up to 26 days. A mean peak plasma level of 5.65 ± 2.61 ng/ml was observed at 3 h, and plasma levels decreased gradually over time. Taspoglutide in SRF form showed an elimination half-life of 6.8 ± 2.4 days, an AUC of 41.55 ±10.26 ng.day/ml and an absolute bioavailability of 74.5 ± 27.7%. The in vivo input profile indicated that taspoglutide is gradually absorbed, achieving 7.2 ± 4.9% and 74.5 ± 27.7% absorption, respectively, at 1 and 26 days (13).

The sustained-release profile shown by SRF taspoglutide in this pioneering animal study warranted subsequent analysis in humans.

The first human pharmacokinetic assessment of taspoglutide was conducted as part of a randomized, double-blind, parallel-group clinical study. Thirty-five subjects with type 2 diabetes under metformin treatment were administered a continuous s.c. infusion of either 104, 200, 400 or 800 μg/day of taspoglutide for 7 days. Mean steady-state plasma concentrations of taspoglutide ranged from 0.053 ± 0.017 ng/ml (104 μg/day) to 0.372 ± 0.111 ng/ml (800 μg/day) and increased in a linear manner. Along the same line, the $AUC_{0\rightarrow\infty}$ increased with escalating doses of taspoglutide (104 μg: 9.59 ± 2.67 ng.h/ml; 200 μg: 18.31 ± 4.10 ng.h/ml; 400 μg: 31.17 ± 5.98 ng.h/ml; 800 μg: 64.42 ± 18.27 ng.h/ml), further evidencing that taspoglutide had a linear pharmacokinetic profile when given continuously for 7 days (14). A similar study evaluated the pharmacokinetic behavior of taspoglutide when given over a longer period of time, and included 12 patients with type 2 diabetes on metformin receiving continuous s.c. infusion of taspoglutide for 28 days (400 μg/day). Pharmacokinetic assessments were performed predose (day –1) and on days 0, 6 and 27. The authors concluded that taspoglutide plasma levels were constant throughout the study, with a steady state of 0.233 ± 0.054 ng/ml (15).

The pharmacokinetic and pharmacodynamic profiles of a single injection of a sustained-release formulation of taspoglutide have also been evaluated. A total of 48 subjects with type 2 diabetes were enrolled in three sequential cohorts. In each cohort, 12 subjects were randomized to a single s.c. injection of taspoglutide (1, 8 or 30 mg in a sustained-release formulation) and 4 subjects to placebo. Following administration of 8 and 30 mg taspoglutide, plasma exposures were maintained for 14 days in nearly all subjects. Mean $C_{max}$ was reached within 24 h postdose for all doses, with the maximum exposure achieved, as expected, with the 30-mg dose. The AUCs increased in a dose-dependent manner, with $AUC_{0\text{-}14\ days}$ of 6.40 ± 1.01, 14.7 ± 5.31 and 54.6 ± 33.5 ng.h/ml, respectively, in the 1-, 8- and 30-mg groups. Mean $C_{max}$ was 0.0547 ± 0.0293, 0.1180 ± 0.0752 and 0.372 ± 0.225 ng/ml, respectively, in the 1-, 8- and 30-mg groups. These results indicated that taspoglutide may be suitable for weekly or biweekly administration (16).

## Safety

Safety analyses of taspoglutide were performed concurrently with pharmacokinetic and efficacy evaluations during clinical studies. In a double-blind study, 35 subjects with type 2 diabetes under metformin treatment were randomized to a continuous s.c. infusion of 104, 200, 400 or 800 μg/day of taspoglutide for 7 days. Treatment with taspoglutide was well tolerated overall. However, an increased incidence of gastrointestinal events (n = 14) was observed in subjects receiving 800 μg/day (14). In a similar clinical study assessing continuous s.c. infusion of taspoglutide (400 μg/day) for 28 days, 9 of 12 patients with type 2 diabetes receiving the GLP-1 analogue presented gastrointestinal side effects. All of these events occurred during the first 24 h of treatment and resolved spontaneously within 3 days (15).

A more comprehensive study evaluating the safety and tolerability of increasing doses of taspoglutide was conducted recently. Patients inadequately controlled by metformin received either placebo or 20 mg of taspoglutide s.c. weekly for 4 weeks, followed by either maintenance at 20 mg (20/20), or titration up to 30 mg (20/30) or 40 mg (20/40) weekly with matched placebo for an additional 4 weeks. Subjects were followed for 4 weeks after the last dose. The study included 133 patients who were randomized to the aforementioned groups. The overall incidence of adverse events was 38% in the placebo arm and 66%, 73% and 63%, respectively, in patients in the 20/20, 20/30 and 20/40 treatment arms. The most common event was nausea, which was transient and mild to moderate. It appeared early during therapy and resolved without treatment in most cases. No patients withdrew due to nausea. Eighty-eight percent of randomized subjects completed the trial, with 1 withdrawal in the placebo arm, 3 in the 20/20 arm and 6 each in the 20/30 and 20/40 treatment groups. Only 7 withdrawals (including the placebo) were due to adverse events. The proportion of patients withdrawn due to gastrointestinal events was 6% (2 subjects) in the 20/30 arm and 3% (1 subject) in the 20/40 arm. Two serious adverse events were reported: cardiac arrhythmia in a patient given placebo and a possible recurrence of prostate cancer in an active arm. The latter was judged by the investigators to be unrelated to taspoglutide administration. There were no clinically significant ECG or laboratory abnormalities. It was concluded from the study that taspoglutide when administered weekly at the mentioned escalating doses was safe and well tolerated. Indeed, dose escalation was not associated with any deterioration of the tolerability profile (17). A clinical study evaluating single doses of taspoglutide (1, 8 or 30 mg) in patients with type 2 diabetes inadequately controlled with metformin also found that the most common adverse events consisted predominantly of transient gastrointestinal symptoms (16).

## Clinical Studies

The first assessment of the efficacy of taspoglutide as an antidiabetic drug in humans was conducted in a randomized, double-blind, parallel-group study that investigated the dose–response relationship of four different taspoglutide doses in comparison to placebo. Fifty-one patients with type 2 diabetes (40 males; age = 55 ± 7.5 years; BMI = 29.3 ± 3.5 $kg/m^2$) under metformin treatment were randomized to a continuous s.c. infusion of 104, 200, 400 or 800 μg/day of taspoglutide (35 patients) or placebo over 7 days. Treatment with taspoglutide significantly reduced mean 24-h blood glucose AUC, with the most pronounced changes in the 800 μg/day dose group (–87.4 ± 7.8 h.mmol/l vs. –35.3 ± 5.2 h.mmol/l on place-

bo). In addition, taspoglutide treatment was associated with an increase in 24-h insulin AUC and reductions in glucagon levels. In summary, taspoglutide administered over 7 days led to notable decreases in blood glucose and glucagon concentration, as well as increases in insulin levels (14).

Another randomized, double-blind, parallel-group clinical study investigated whether taspoglutide was also effective over a longer treatment period. In this case, taspoglutide was administered for 28 days. Eighteen patients with type 2 diabetes (12 males; age = 56 ± 1.5 years; BMI = 29.7 ± 0.6 kg/m$^2$) on treatment with metformin were randomized to adjunctive treatment with continuous s.c. infusion of taspoglutide (400 μg/day; 12 patients) or placebo. Taspoglutide markedly improved the 24-h blood glucose profiles on the first day of treatment. Of note, this effect was sustained over the entire treatment period. Reductions from baseline values with taspoglutide were significantly greater than with placebo for 24-h blood glucose AUC (day 27: –56.79 ± 5.08 h.mmol/l vs. –13.57 ± 7.21 h.mmol/l) and fasting blood glucose concentrations (day 28: –2.71 ± 0.21 mmol/l vs. –0.95 ± 0.30 mmol/l). There was also a trend for lower HbA1c (–1.14 ± 0.1% vs. –0.8 ± 0.14%) and reduced body weight (–1.9 ± 0.5 kg vs. –1.1 ± 0.5 kg). This study indicated that taspoglutide administered to patients with type 2 diabetes over 28 days achieved a marked and sustained improvement in glycemic control (15).

Single doses of taspoglutide have also been shown to be effective. Forty-eight subjects with type 2 diabetes (33 males; age = 56 ± 7 years; BMI = 30.4 ± 3.0 kg/m²) inadequately controlled with metformin (> 2 g/day) were enrolled in three sequential cohorts. In each cohort, 12 subjects were randomized to a single s.c. injection of taspoglutide at doses of 1, 8 or 30 mg. In comparison to placebo, a single dose of 30 mg taspoglutide significantly reduced 24-h blood glucose AUC for up to 14 days (–65.1 h.mmol/l), with decreases in both fasting and postprandial blood glucose concentrations. In addition, subjects receiving the 30-mg dose experienced a progressive weight loss (16).

A recent phase II study provided further evidence for the efficacy of taspoglutide when administered weekly. In this study, diabetic patients inadequately controlled with metformin received either placebo or an s.c. injection of 20 mg taspoglutide weekly for 4 weeks, followed by either maintenance dosing at 20 mg (20/20), or titration up to 30 mg (20/30) or 40 mg (20/40) weekly with matched placebo for an additional 4 weeks. Subjects were then followed for 4 weeks after the last dose. The study included 133 patients (age = 57 ± 9 years; BMI = 32.4 ± 5.4 kg/m²; HbA1c = 7.9 ± 0.7%; duration of diabetes = 7 ± 5 years) who were equally distributed to the four arms. Despite the short treatment duration, significant improvements in glycemic control were observed in all active groups. The changes in FPG levels were –2.3, –1.6 and –2.2 mmol/l, respectively, in the 20/20, 20/30 and 20/40 versus –0.6 mmol/l in the placebo group. At the end of treatment, the percentage of patients reaching HbA1c of 7% or less was 72% (20/20 group), 53% (20/30 group) and 70% (20/40 group) versus 19% on placebo (17).

Other recent phase II trials have aimed to evaluate the efficacy of a slow-release taspoglutide formulation in patients with type 2 diabetes not well controlled by metformin (> 1.5 g/day). Three hundred and six subjects (age = 55 ± 8 years; BMI = 32.7 ± 5.0 kg/m²; HbA1c = 7.9 ± 0.7 %; duration of diabetes = 5 ± 5 years) were randomized to 8 weeks of treatment with placebo or taspoglutide at 5, 10 or 20 mg weekly (QW) or 10 and 20 mg once every 2 weeks (Q2W) and followed for 4 additional weeks. The investigators found significant reductions in HbA1c after 8 weeks of treatment: –1.0 ± 0.1% (5 mg QW), –1.2 ± 0.1% (10 mg QW), –1.2 ± 0.1% (20 mg QW), –1.0 ± 0.1% (10 mg Q2W) and –1.0 ± 0.1% (20 mg Q2W), compared to placebo (–0.2 ± 0.1%). The proportion of patients reaching a target HbA1c of 7% or less was 59% (5 mg QW), 79% (10 mg QW), 81% (20 mg QW), 44% (10 mg Q2W) and 63% (20 mg Q2W) vs. 17% in the placebo group. Interestingly, body weight decreased progressively in a dose-dependent manner, with significant reductions from baseline in the 10- (–2.0 ± 0.3 kg) and 20-mg (–2.8 ± 0.3 kg) QW groups, as well as in the 20-mg Q2W arm (–1.9 ± 0.3 kg). The researchers concluded that weekly administration of taspoglutide leads to significant improvements in glycemic control and weight loss, and represents a promising treatment option for patients with type 2 diabetes (18).

As part of the aforementioned study, the same slow-release taspoglutide formulation was evaluated on several parameters of β-cell function. Volunteers underwent a 4-h mixed meal test performed under postabsorptive conditions at baseline (PRE) and 1 week after the last injection of active drug or placebo (POST). After 8 weeks of treatment, fasting plasma glucose (FPG) decreased by 21%, 24% and 26%, respectively, compared to PRE in the 5-, 10- and 20-mg QW groups (–8% with placebo). In the Q2W arm, FPG declined by 12% on 10 mg and 16% on 20 mg. Taspoglutide decreased 2-h postprandial plasma glucose (2h-PPG) by 17% (5 mg), 25% (10 mg) and 22% (20 mg) in the QW groups (–9% with placebo), as well as glucose AUC, which decreased by 21%, 26% and 23%, respectively, in the 5-, 10- and 20-mg groups (–8% on placebo). In the Q2W arm, 2h-PPG decreased by 13% and 16%, respectively, and glucose AUC declined by 11% and 15%, respectively, in the 10- and 20-mg groups. Insulin secretion rate (ISR) improved significantly during fasting. Similarly, there was an improvement in total insulin response during the 4-h postprandial period (average: +9 nmol/m$^2$ vs. placebo). Both changes were directly proportional to the drug dose. The ΔAUC-ISR/ΔAUC-glucose calculated during the first 2 h after the meal clearly improved on all weekly regimens. β-Cell glucose sensitivity (i.e., slope of the dose–response curve of ISR vs. glucose concentration) was significantly enhanced across the board. These data indicated that taspoglutide improves β-cell function in patients with type 2 diabetes treated with metformin, and further posited this novel long-acting human GLP-1 analogue as a potentially effective drug for treating this disorder (19).

*Table I: Ongoing phase III taspoglutide clinical trials (from ClinicalTrials.gov Web site).*

| Identifier/Sponsor | Description | Interventions | Outcomes |
|---|---|---|---|
| NCT00744926<br>Roche | Taspoglutide vs. placebo for the treatment of type 2 diabetes inadequately controlled with diet and exercise | Taspoglutide<br>Placebo | HbA1c<br>FPG<br>BW<br>MTT response<br>β-Cell function<br>Safety |
| NCT00744367<br>Roche | Taspoglutide vs. placebo for the treatment of type 2 diabetes inadequately controlled with metformin plus pioglitazone | Taspoglutide<br>Placebo<br>Pioglitazone<br>Metformin | HbA1c<br>FPG<br>BW<br>β-Cell function<br>Safety |
| NCT00754988<br>Roche | Taspoglutide vs. sitagliptin for the treatment of type 2 diabetes inadequately controlled with metformin | Taspoglutide<br>Sitagliptin<br>Placebo<br>Metformin | HbA1c<br>FPG<br>BW<br>Lipid profile<br>β-Cell function<br>Safety |
| NCT00755287<br>Roche | Safety, tolerability and effect on glycemic control of taspoglutide vs. insulin glargine in insulin-naïve type 2 diabetes patients inadequately controlled with metformin plus sulfonylurea | Taspoglutide<br>Insulin<br>Metformin | HbA1c<br>FPG<br>BW<br>Hipoglycemia<br>Lipid profile<br>MTT response<br>Safety |
| NCT00717457<br>Roche | Taspoglutide vs. exenatide for the treatment of type 2 diabetes inadequately controlled with metformin, thiazolidinedione or a combination of both | Taspoglutide<br>Exenatide | HbA1c<br>Fasting BW<br>MTT response<br>β-Cell function |

FPG, fasting plasma glucose; BW, body weight; MTT, meal test tolerance.

Currently there are five ongoing phase III clinical trials (20-24) evaluating taspoglutide for the treatment of patients with type 2 diabetes inadequately controlled with diet and exercise or with other approved antidiabetic agents such as metformin (Table I). One of these clinical trials will specifically compare the antidiabetic properties of taspoglutide versus exenatide, the first approved incretin analogue.

## Sources

F. Hoffmann-La Roche, Ltd. (rights acquired from Ipsen to market taspoglutide worldwide except Japan); Tejin Pharma, Ltd. and Chugai Pharmaceutical Co., Ltd. are developing taspoglutide jointly in Japan.

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