ERS Investor & Analyst Event
Munich
Tuesday 9th September 2014
Darrell Baker
SVP, Global Head of Respiratory
<table>
<thead>
<tr>
<th>Agenda</th>
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</thead>
<tbody>
<tr>
<td><strong>GSK’s Respiratory Portfolio</strong></td>
<td>Darrell Baker, Global Head of Respiratory at GSK</td>
<td>13:45 – 14:00</td>
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<tr>
<td><strong>Eosinophils Research in COPD</strong></td>
<td>Professor Neil Barnes, Respiratory Franchise Medical Head at GSK</td>
<td>14:00 – 14:10</td>
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<tr>
<td><strong>Eosinophils – Clinical Experience in Severe Asthma</strong></td>
<td>Professor Ian Pavord, University of Oxford</td>
<td>14:10 – 14:25</td>
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<td><strong>Mepolizumab Phase III data in Severe Asthma</strong></td>
<td>Steven Yancey, Medicine Development Leader at GSK</td>
<td>14:25 – 14:45</td>
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<td><strong>Q&amp;A</strong></td>
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<td>14:45 – 15:45</td>
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Respiratory portfolio in transition – new portfolio provides platform for continued market leadership

£21bn global respiratory market

33% GSK share of global market

Anoro Ellipta allows access to £4.9bn bronchodilator market

Breo Ellipta approved & launched
Anoro Ellipta approved & launched
Incruse Ellipta approved
Arnuity Ellipta approved

5 additional products in late stage development
• mepolizumab
• ICS/LABA/LAMA (closed triple)
• VI monotherapy
• ICS/LAMA
• MABA

Source: GSK R3 Model based on IMS Health June 2014
Breo Ellipta / Relvar Ellipta launches underway

- Approved in over 50 markets globally
- Launched in 19 markets including US (for COPD only), Japan (asthma only), UK, Germany, Denmark, Sweden, Mexico, Chile, Brazil.

US access building as at July:
- Commercial: ~50%
- Medicare Part D: ~70%

US market shares (42 weeks to 22 Aug14)
- NBRx is 4.3% overall and 11.1% for pulmonologists
- TRx is 1.18%

- BREO ELLIPTA filed in US for asthma in June 2014
- SUMMIT recruitment complete; data now expected in 2015
Anoro Ellipta launches underway

The first once-daily dual bronchodilator in US for treatment of COPD

- Approved in 38 markets globally
- Launched in 8 markets including US, Canada, UK, Germany, Chile, Denmark, & Japan

US access building as at July:
- Commercial: ~75%
- Medicare Part D: ~30%

US market shares (18 weeks to 22 Aug 14):
- NBRx is 4.1% overall and 9.4% for pulmonologists
- TRx is 0.8%

- Anoro v tiotropium H2H data – significantly improved lung function (trough FEV1 at Day 169) compared with tiotropium.
Upcoming catalysts in our respiratory franchise

- *Incruse* approved in US and Europe – launch anticipated by end of the year
- *Arnuity* approved in US – launch anticipated in 2015
- Mepolizumab severe asthma filing by end of 2014
- Phase 3 studies commenced in Eosinophilic Granulomatosis with Polyangiitis in Feb 2014 and COPD in April 2014
- Closed triple for COPD (UMEC/FF/VI) Ph III IMPACT started July 2014
- Breo Ellipta, PDUFA anticipated Q2 for asthma file
- SUMMIT recruitment completed in March 2014, read out in 2015
- Salford Lung Studies:
  - COPD recruitment due to complete end 2014; 12 month treatment period
  - Asthma recruiting
Seretide comparator study DB2116134
Anoro Ellipta vs. Seretide

- A 12-week, randomised, double-blind, double-dummy, multi-centre study to evaluate the efficacy and safety of Anoro Ellipta and Seretide in subjects with COPD

Primary objective
- To compare the efficacy (defined by 0-24hr wm FEV$_1$) of Anoro Ellipta 55/22mcg* once-daily and Seretide 500/50mcg twice-daily in subjects with COPD who have a history of infrequent exacerbations

Secondary objective
- To compare the effects of Anoro Ellipta and Seretide on safety and patient-reported outcomes relating to health-related quality of life in subjects with COPD

Patients and treatment
- Patients were randomised to Anoro Ellipta 55/22mcg or Seretide 500/50mcg in a 1:1 ratio

Main entry criteria
- Age 40+
- COPD as per American Thoracic Society (ATS)/European Respiratory Society (ERS) definition
- Smoking history ≥10 pack-years
- Post-bronchodilator FEV$_1$ ≤70% predicted
- No history of ≥1 COPD exacerbations within 12 months, that required oral corticosteroids, antibiotics and/or hospitalisation
- Use of ICS and other ICS/LABA (non-FSC) was not permitted during the trial
- LABAs, LAMAs, theophyllines, PDE4s, LTMs, and ipratropium also not allowed
- mMRC score ≥2 (0–4 point scale) – walks slower than people of the same age because of breathlessness, or has to stop for breath when walking at own pace
- No current diagnosis of asthma

*Each UMEC delivered dose of 55mcg corresponds to pre-dispensed dose of 62.5mcg. Each VI delivered dose of 22mcg corresponds to a pre-dispensed dose of 25mcg

Anoro Ellipta significantly improved FEV$_1$ compared with Seretide

Primary endpoint: WM FEV1 (0–24h) on Day 84

- Anoro Ellipta showed a statistically significant improvement in mean change from baseline WM FEV$_1$ (0–24h) compared with Seretide by 80ml (95% CI: 46, 113; p<0.001) in subjects with moderate to severe COPD and infrequent COPD exacerbations$^1$

Patient profiles for the new portfolio

**COPD**

**Patients with COPD who are breathless**

*Anoro®* vs *Ellipta®*
- Initial maintenance bronchodilator treatment for patients with COPD who are breathless
- Age: 60
- Diagnosed with COPD: 2 years ago
- Former smoker: 24 pack-years
- FEV₁: 70% predicted
- Primary clinical concern: breathlessness
- Primary lifestyle concern: being able to continue working until his planned retirement in 5 years

- Until recently enjoyed a relatively active lifestyle as breathlessness was controlled with rescue medication
- Can no longer complete everyday physical activities like walking up stairs or going to the shops, without stopping to catch his breath
- His quality of life is deteriorating, and he needs a treatment that can offer him the chance of continuing to work

**COPD**

**Patients with COPD who have a history of exacerbations**

*Relvar®* vs *Ellipta®*
- For symptomatic treatment of patients with COPD with a FEV₁ < 70% predicted normal (post-bronchodilator) and a exacerbation history
- Age: 59
- Diagnosed with COPD: 6 months ago
- Current smoker: 10 cigarettes/day
- FEV₁: 54% predicted
- Primary clinical concern: a history of exacerbations
- Primary lifestyle concern: increasing anxiety about his condition

- Had one course of oral steroids for an exacerbation in the winter months, now using SABA as needed
- Jorge is adjusting to life with a confirmed COPD diagnosis, and trying to quit smoking
- However, his recent exacerbation has set him back considerably. He needs a treatment that will reduce his risk of exacerbating again

**COPD**

**Patients with COPD who have a history of exacerbations and require further symptom relief**

*Incruse®* vs *Ellipta®* in combination with an ICS/LABA
- For patients with COPD with a history of exacerbations who require further symptom relief
- Age: 58
- Diagnosed with COPD: 8 years ago
- Former smoker: 30 pack-years
- FEV₁: 44% predicted
- Primary clinical concern: continuing symptoms and a history of exacerbations
- Primary lifestyle concern: struggling to walk which is preventing her from doing daily activities and is slowly becoming housebound

- Has a history of exacerbations, one of which left her hospitalised
- She is also increasingly breathless when walking
- Due to her breathlessness, her activity levels have fallen, reducing her fitness and increasing her breathlessness further

**Asthma**

**Patients with asthma who are uncontrolled on ICS and "as needed" SABAs**

*Relvar®* vs *Ellipta®*
- For patients with asthma who are uncontrolled on ICS and "as needed" SABAs
- Age: 39
- Diagnosed with asthma: 25 years ago
- Former smoker: No
- FEV₁: 78%
- Primary clinical concern: ongoing asthma symptoms
- Primary lifestyle concern: doesn’t want to be slowed down by her asthma

- Olivia is a busy mum of three with a full-time job
- She ‘puts up’ with her symptoms as she doesn’t feel she has the time to manage them properly
- Dislikes being on inhalers as she feels tied to asthma, but tries to remember to use them

*Incruse® Ellipta® for symptom relief, ICS/LABA to reduce exacerbation risk. *Relvar®* Ellipta® Ellipta® for symptom relief, ICS/LABA to reduce exacerbation risk. Please refer to the EU, the only ICS/LABA that has been studied in combination with *Incruse®* Ellipta® is *Relvar®* Ellipta®.
Steven Yancey
Medicine Development Leader, mepolizumab
Objectives/design of the Phase III asthma programme

MEA115588 (MENSA)

To evaluate the efficacy of mepolizumab 75 mg intravenous (i.v.) or 100 mg subcutaneous (SC) every 4 weeks versus placebo on the frequency of clinically significant exacerbations in adult and adolescent subjects with severe eosinophilic asthma.

MEA115575 (SIRIUS)

To compare the effects of 100 mg subcutaneous (SC) mepolizumab adjunctive therapy with placebo on reducing the use of maintenance oral corticosteroids (OCS) in systemic corticosteroid dependent subjects with severe eosinophilic asthma.
Asthma and eosinophilic inflammation

Over-expression of eosinophils
### MENSA: Design and patient identification

**Visit 1:** Random Assignment 1:1:1

- **Visit 2 Run-in period**
  - Week -1 to -6

**Investigational Product Administered**

- **Visit 2**
  - Random Assignment 1:1:1
  - **Visit 1 Screen**
  - **Week Visit** 0 2 4 3 5 8 6 12 16 7 20 8 24 9 32 10 40 **Follow-up**

**Primary Efficacy Endpoint**

- **Week** 0 4 8 12 16 20 24 28 32 40
- **Visit** 2 3 4 5 6 7 8 9 10

**Investigational Product Administered**

- Mepolizumab 75mg IV and Placebo SC
- Mepolizumab 100mg SC and Placebo IV
- Placebo IV and Placebo SC
Results: Primary Endpoint

Reduction in Exacerbations

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Placebo</th>
<th>mepolizumab 75 mg IV</th>
<th>mepolizumab 100 mg SC</th>
</tr>
</thead>
</table>

Cumulative number of exacerbations

- Placebo
- mepolizumab 75 mg IV
- mepolizumab 100 mg SC

Time (weeks)

Cumulative number of exacerbations

- Placebo: Linear increase
- mepolizumab 75 mg IV: Steeper increase
- mepolizumab 100 mg SC: Steeper increase

p < 0.001
Secondary Endpoint

Changes in Pre-BD FEV$_1$

Errors bars represent 95% CI

p<0.001
Secondary Endpoint
Changes in St George’s Respiratory Questionnaire

- Placebo: 75 mg IV
- 100 mg SC

Change from baseline in SGRQ score:
- Placebo: 9 points difference*
- 75 mg IV: 15.4 points difference*
- 100 mg SC: 16 points difference*

*p<0.001
Key Results by Higher Blood Eosinophil Counts
(≥500 cells/µL)

Figure S4A. Reduction of Clinical Significant Exacerbations Across the Three Treatment Groups at Week 32

- Placebo: 2.26 exacerbations per year
- 75 mg IV: 0.58 exacerbations per year
- 100 mg SC: 0.46 exacerbations per year

80% difference
74% difference

Figure S4B. Change from Baseline in Pre- and Post-bronchodilator FEV₁ Compared to Placebo at Week 32

- Pre-BD: Placebo 134 mL, 75 mg IV 319 mL, 100 mg SC 266 mL
- Post-BD: Placebo 91 mL, 75 mg IV 409 mL, 100 mg SC 313 mL

222 mL
# Summary of Adverse Events

<table>
<thead>
<tr>
<th>Event Category</th>
<th>Placebo N=191</th>
<th>mepolizumab IV N=191</th>
<th>mepolizumab SC N=194</th>
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</thead>
<tbody>
<tr>
<td><strong>All AEs, n (%)</strong></td>
<td>158 (83)</td>
<td>161 (84)</td>
<td>152 (78)</td>
</tr>
<tr>
<td>Non-asthma events</td>
<td>157 (82)</td>
<td>161 (84)</td>
<td>152 (78)</td>
</tr>
<tr>
<td>Asthma worsening</td>
<td>29 (15)</td>
<td>18 (9)</td>
<td>13 (7)</td>
</tr>
<tr>
<td>Drug-related*</td>
<td>30 (16)</td>
<td>33 (17)</td>
<td>39 (20)</td>
</tr>
<tr>
<td>Led to withdrawal</td>
<td>4 (2)</td>
<td>0</td>
<td>1 (&lt;1)</td>
</tr>
<tr>
<td><strong>SAEs, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>On-treatment</td>
<td>27 (14)</td>
<td>14 (7)</td>
<td>16 (8)</td>
</tr>
<tr>
<td>Investigator assigned as drug-related</td>
<td>1 (&lt;1)</td>
<td>0</td>
<td>1 (&lt;1)</td>
</tr>
<tr>
<td>Fatal</td>
<td>1 (&lt;1)</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*Status assigned by the investigators while masked to treatment group
SIRIUS: Design and patient identification

Primary Efficacy Endpoint assessed at week 24 (Exit Visit)

Investigational Product SC every 4 weeks

Visit 1
-8 to -3 weeks

Visit 2

Week
0
3
4
5
8
6
12
7
16
8
20
24

OCS Optimisation Phase
Induction Phase
OCS Reduction Phase
Maintenance Phase

mepolizumab 100mg SC
Placebo SC
Results: Primary endpoint of OCS reduction

OR = 2.39 (95% CI, 1.25-4.56)  
P = 0.008

Other: no decrease in OCS dose, or lack of control during weeks 20-24 or withdrawal from treatment
Results: Median OCS reduction during the study

Median OCS change from baseline (%)

- Placebo
- mepolizumab 100mg SC

* P=0.007
Changes in Asthma Control Questionnaire

![Graph showing changes in ACQ-5 score over time for Placebo and mepolizumab 100mg SC. The p-value is 0.004.](image)

Mean ACQ-5 Score

Time (weeks)

- Placebo
- mepolizumab 100mg SC

p=0.004
Reduction in Exacerbations

Exacerbation rate per year

Placebo

2.2

mepolizumab

1.4

32 % reduction*

* P=0.042
## Summary of Adverse Events

<table>
<thead>
<tr>
<th>Adverse Event Type</th>
<th>Number (%) of Patients</th>
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<tbody>
<tr>
<td></td>
<td>Placebo N=66</td>
</tr>
<tr>
<td>All AEs</td>
<td></td>
</tr>
<tr>
<td>Non-asthma events</td>
<td>60 (91)</td>
</tr>
<tr>
<td>Asthma worsening</td>
<td>8 (12)</td>
</tr>
<tr>
<td>Drug-related*</td>
<td>12 (18)</td>
</tr>
<tr>
<td>Led to withdrawal from study</td>
<td>3 (5)</td>
</tr>
<tr>
<td>SAEs</td>
<td></td>
</tr>
<tr>
<td>On-treatment</td>
<td>12 (18)</td>
</tr>
<tr>
<td>Fatal</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Any on-treatment AE</td>
<td>61 (92)</td>
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</table>

*Status assigned by the investigators while masked to treatment group
Conclusions – Asthma

**MENSA**

mepolizumab: PhIII data demonstrated potential as an add-on therapy in patients with severe eosinophilic asthma, producing a **clinically and statistically significant (~50%) reduction** in the **exacerbation rate** compared with placebo

mepolizumab produced a **similar treatment effect** in exacerbations, lung function and quality of life measures regardless of the **route of administration (IV or SC)**

mepolizumab was **well-tolerated** with a safety profile similar to that of placebo

**SIRIUS**

mepolizumab: PhIII data in patients with severe eosinophilic asthma and on daily use of oral corticosteroids, demonstrated potential to **reduce OCS while maintaining control**

The validity of this OCS reduction approach was supported by **stability of FEV₁ and ACQ-5** over the course of the study

mepolizumab was **well-tolerated** with a safety profile similar to that of placebo

mepolizumab is in development for severe eosinophilic asthma in patients who exacerbate despite high-dose oral or inhaled corticosteroids (ICS) and an additional controller such as long-acting beta-2 agonist. In addition, mepolizumab is being investigated in COPD and Eosinophilic Granulomatosis with Polyangiitis (EGPA). mepolizumab is not approved anywhere in the world