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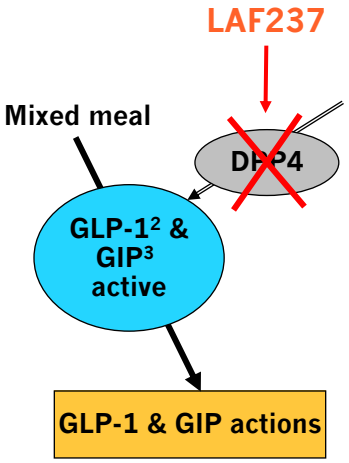
LAF237 – Oral DPP4[1] Inhibitor with Potential for Sustainable Diabetes Control

- First in a highly attractive new class of compounds (incretin enhancer)
- Effective as monotherapy and in combination
- Effectively reduces HbA1c
- Good tolerability with no nausea and no significant effect on weight
- Has the potential for disease modification based on islet-cell effects



1 Dipeptidyl peptidase IV
2 Glucagon-like-peptide-1
3 Gastric inhibitory polypeptide

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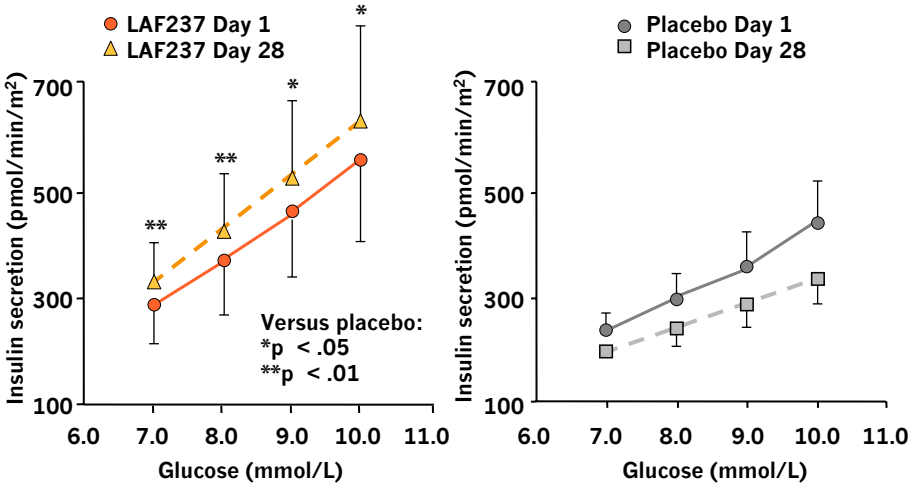
LAF237 Increases β-Cell Responsiveness to Glucose in T2DM



Adapted from Mari A, et al. J. Clin Endocrinol Metab 90:4888-4894, 2005

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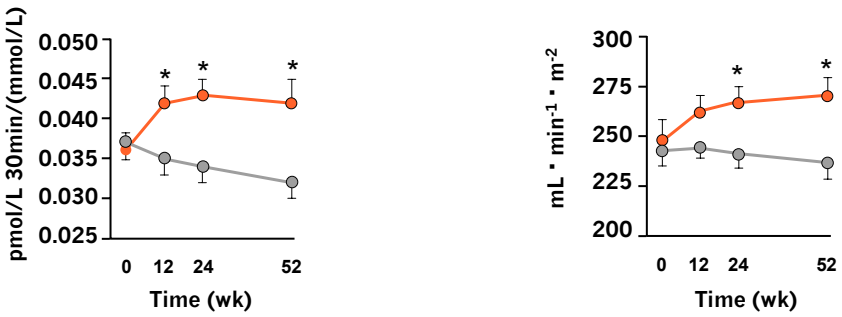
LAF237 Improves and Sustains Islet Cell Function and Insulin Sensitivity over 1 year in T2DM

Patients failing on stable metformin therapy

β-cell function (insulin secretion)

LAF237/metformin
Placebo/metformin

Insulin sensitivity



*P < .05 vs. placebo; †P < .01 vs. placebo

Adapted from Ahren B, et al. *Diabetes Care*. 2005;28:1936-1940.

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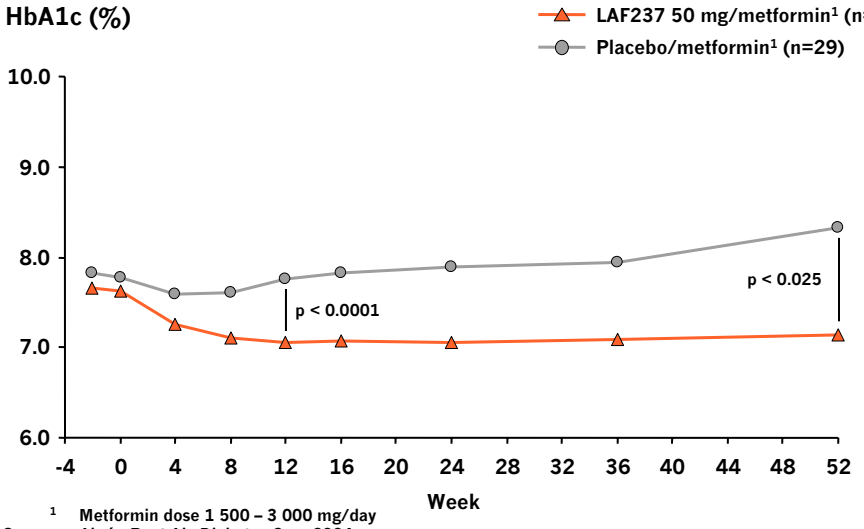
Improvements in Islet Cell Function and Insulin Sensitivity With LAF237 Support Sustained Efficacy Seen Over 1 year



[1] Metformin dose 1 500 – 3 000 mg/day
Source: Ahrén B. et Al., Diabetes Care 2004

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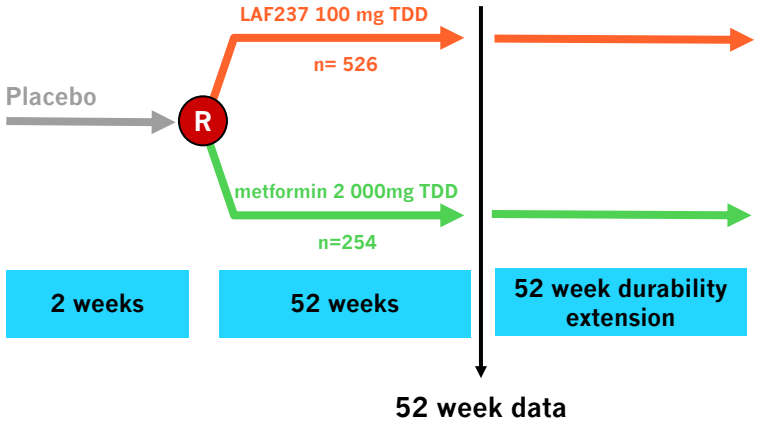
Phase III Trial Design for Study 2309 – Long-term LAF237 Monotherapy

Drug naïve patients with T2DM and HbA1c 7.5-11%
Objective - HbA1c reduction at 12 months and maintenance to 2 years



Source: Study 2309 data on file

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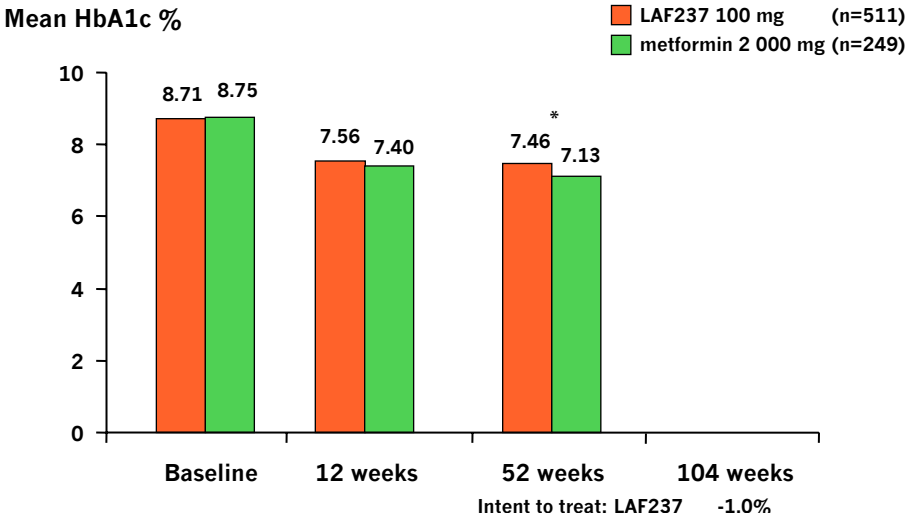
52 Week Data with Monotherapy Confirm Early and Sustained Reductions in HbA1c



*p < 0.05 versus LAF237
Source: Study 2309 data on file per protocol population

Intent to treat: LAF237 -1.0%
metformin -1.4%

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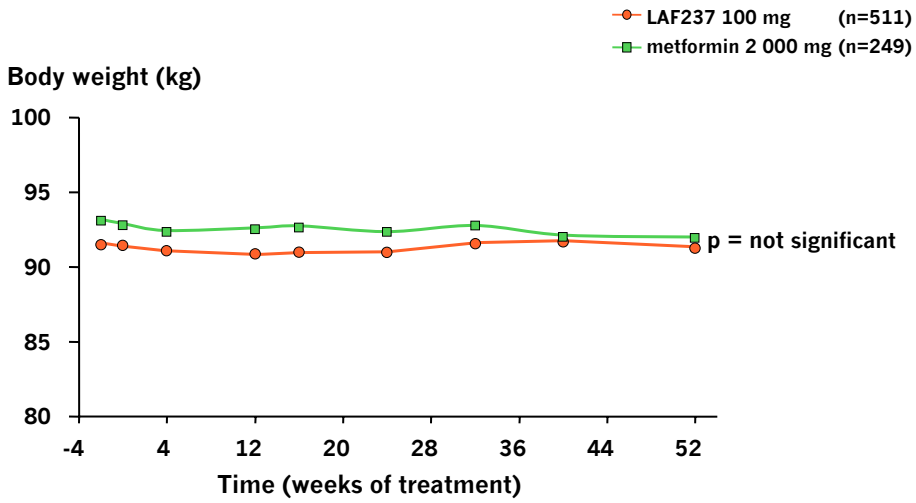
Both LAF237 and Metformin Demonstrate Body Weight Neutrality Unlike SUs[1] and TZDs[2]



[1] Sulfonylureas [2] Thiazolidinediones
Source: Study 2309 data on file

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LAF237 is Better Tolerated than Metformin

AEs of special interest	LAF237 100 mg (%) (n=526)	metformin 2 000 mg (%) (n=254)
Hypertension	3.7	4.8
Edema	2.5	3.6
Diarrhea	6.0	26.2
Paresthesia	0.8	2.0
Nausea	3.3	10.3
Myalgia	2.3	0.8
Hypoglycemia	0.6	0.4
ECG[1] abnormalities	11.0	12.0

[1] Electrocardiogram
Source: Study 2309 data on file

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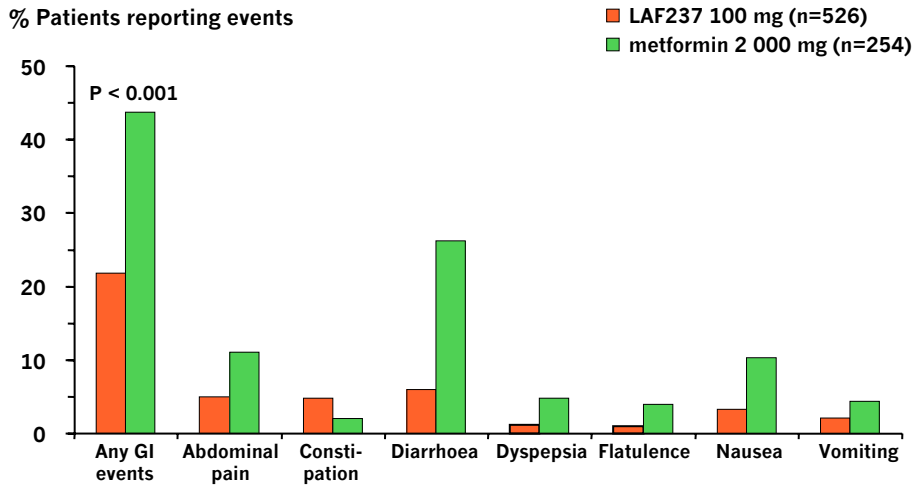
LAF237 Has a Superior GI Tolerability Profile to Metformin



Source: Study 2309 data on file

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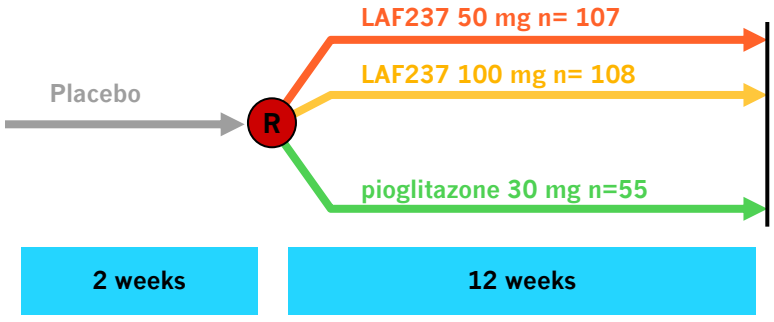
Phase III Trial Design for Study 2329 – LAF237 Dose Comparison

Drug naïve patients with T2DM and HbA1c 9-11%

Primary objective: HbA1c reduction from baseline – LAF237 50 mg and 100 mg total daily dose

Pioglitazone used as a positive control for study validation



Source: Study 2329 data on file

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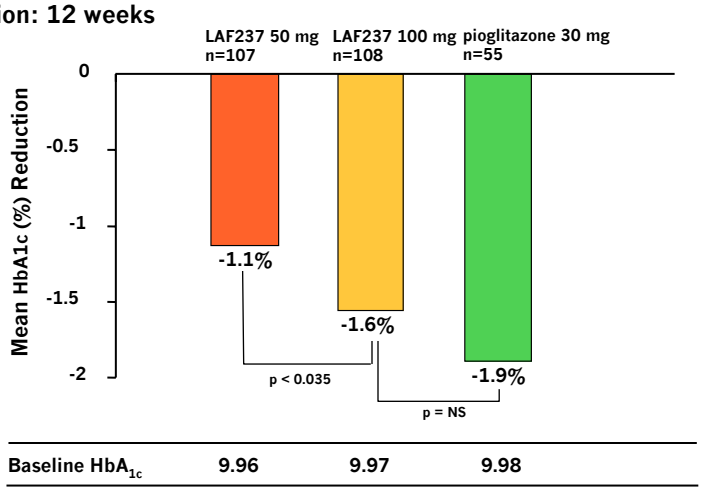
LAF237 Achieves Excellent, Dose-proportional Reductions in HbA1c

Duration: 12 weeks



Source: Study 2329 data on file

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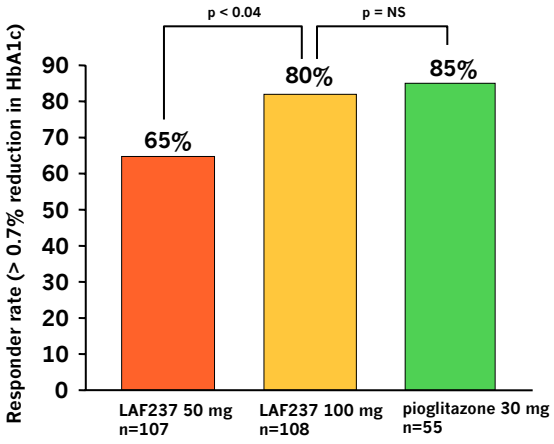
LAF237 Demonstrates Excellent Responder Rates

Duration: 12 weeks



Source: Study 2329 data on file

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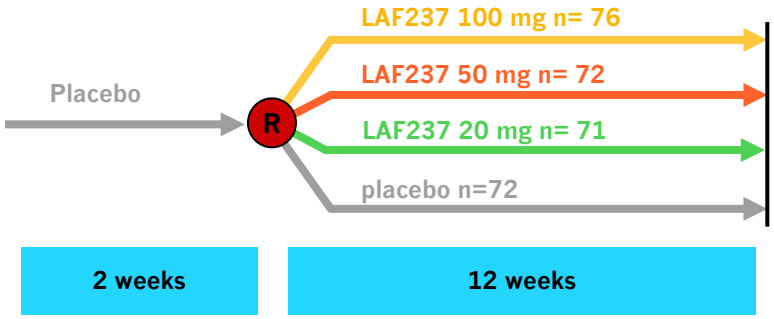
Phase IIb Trial Design for Study 1202- LAF237 Dose-ranging Study

Drug naïve patients with T2DM and HbA1c 7.5-11%

Primary objective: HbA1c reduction from baseline – LAF237 20 mg, 50 and 100 mg vs. placebo



Source: Study 1202 data on file

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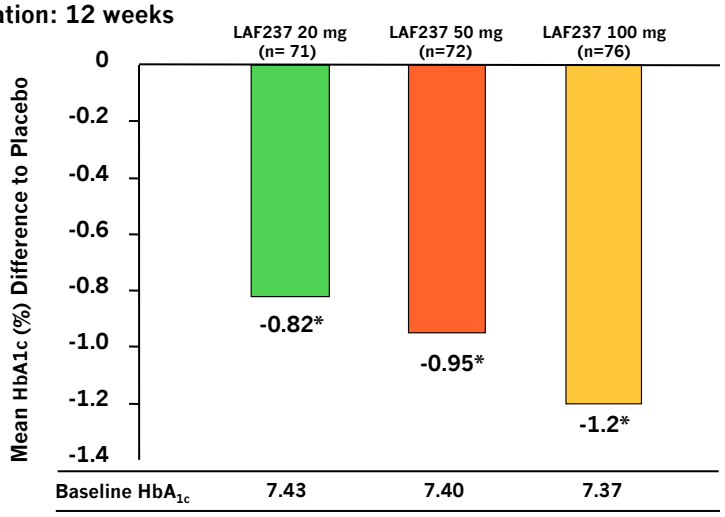
LAF237 Demonstrates Excellent, Dose-proportional Reduction in HbA1c

Duration: 12 weeks



Source: Study 1202 data on file *p < 0.001 versus placebo and baseline

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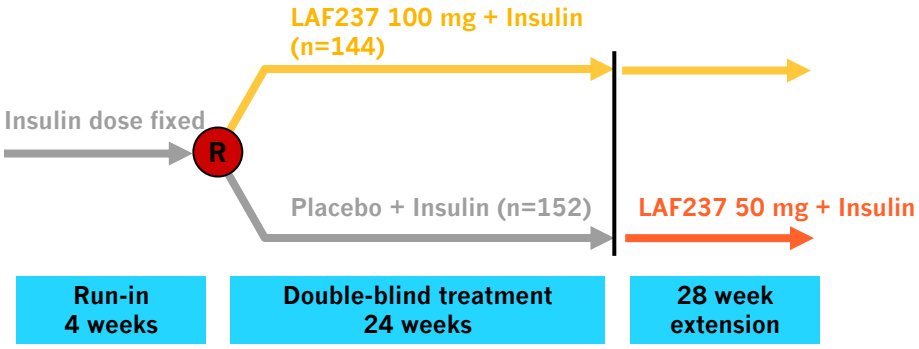
LAF237 Phase III Trial Design for Study 2311 Add-on to Insulin

Patients with T2DM on insulin, HbA1c 7.5–11%
Primary objective: To improve metabolic control as add-on to insulin



Source: Study 2311 data on file

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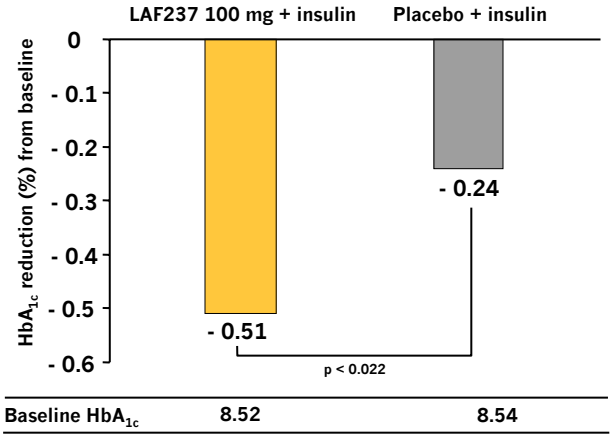
LAF237 Significantly Reduces HbA1c in T2DM Patients Requiring Insulin

Duration: 24 weeks



Source: Study 2311 data on file

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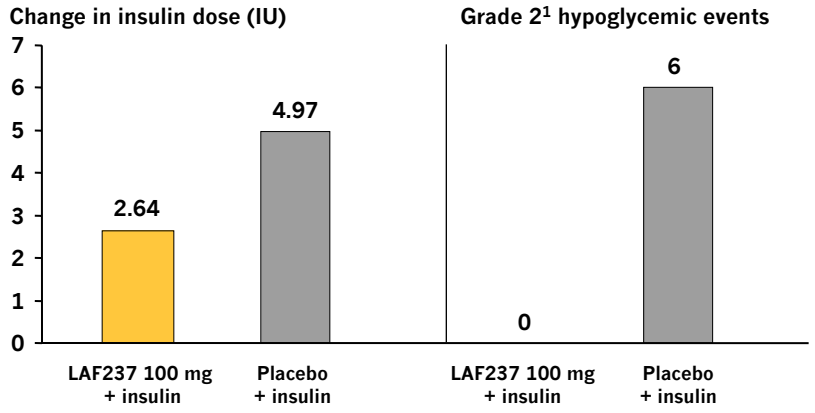
Reductions of HbA1c Achieved With Less Insulin Requirements and No Severe Hypoglycemic Events

Duration: 24 weeks



[1] Blood glucose < 3.1 and symptoms suggestive of hypoglycemia and patient unable to initiate self treatment

Source: Study 2311 data on file

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LAF237 New Phase IIb/III Data Summary

New Phase IIb/III data confirms that LAF237

- Reduces HbA1c levels in a dose-proportional, clinically meaningful manner in monotherapy and combination with insulin
- Sustains meaningful HbA1c reductions out to one year
- Has neutral body weight effects associated with HbA1c improvements
- Is very well tolerated
- Is associated with fewer severe hypoglycemic episodes when added to insulin
- Has the ideal profile as 'first drug of choice' for combination treatment due to efficacy and safety profile, lack of drug-drug interactions and complementary mechanism of action

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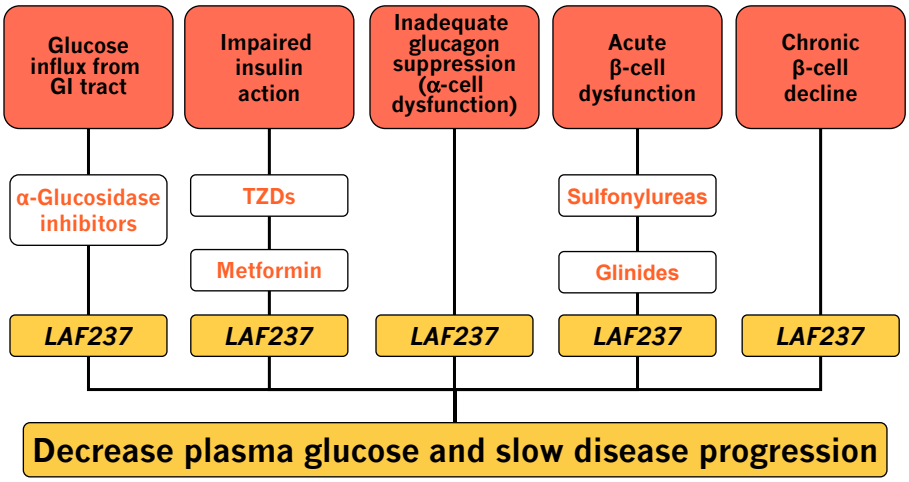
LAF237 Addresses Multiple Important Defects in T2DM Treatment



Adapted from DeFronzo RA. *Br J Diabetes Vasc Dis.* 2003;3(suppl 1):S24–S40

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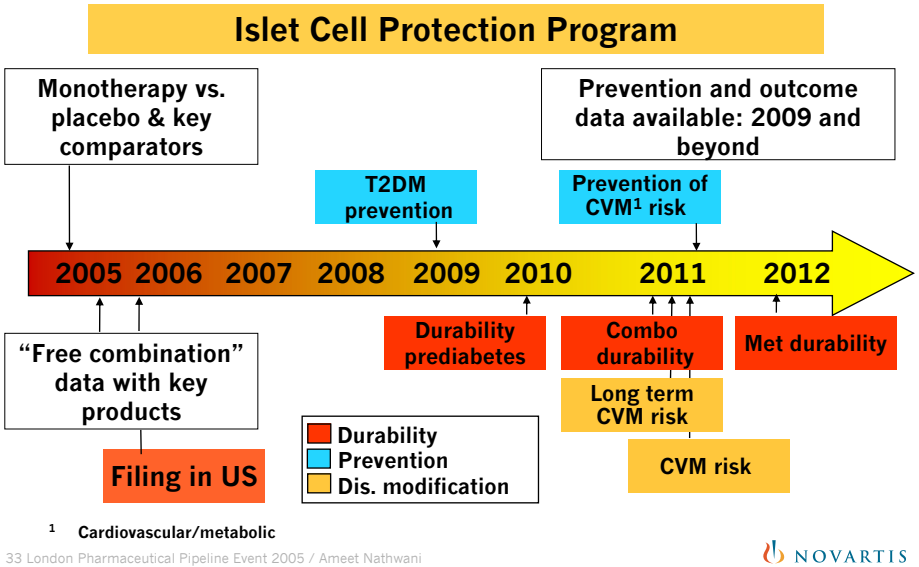
Overview of Timing of Study Starts and Expected Data for LAF237



[1] Cardiovascular/metabolic

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Summary and Conclusions

- Pancreatic islet dysfunction is the key determinant of the onset and progression of type 2 diabetes
- Clinical data confirms that LAF237 restore insulin sensitivity and normalises islet cell function long-term in patients with T2DM
- New phase IIb/III data shows that LAF237 has the ability to sustain reductions in HbA1c to clinically meaningful levels long-term in monotherapy and combination with insulin
- Further pivotal clinical data will be available in early 2006

An extensive clinical trials program with LAF237 will define the role of islet cell protection in

- **Delaying onset of T2DM (prevention)**
- **Slowing progression and maintaining control in T2DM (durability)**
- **Reducing CVM complications (disease modification)**

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