ADA Analyst Presentation
Saturday 9th June

Carlo Russo
Senior Vice-President & Albiglutide Team Leader, GSK
# Agenda

| Welcome & introduction to the Harmony Clinical Programme | Carlo Russo  
Senior Vice-President, Albiglutide Team Leader |
|----------------------------------------------------------|----------------------------------------------------------|
| Results from Harmony 6 & Harmony 7 | Dr Richard E. Pratley  
Director, Florida Hospital Diabetes Institute, USA |
| The Evolution of Type 2 Diabetes Treatment | Professor Philip Home  
Professor of Diabetes Medicine, Newcastle University, UK |
<p>| Q&amp;A discussion | |
| Refreshments | |</p>
<table>
<thead>
<tr>
<th>Study</th>
<th>Background Therapy</th>
<th>Comparators</th>
<th>No. of Patients Randomized</th>
<th>Primary Endpoint</th>
<th>Estimated LPLV</th>
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<tbody>
<tr>
<td>H2H vs liraglutide</td>
<td>Metformin, pioglitazone, glimepiride, or combination</td>
<td>Liraglutide</td>
<td>841</td>
<td>32 weeks</td>
<td>COMPLETED Presented at ADA 2012</td>
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<td>HARMONY 7</td>
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<td>Add-on to insulin glargine</td>
<td>Basal insulin glargine</td>
<td>Prandial insulin</td>
<td>586</td>
<td>6 months</td>
<td>COMPLETED Presented at ADA 2012</td>
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<td>HARMONY 6</td>
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<td>Renal impairment</td>
<td>Metformin, pioglitazone, glimepiride, or combination</td>
<td>Sitagliptin</td>
<td>507</td>
<td>6 months</td>
<td>Jul 2012</td>
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<td>HARMONY 8</td>
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<td>Monotherapy</td>
<td>Diet &amp; exercise (treatment-naïve patients)</td>
<td>Placebo</td>
<td>309</td>
<td>1 year</td>
<td>Jan 2013</td>
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<td>HARMONY 2</td>
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<td>Add-on to pioglitazone</td>
<td>Pioglitazone ± metformin</td>
<td>Placebo</td>
<td>310</td>
<td>1 year</td>
<td>Jan 2013</td>
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<td>Add-on to metformin + SU</td>
<td>Metformin + glimepiride</td>
<td>Pioglitazone or placebo</td>
<td>685</td>
<td>1 year</td>
<td>Mar 2013</td>
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<td>HARMONY 5</td>
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<td>H2H vs insulin glargine</td>
<td>Metformin or metformin + SU</td>
<td>Insulin glargine</td>
<td>779</td>
<td>1 year</td>
<td>Feb 2013</td>
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<td>HARMONY 4</td>
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<td>Add-on to metformin</td>
<td>Metformin</td>
<td>Sitagliptin, glimepiride, or placebo</td>
<td>1049</td>
<td>2 years</td>
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Harmony 6 Results
Add-on to Insulin Glargine vs prandial Lispro Insulin in Subjects With Type 2 Diabetes Mellitus

Richard Pratley MD
Director, Florida Hospital Diabetes Institute & Diabetes Professor, Sanford Burnham Medical Research Institute, Florida, US
Harmony 6 Study Design

Study Design

- Randomized, open-label active controlled, parallel group study
- Optional up-titration of albiglutide 30→50 mg weekly, starting at Week 8
- Titration of basal and pre-prandial insulin, to meet pre-specified protocol criteria
- Primary Endpoint: 26 weeks
- Study Duration: 52 weeks
- 586 randomized; 566 received treatment

Primary Endpoints:
- Non-inferiority vs lispro
- Superiority vs lispro, if non-inferiority met

Other Endpoints:
- Time to, and % requiring rescue
- Weight
- Hypoglycemia
- QoL
- FP
Overall Conclusions

- **Efficacy**
  - Both albiglutide and lispro produced clinically significant reductions in HbA1c from baseline (-0.82 % vs -0.66%, respectively)
  - Albiglutide met the non-inferiority endpoint for HbA1c vs. lispro (p<0.0001) at 26 weeks, and only just missed showing superiority (p=0.0533)
  - The FPG trend mirrored the HbA1c curve, with greater reduction in the albiglutide treatment arm than the pre-prandial Lispro arm
  - The observed weight change at Week 26 in the albiglutide arm was statistically greater than the pre-prandial insulin arm (-0.73 kg vs +0.81 kg)
  - No meaningful difference between treatment groups when viewed by subgroup (background OAD, gender, race, etc)
  - Efficacy and weight loss in the albiglutide arm were maintained through 52 weeks
Overall Conclusions

- **Safety**
  - The 52 week nausea/vomiting rates for albiglutide were consistent with Harmony 7. Rates were higher in the albiglutide arm compared to Lispro:
    - Nausea: 13.0% with albiglutide and 2.1% with Lispro
    - Vomiting: 7.0% with albiglutide and 1.4% with Lispro
    - Hypoglycemia at week 52: 32.6% with albiglutide and 49.8% with Lispro
    - Three events of severe hypoglycemia in the pre-prandial Lispro arm vs zero in the albiglutide arm
  
- Rates of events of special interest at Week 52 with albiglutide were consistent between this study and Harmony 7:
  - Injection site reactions: 9.5% with albiglutide and 5.3% with Lispro
  - Acute pancreatitis: Zero events with both albiglutide and Lispro
  - Thyroid nodules/neoplasm: one subject who received one dose of albiglutide with calcitonin elevated at baseline & subsequently determined to be MEN positive, and no subjects with Lispro
Harmony 7 Results
A Randomized, Open-Label, Parallel-Group, Multicenter Study to Determine the Efficacy and Safety of Albiglutide as Compared With Liraglutide in Subjects With Type 2 Diabetes Mellitus
Harmony 7 Study Design

Study Design

- Randomized, double-blind, active-controlled, parallel-group study
- Titration protocol of albiglutide 30 → 50 mg QW and liraglutide (1.2 → 1.8 mg QD)
- Study duration: 32 weeks
- Primary endpoint: Change in HbA\textsubscript{1c} from baseline as compared with liraglutide

Primary endpoints
- Noninferiority (≥ superiority) vs liraglutide

Other endpoints
- FPG
- Time to rescue
- Weight
- Hypoglycemia
- QoL

Inadequate control on Met, TZD, SU, or combination
N = 800
HbA\textsubscript{1c}: 7%-10%
Overall conclusions

- Liraglutide (once daily) and albiglutide (once weekly) clinically and statistically reduced HbA1c from baseline. \((-0.78\% \text{ with ALBI and } -0.99\% \text{ with LIRA [treatment difference: } 0.21\% P < .001]\))

- The treatment difference did not meet non-inferiority criteria. (95% CI: 0.08-0.34%).

- Albiglutide was generally well tolerated and had a better GI tolerability than liraglutide.

- Both agents showed reductions in weight loss, but this was better with liraglutide (LIRA \([-2.19 \text{ kg}]\) greater than ALBI \([-0.64 \text{ kg}]\)).
Type II diabetes: An evolving treatment landscape

Professor Philip Home
Professor of Diabetes Medicine, Newcastle University, UK