

## Galvus® – the most comprehensively studied DPP-4 inhibitor

- >7 000 patients enrolled in clinical studies
- >4 500 patients exposed to Galvus®
  - >1 300 patients exposed ≥52 weeks
  - >300 patients exposed for 104 weeks
- >2 300 patient years of experience
- Studies in monotherapy, add-on to metformin, add-on to sulfonylurea, add-on to insulin, add-on to TZD and initial combination with pioglitazone
- Extensive phase IIIB program ongoing including GLORIOUS outcome program investigating diabetes prevention, progression and cardiovascular outcomes

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## Galvus® – clinical AE profile comparable to placebo

Event Rate Patients per 100 SYE <sup>1</sup>	Galvus® 100 mg daily n=1 855	met up to 2 g daily n=252	rosi 8 mg daily n=267	pio 30 mg daily n=216	placebo n=347
<b>Any</b>	119.4	88.55	147.3	136.8	177.5
<b>Nasopharyngitis</b>	14.18	11.18	17.23	8.87	18.1
<b>Headache</b>	12.73	8.39	12.06	10.13	14.65
<b>Dizziness</b>	10.87	6.99	9.47	12.67	12.07
<b>URTI</b>	9.84	6.99	6.89	10.13	13.79
<b>Diarrhea</b>	5.38	30.76	6.03	6.33	8.62
<b>Nausea</b>	5.28	12.12	1.72	3.8	8.62
<b>Edema peripheral</b>	4.35	4.19	9.47	21.53	3.45
<b>Abdominal pain</b>	2.07	8.39	1.72	2.53	3.45

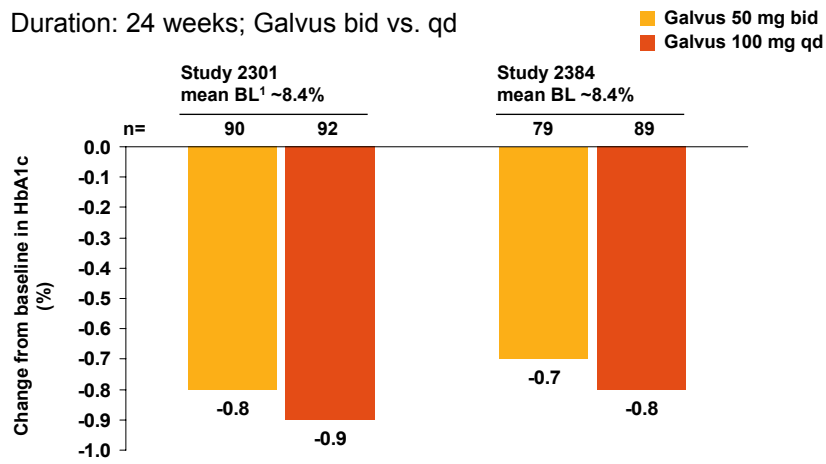
<sup>1</sup> Subject-years Exposure; AE=adverse event; Met=metformin; Rosi=rosiglitazone; AEs ≥ 5% Incidence; the column Galvus 100 mg daily refers to pooled data from trials with 50 mg bid and 100 mg qd Data on file, Novartis Pharmaceuticals

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## Galvus® – new data confirm once daily efficacy

Duration: 24 weeks; Galvus bid vs. qd



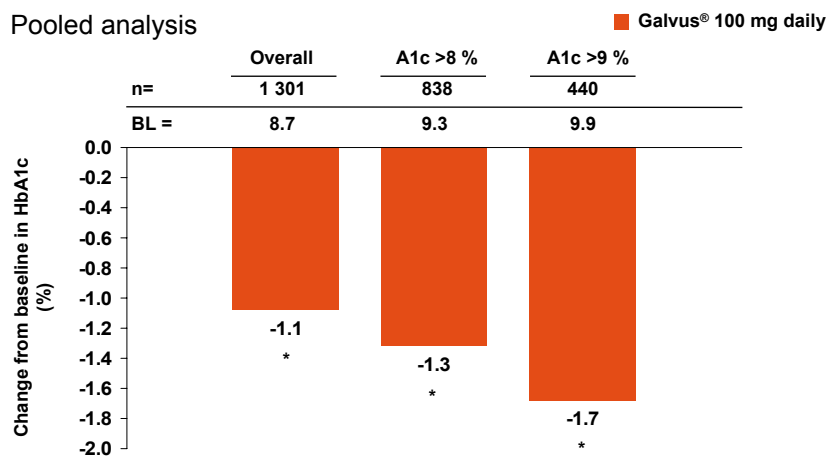
<sup>1</sup> Baseline  
Primary ITT population  
P < 0.01 vs. PBO in both studies. 50 mg qd dose is not included  
Data on file, Novartis Pharmaceuticals, LAF237A2301 and 2384

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## Galvus® – very effective as monotherapy

Pooled analysis



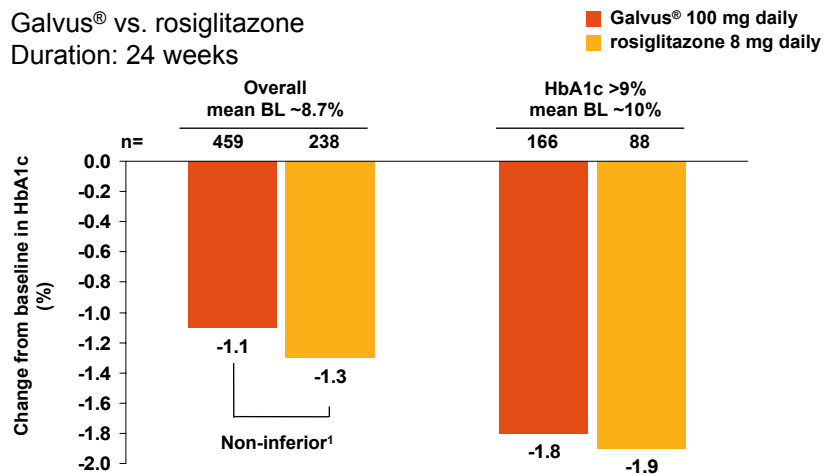
Pooled analysis from LAF237A2301, 2309, 2327, 2355 (at 24 weeks), primary efficacy ITT population; BL=baseline  
\* P < 0.01 from BL  
Data on file, Novartis Pharmaceuticals

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## Galvus® – as effective as 8 mg rosiglitazone

Galvus® vs. rosiglitazone  
Duration: 24 weeks



BL=baseline; Primary ITT population

<sup>1</sup> CI = (-0.01, 0.39) (noninferiority margin is defined by CI upper limit 0.4%)

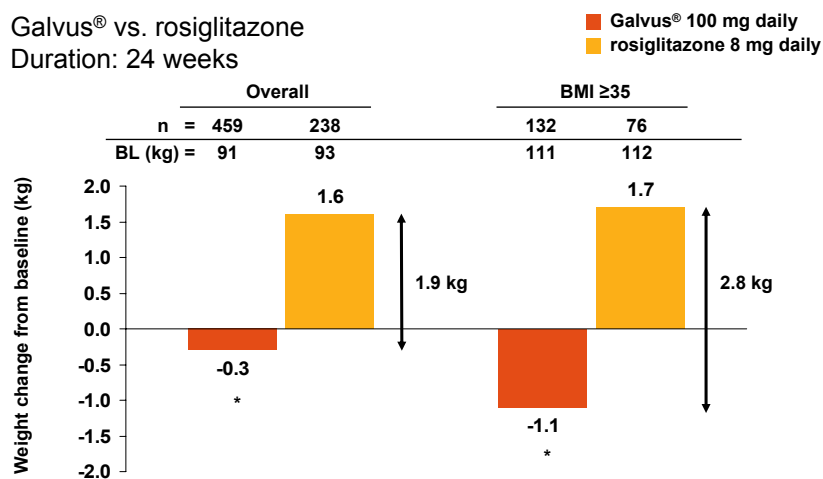
Data on file, Novartis Pharmaceuticals, LAF237A2327; Abstract 557P ADA-2006

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## Galvus® – relative weight loss to rosiglitazone

Galvus® vs. rosiglitazone  
Duration: 24 weeks



\*P<0.001 vs. rosiglitazone (primary ITT population)

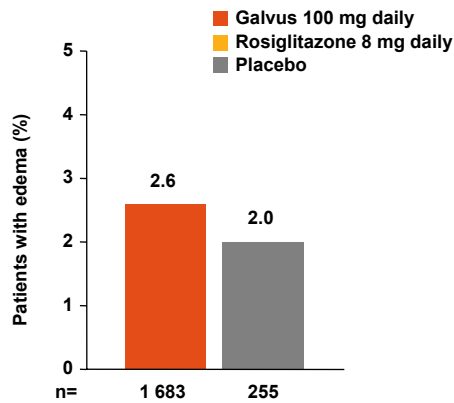
Data on file, Novartis Pharmaceuticals, LAF237A2327; Abstract 557P ADA-2006

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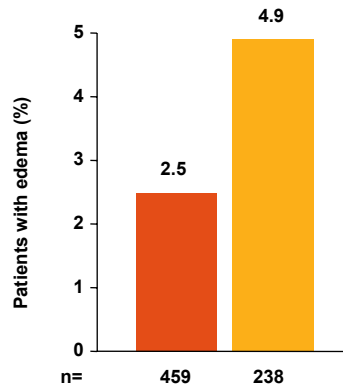


## Galvus® – placebo-like incidence of edema, and less than rosiglitazone

Galvus vs. placebo<sup>1</sup>



Galvus vs. rosiglitazone<sup>2</sup>



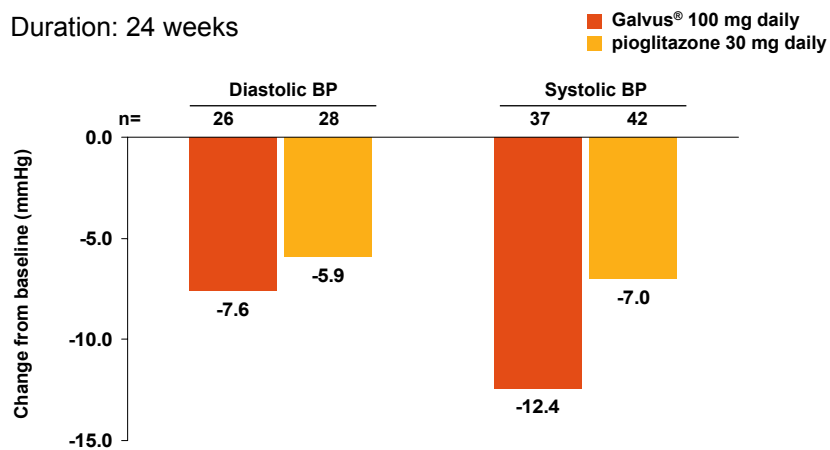
<sup>1</sup> Pooled safety data: Summary of Clinical Safety dated 14 July 2006, Table 4-23

<sup>2</sup> Schweizer A, et al. Diabetologia 2006; 49 (suppl1): 479, Abstract 0790.

Edema-related events include pitting edema, peripheral edema, and other edema

## Galvus® – new data shows favorable effect on BP vs. pioglitazone in hypertensive patients

Duration: 24 weeks



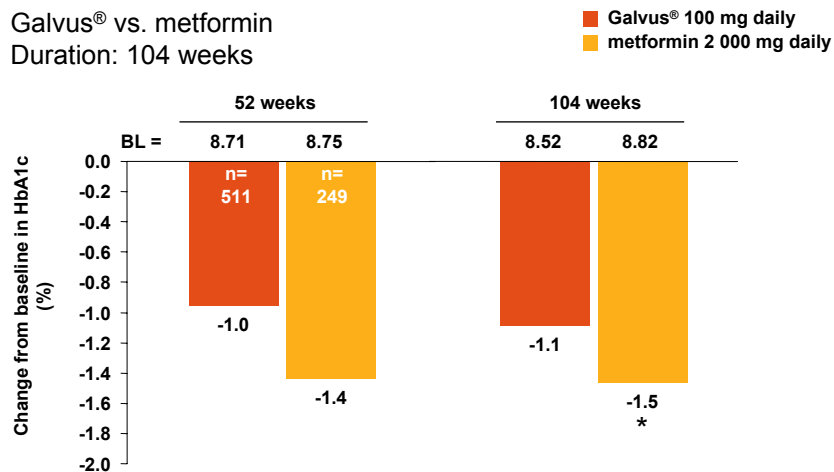
BP = blood pressure

Patient group defined as DBP >90 and SBP >140 mmHg

Data on file, Novartis Pharmaceuticals, LAF237A2335

## Galvus® – sustained efficacy out to 2 years

Galvus® vs. metformin  
Duration: 104 weeks



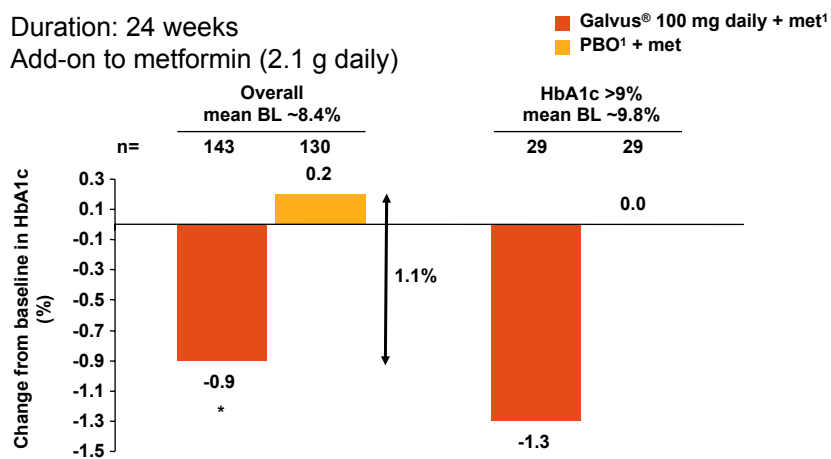
Source: Data on file, Novartis Pharmaceuticals Galvus study 2309 \*  $p < 0.05$ , did not meet endpoint of non-inferiority vs. metformin Extension ITT population, all data were used regardless whether patients were on-rescue medication or not Missing values were imputed using last observation carried forward method.

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## Galvus® – highly effective in combination with metformin

Duration: 24 weeks  
Add-on to metformin (2.1 g daily)



<sup>1</sup> Met=metformin; PBO=placebo; primary ITT population  
\*  $P < 0.01$  difference vs. PBO; 50 mg qd dose is not included  
Data on file, Novartis Pharmaceuticals, LAF237A2303; Abstract 121 OR ADA-2006

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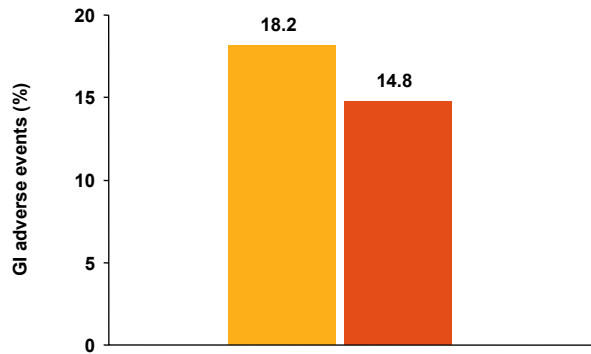


## Galvus® – trend to reduce metformin-induced GI events when used in combination

Duration: 24 weeks

Add-on to metformin (2.1 g daily)

Galvus® 100 mg daily + met (n=63)  
PBO + met (n=62)



met=metformin; PBO=placebo; GI=Gastrointestinal  
50 mg qd dose is not included

Data on file, Novartis Pharmaceuticals, LAF237A2303; Abstract 121 OR ADA-2006

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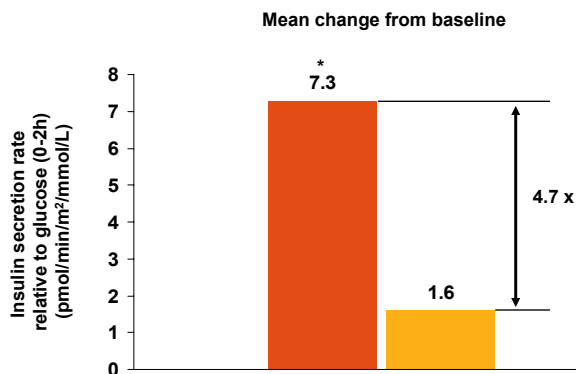


## Galvus® – nearly 5-fold enhancement of $\beta$ -cell function when added to metformin

Duration: 24 weeks

Add-on to Metformin (2.1 g daily)

Galvus® 100 mg daily + met (n=56)  
PBO + met (n=54)



met=metformin; PBO=Placebo; Primary ITT population

\*P<0.001 vs. PBO + met

Data on file, Novartis Pharmaceuticals, LAF237A2303; Abstract 121 OR ADA-2006

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## Galvus® – a potent and highly selective DPP-4 inhibitor (1/2)

- **Robust efficacy**
  - New data confirm once daily dosage
  - Pooled monotherapy data shows -1.1% reduction in HbA1c in initial use by treatment-naïve patients
  - As effective as highest dose TZD
  - New data demonstrate sustained efficacy out to 2 years
  - Additional -1.1% improvement when added to patients failing to achieve HbA1c goal on metformin

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## Galvus® – a potent and highly selective DPP-4 inhibitor (2/2)

- **Excellent tolerability**
  - Low incidence of hypoglycemia
  - Superior GI tolerability vs. metformin (especially diarrhea)
  - Trend to reduce GI effects when added on to metformin
  - Weight loss compared to TZD
  - Placebo-like edema with less edema than pioglitazone
- **Islet-cell effects suggest potential for long-term disease modification**
  - Nearly 5 fold increase in beta-cell function
  - Improvement in insulin sensitivity by euglycemic clamp
  - Improves first-phase insulin response
  - Meaningful reductions of BP overall and in hypertensive patients

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## Galvus® – GLORIOUS outcomes program

A program of five studies planned to demonstrate the disease modification potential of Galvus®

Study	Summary
1	Prevent progression to type 2 diabetes in patients with impaired fasting glucose or impaired glucose tolerance
2	Prevent progression to type 2 diabetes in Asian patients with impaired glucose tolerance
3	Slow progression and demonstrate long-term durability in early type 2 diabetes
4	Slow progression and demonstrate long-term durability in combination with metformin in type 2 diabetes
5	Prevention of progression to diabetes and reduction of cardiovascular events in high CV risk patients

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## Novartis CVM launch portfolio – best in class



- Powerful BP control through two complementary actions
- Up to 43 mmHg drop with single pill convenience
- Positive Opinion from CHMP 17 November



- First direct renin inhibitor
- Potential to become a New Standard in hypertension



- FDA action expected in February 2007
- The most widely studied DPP IV inhibitor
- As effective as a TZD without the limitations

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