

Anti-diabetic agents: new therapies in an expanding market

Paris, 22nd June 2006

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Ipsen today



Who we are, what we do: “innovation for patient care”

An innovation driven International Specialty Pharmaceutical Group with more than 75 years of operations

A world-class Group

A diversified and balanced portfolio of products with more than 20 field proven products

A longstanding presence in primary care in France

A clear strategic focus on fast-growing specialist care worldwide

A differentiating R&D capability

A recognised strategic partner

A strong management track-record

- > 100 countries. c.4,000 employees.
- 2005 Sales: €807 m. 2005 EBIT: €185 m (23.0% margin).
- 47% of 2005 sales
- Gastroenterology, cognitive disorders and cardiovascular.
- 49% of 2005 sales
- Oncology, neuromuscular disorders and endocrinology
- Focused on (i) hormone-dependent diseases, (ii) peptide and protein engineering and (iii) innovative delivery systems.
- 700 staff, 2005 budget: 20.9% of sales.
- Alliances with international industry leaders in US, Europe and Japan and best-in-class universities around the world.
- Experienced and international management.

A diversified and balanced portfolio of products

**Primary care:
a sound business platform**

+4.4%

**05/04
sales growth**

+10.4%

**Specialist care:
Growth engines**

Gastroenterology

18% of sales

Smecta®

- France and China: 66% of sales

+4.9%

+6.0%

Decapeptyl®

- G5: 67% of sales

Oncology

26% of sales

Cognitive disorders

15% of sales

Tanakan®

- France: 73% of sales

+4.0%

+20.4%

Somatuline®

- G5: 70% of sales
- Filing scheduled in the US

Endocrinology

11% of sales

Cardiovascular

14% of sales

Nisis/Nisisco®

- France: 100% of sales

+4.3%

+12.4%

Dysport®

- G5: 51% of sales
- Filing scheduled in the US

Neuromuscular Disorders

12% of sales

Focused investments in primary care to nourish cash flow generation and grow specialist care worldwide

Differentiating R&D: a unique convergence of capabilities

A differentiating R&D focused on...

- 1 Hormone dependent diseases
- 2 Peptide and protein engineering
- 3 Innovative delivery systems

A competitive R&D capability with...

- 1 4 R&D specialized centres (Boston, Paris, Barcelona, London)
- 2 A staff of 700
- 3 20.9% of sales spent on R&D in 2005
- 4 A unique convergence of technological platforms

A recognised strategic partner

Ipsen has built a strong network of centres of research excellence and industry leaders

“International Specialty Pharma” business model

Mission Statement

To be a worldwide best-in-class provider of innovative drugs, addressing unmet medical needs in its targeted therapeutic areas

Strategic Priorities

- ① **GROW** top-line and profits in the **specialist care** by providing innovative drug therapy
- ② **OPTIMISE** returns of **primary care** through selected product life cycle management, partnerships and focused investments
- ③ **GLOBALISE** through active geographical expansion policy

Key Company Levers

- ① Strong R&D Capabilities
- ② Extended International Network
- ③ Experienced and Proactive Teams
- ④ Financial Flexibility

Key Growth Boosters

- ① US expansion
- ② Strong R&D pipeline
- ③ Partnerships

Growth boosters

US expansion

4 NDA's in the pipeline:

- Somatuline® : filing in 2006
- Dysport® : filing in 2007 in cervical dystonia
- Reloxin® : partnered in aesthetic medicine
- OBI-1: currently in phase II

Strong R&D pipeline

Differentiating R&D, delivering innovative products:

- BIM 51077 (GLP-1)
- BN 83495 (STX-64)
- OBI-1

Partnership in aesthetic medicine

Partnership with Medicis in the US:

- World leader in dermal fillers with Restylane™
- Innovative and synergistic R&R™ concept
- Filing forecasted in 2007

A strong R&D pipeline to fuel future growth: 7 NCEs

		Compound	Indication	Current Status
Specialist Care	Oncology	Decapeptyl®	Combination and longer release formulation	Phase II/III
		BN 83495 (STX 64)	Post-menopausal breast cancer	Phase I
		BN 2629 (SJG-136)	Advanced metastatic cancers	Phase I
		Diflomotecan (BN 80915)	Advanced metastatic cancers	Phase II
		Elomotecan (BN 80927)	Metastatic tumors	Phase I
	Endocrinology	Somatuline® Autogel®	Neuro endocrine tumors Acromegaly	Phase III Filing scheduled in the US in 2006
		BIM 51077	Type 2 diabetes	Phase II
		NutropinAq®	Idiopathic short stature	Phase III
	Neuromuscular Disorders	Dysport®	Cervical Dystonia Myofascial pain	Phase III – Filing scheduled in 2007 in US Phase II
		Dysport® /Reloxin®	Aesthetic medicine	Under regulatory review in Europe Phase III – Filing schedule in 2007 in US
Primary Care	Cognitive Disorders	Tanakan®	Mild cognitive impairment related to age	Phase III
Others	Haematology	OBI-1	Haemophilia	Phase II
	Rheumatology	Febuxostat (TMX-67)	Symptomatic hyperuricaemia	Regulatory strategy to be confirmed during 2006

Note: excludes pre-clinical programmes

Financials at a glance

<i>In €millions</i>	2005	2004	05/04 growth
Sales	807.1	751.5	+7.4%
EBITDA	214.9	194.5	+10.5%
<i>EBITDA margin</i>	26.6%	25.9%	
EBIT	185.3	156.5	+18.4%
<i>EBIT margin</i>	23.0%	20.8%	
Net profit	148.6	117.6	+26.4%
<i>Net margin</i>	18.4%	15.7%	
EPS ⁽¹⁾ (diluted - in €per share)	2.20	2.01	+9.5%
Cash flow from operations	176.9	124.7	+41.8%

Sales at constant perimeter

IFRS, pro forma, 2004 adjusted to exclude disposed GP business in Spain from continuing operations

Note (1): based on average number of shares during the period

Key drivers of future performance

DEVELOP specialist care product portfolio

- Expansion into US
- Active life cycle management

OPTIMISE primary care products

- Selective investment
- Leverage existing sales force infrastructure

MAXIMISE value of R&D pipeline

- Focused development
- Synergistic partnerships

ENHANCE product portfolio and geographical reach

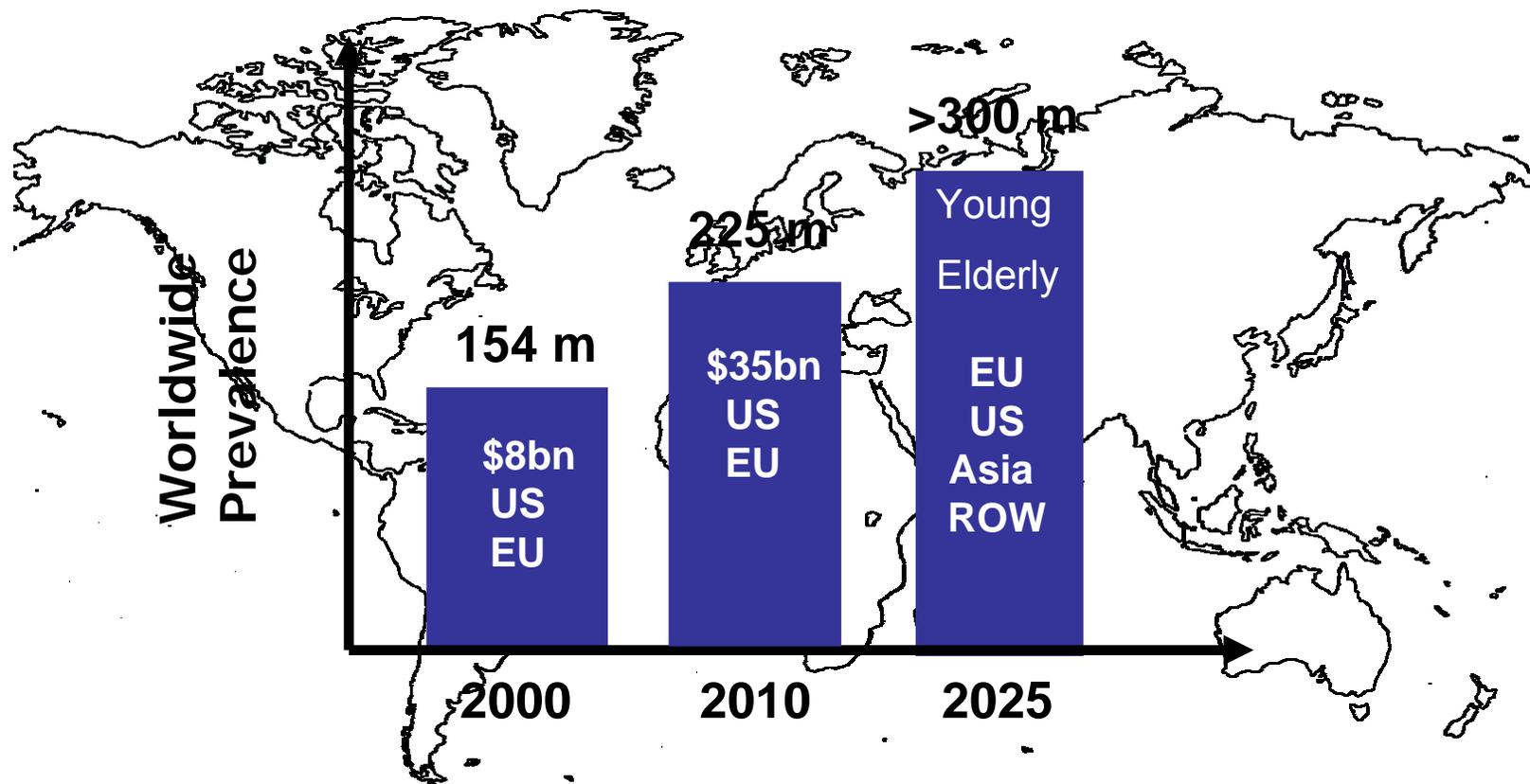
- New products / new indications
- Continue to seek new alliances
- Continue to seek acquisition opportunities

Ipsen: positioned for profitable growth

Focus on diabetes and GLP-1 analogs

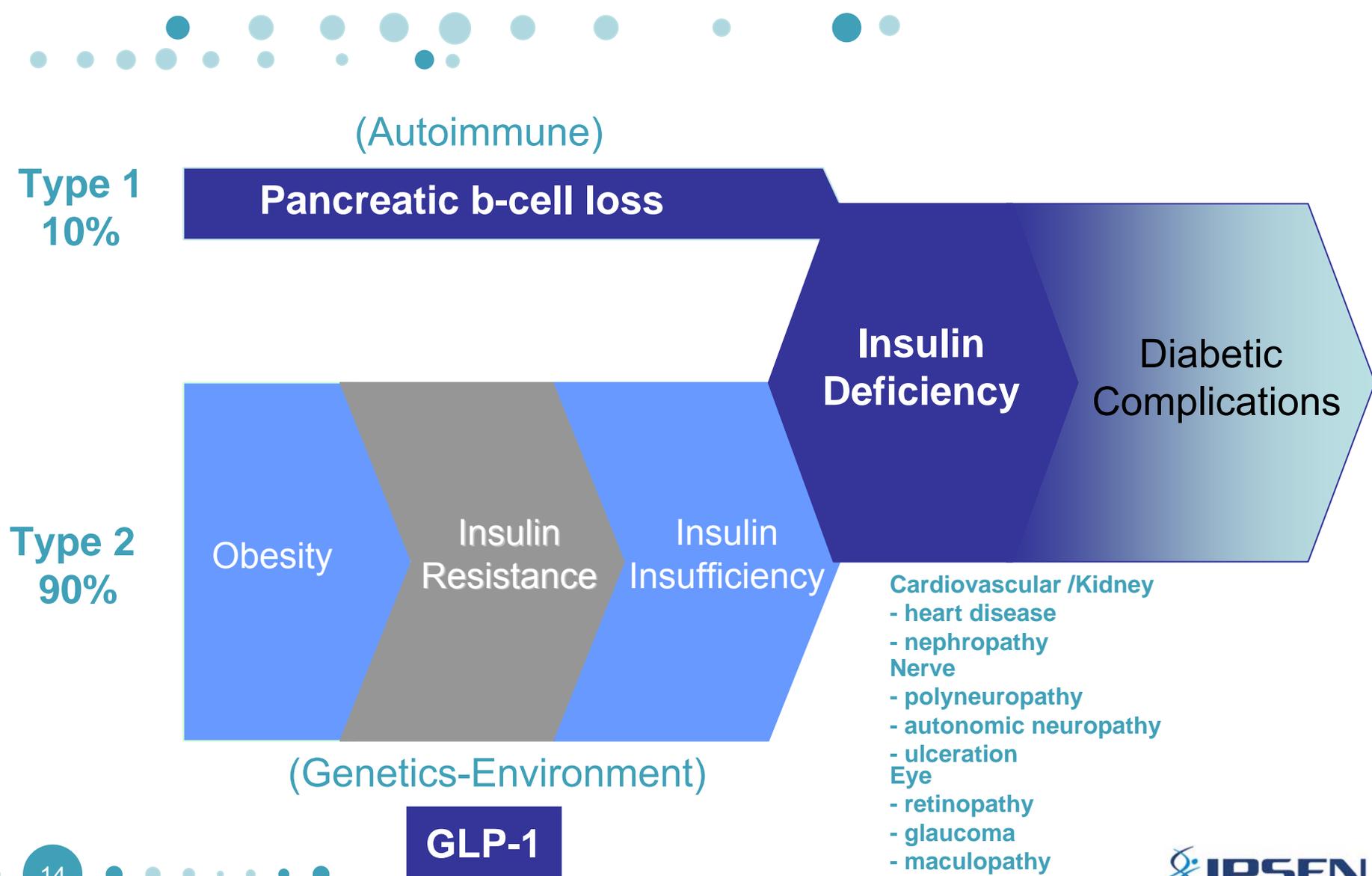


Foreword: the diabetes market is expanding

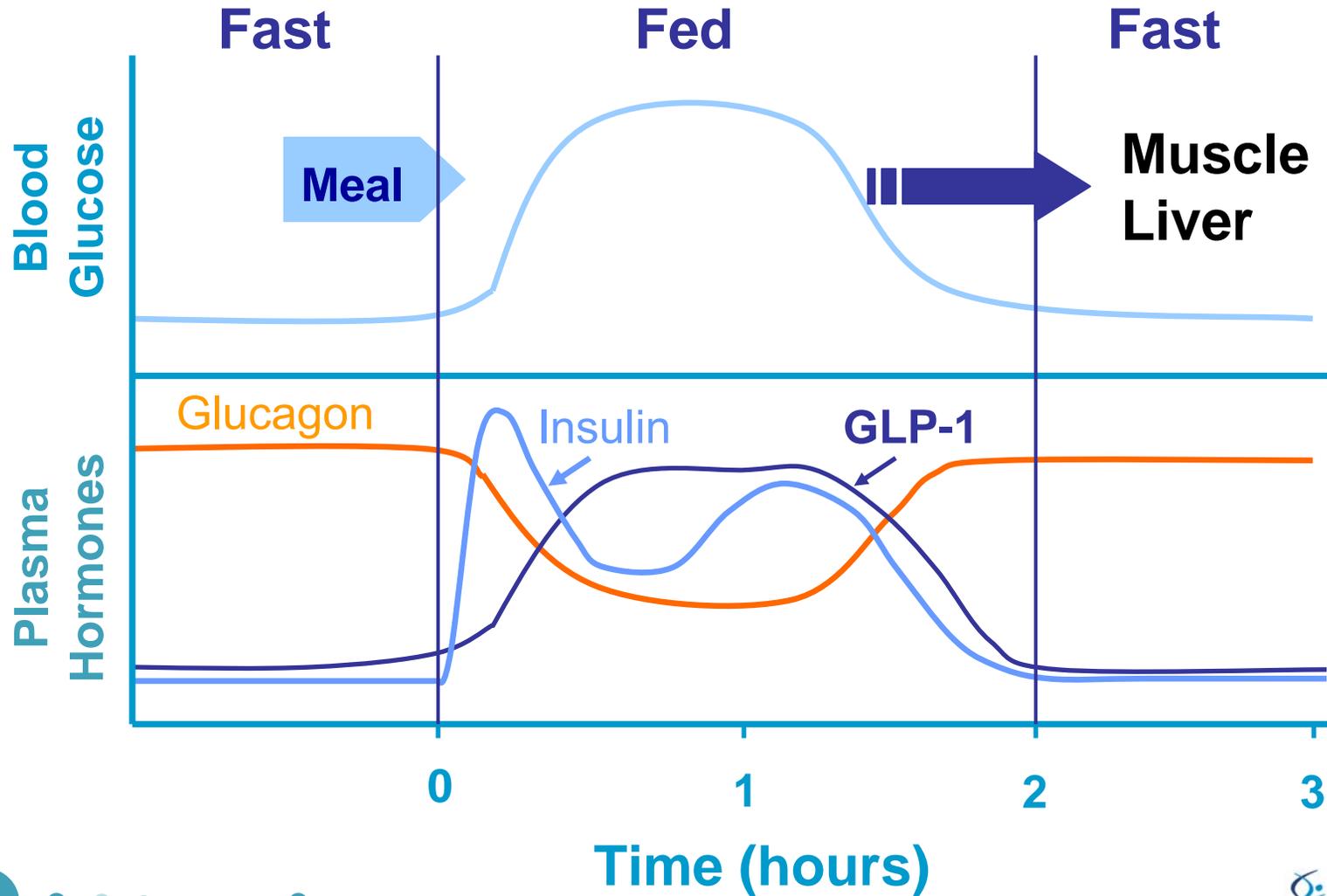


Source: IMS Health Medical Dynamics data, 2002

Diabetes overview: typology



Diabetes overview: regulation of glucose excursions in non-diabetics



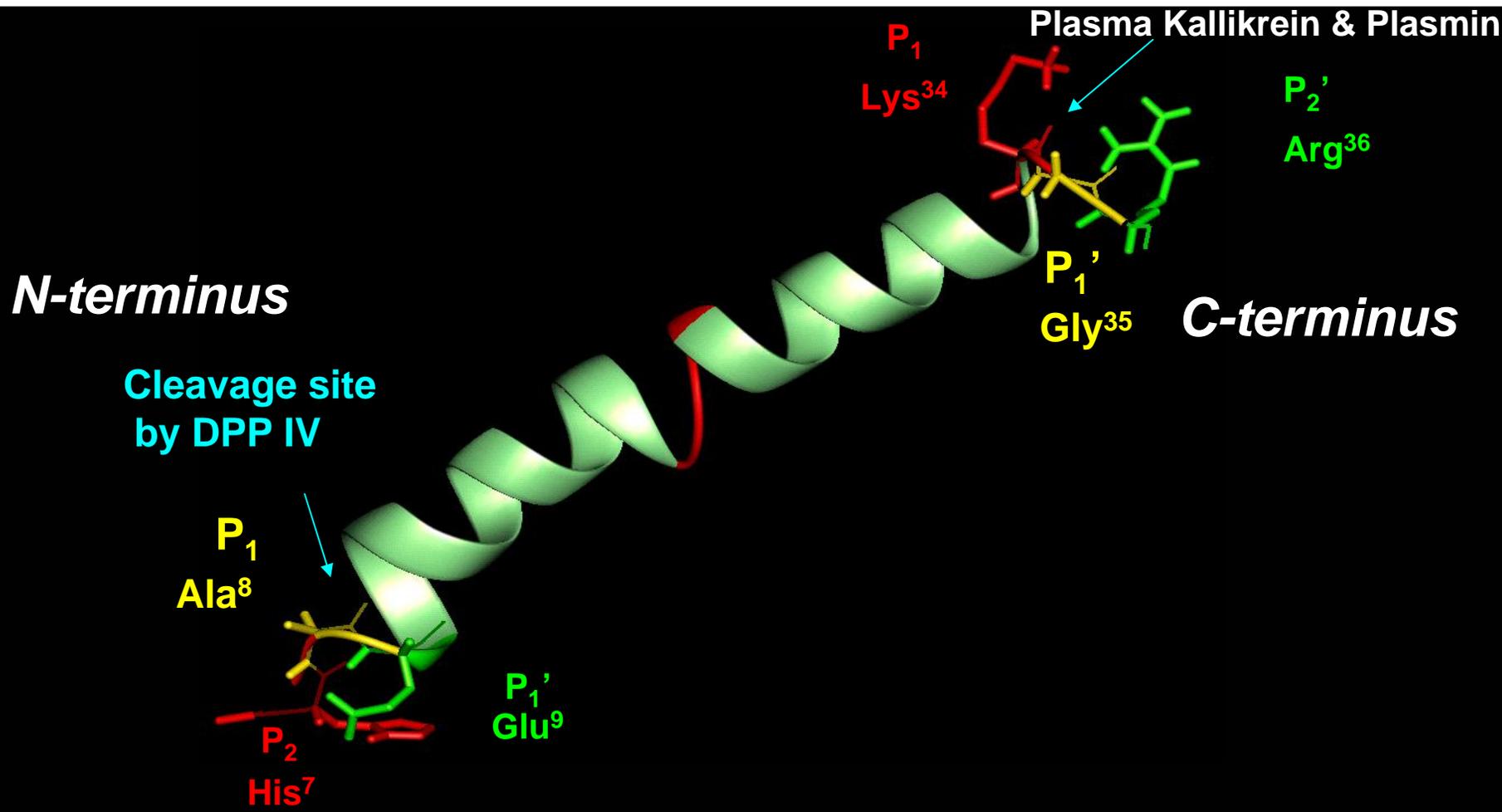
GLP-1 - Potential Treatment for Type II Diabetes

- ✓ Produced by L-cells of intestine
 - 2 forms: GLP-1(7-37)-OH & GLP-1(7-36)NH₂
- ✓ Stimulates insulin secretion and inhibits glucagon release
 - only when plasma glucose elevated = *Glucagon-incretin*
- ✓ Promotes insulin gene expression and proinsulin biosynthesis
- ✓ Induces pancreatic β -cell proliferation/differentiation
- ✓ Slows gastric emptying
 - decreasing postprandial glucose excursions
- ✓ Suppresses appetite
- ✓ Demonstrated effectivity in normal human volunteers and type II diabetic subjects

Goals for Therapeutic GLP-1 Analogs

1. Equal / greater potency as native compound
2. Extended metabolic half-life
 - ✓ native GLP-1 has very short circulating T1/2
 - ✓ ~2min i.v., ~15min s.c.
3. Retention of incretin properties
4. Compatible with novel/sustained formulation
5. Strong patent position

hGLP-1(7-36)NH₂ is Cleaved in Plasma at Both N- & C Termini



Goals for Therapeutic GLP-1 Analogs

1. Equal / greater potency as native compound

<u>Binding:</u> BIM-51077	$K_i = 1.1 \pm 0.15 \text{ nM}$
hGLP-1(7-36)	$K_i = 0.9 \pm 0.11 \text{ nM}$

In Vivo: BIM-51077 8x more active than hGLP-1 (7-36) *in vivo*

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✓ **22-fold more stable in plasma**

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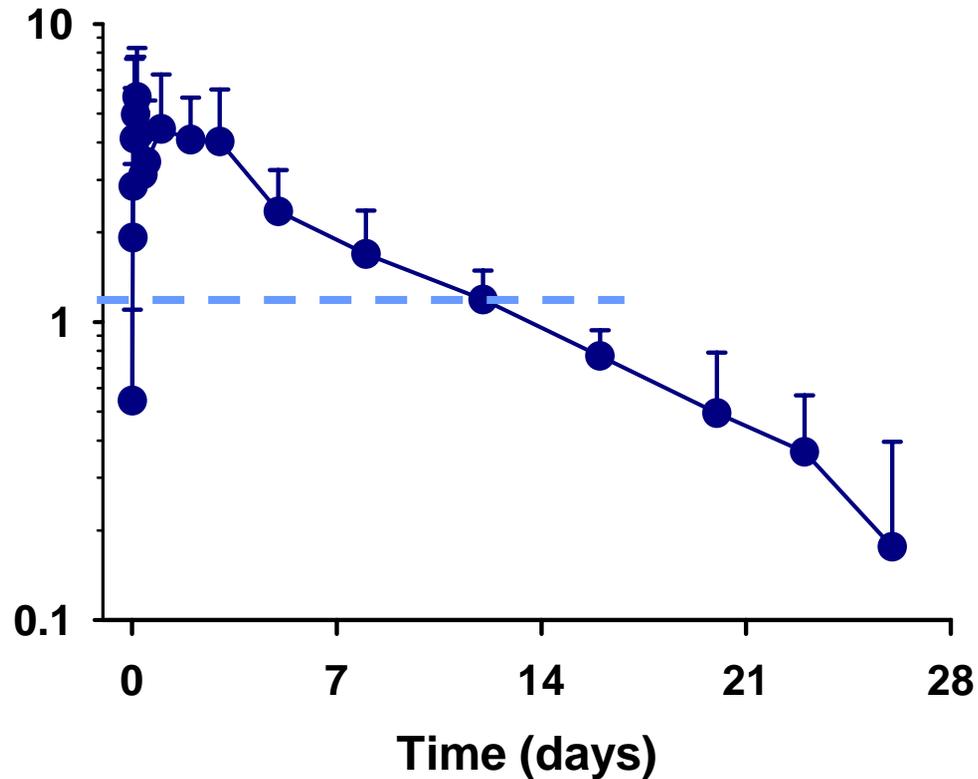
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4. **Compatible with novel/sustained formulation**
 - ✓ **Yes, highly compatible physio-chemical properties**
 - ✓ **High aqueous solubility at neutral pH**
5. Strong patent position

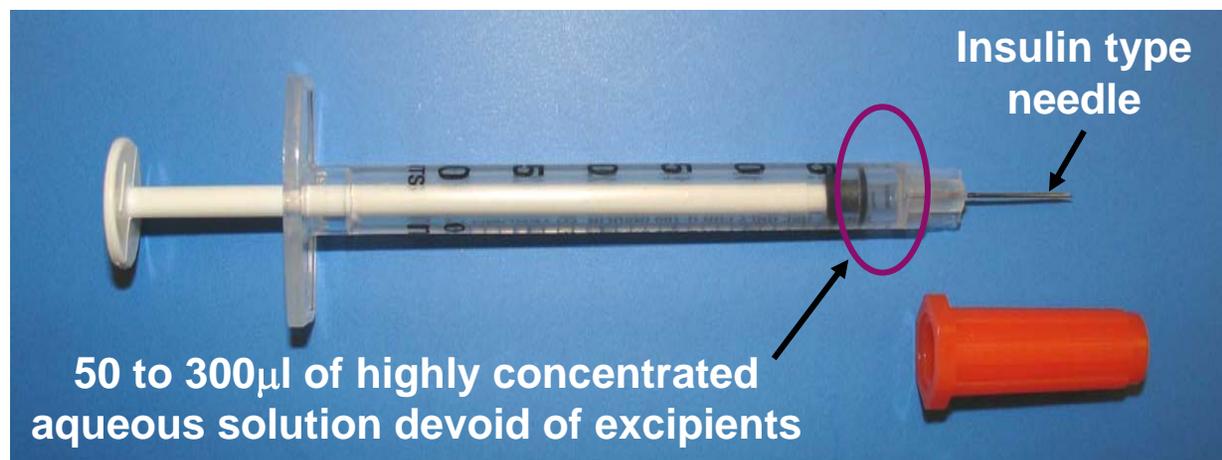
Pharmacokinetic Profile of a SRF Formulation of BIM51077



BIM51077 Plasma Concentration (ng/ml) Achieved in Male Beagle Dogs Following sc Administration of SRF at a Dose Level of 15 mg/dog

Pharmacokinetic Profile of a SRF Formulation of BIM51077

- ✓ A single sc administration of BIM-51077 SRF (15 mg in dogs) maintained BIM-51077 levels within one log for up to 2 weeks with minimal initial burst.
- ✓ BIM51077 plasma levels were detected up to 26 days



Syringe used for BIM51077 SRF

- 0.3mL TERUMO Myjector U-100 with 29G1/2 (0.33 X 12 mm)

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3. Compatible with novel/sustained formulation

- ✓ Yes, highly compatible physio-chemical properties
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5. Strong patent position

- ✓ **Patents covering use and composition of BIM-51077 are issued in the US, Europe, Japan, and many other countries WW**
- ✓ **Further patent applications for various compositions, uses, and processes continue to be filed and actively prosecuted**

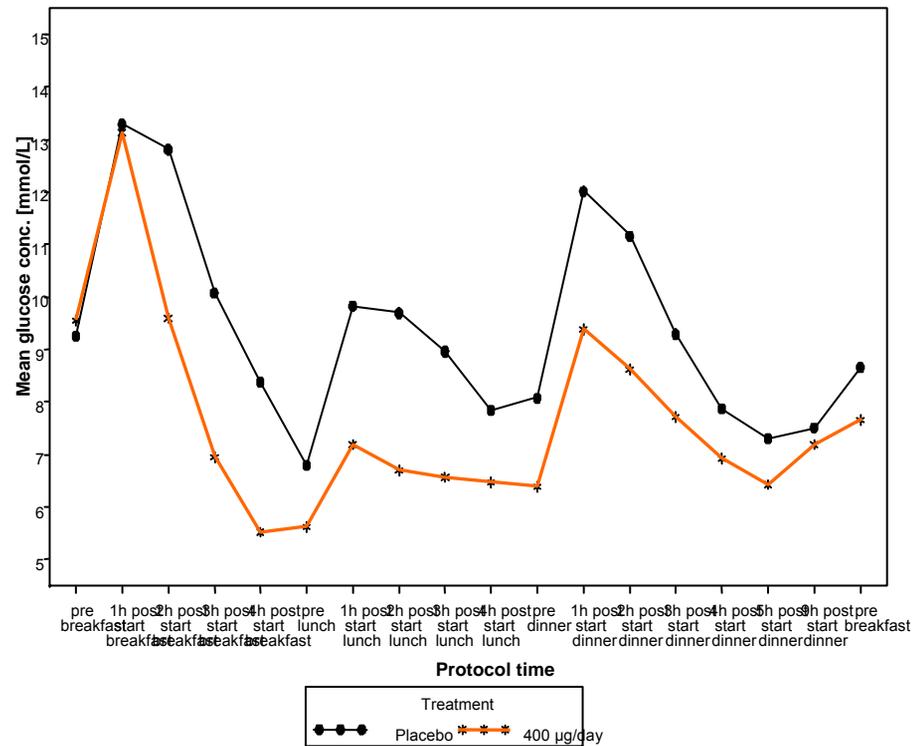
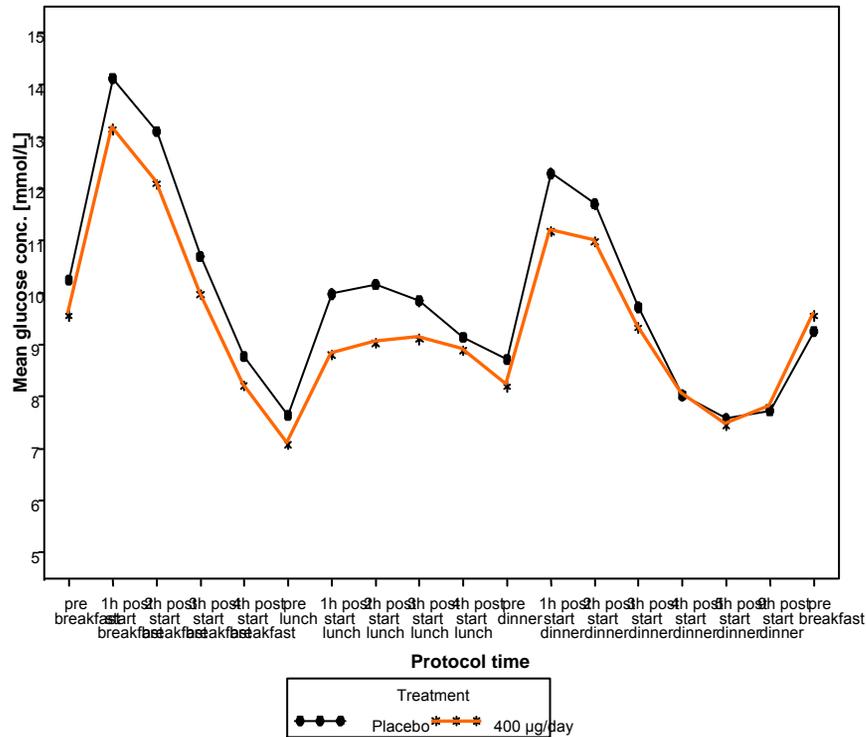
BIM-51077: clinical efficacy and safety



BIM-51077 produced sustained improvement in blood glucose control over 28 days by continuous infusion

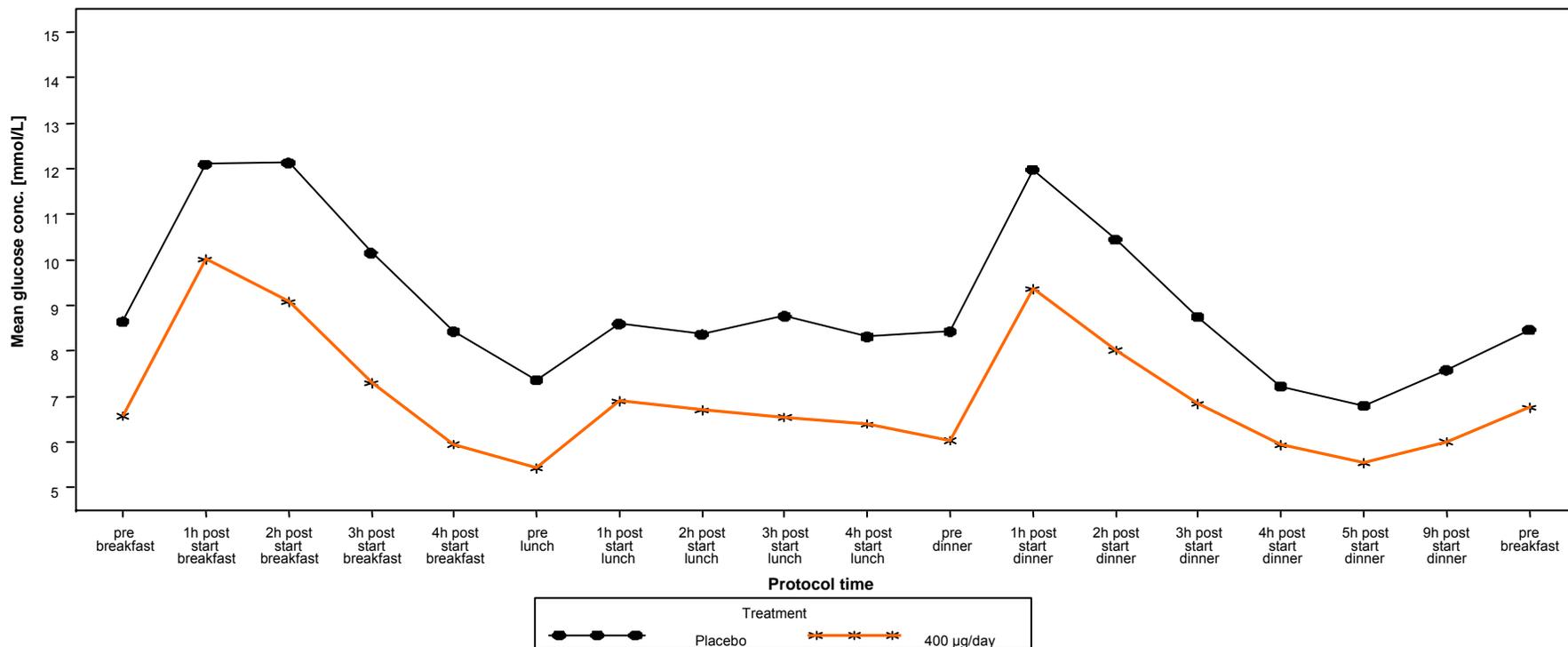
- ✓ 18 patients, Type 2 diabetics treated with metformin
- ✓ 12 active (400µg/day) and 6 placebo
- ✓ 28-day continuous subcutaneous infusion of BIM-51077 IRF

BIM-51077 produced sustained improvement in blood glucose control over 28 days by continuous infusion



BIM-51077 produced sustained improvement in blood glucose control over 28 days by continuous infusion

24-h profile of blood glucose concentrations on Day 28



BIM-51077 produced sustained improvement in blood glucose control over 28 days by continuous infusion

When administered at 400 µg/d dose level over 28 days, BIM-51077 showed:

- ✓ Good safety profile without any antibodies against BIM-51077
- ✓ Significant and rapid effect on 24-h BG after the start of infusion. Effect maintained over 28 days without desensitization
- ✓ Sustained effect on fasting blood glucose over 28 days
- ✓ Trend to increase insulin secretion, to decrease HbA1c, and decrease body weight and appetite

Q&A session

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