Focus on Patients

Patient well-being at the heart of all we do

Be patient focused: Put patients and consumers first
Two key approaches at GSK, in parallel

- **Build trust**
  - No trust, no engagement
  - Trust us, trust your doctor, trust the medicine
  - Trust the data

- **Engage, right through the process**
  - End-to-end-patient connectivity, from early development, to established medicines, to safety monitoring
Transparency, sales and marketing practices

Clinical Transparency

- Online Clinical Trial Register launches
- Scope of the Clinical Study Register expands
- First voluntary posting of HCP research payments in US (1Q2011)
- Clinical Register reaches 5,000 results summaries; 1,000 monthly visitors
- All Trials Campaign: commit to publish clinical study reports
- GSK first to grant access to anonymised patient-level data
- GSK patient level data access site becomes multi sponsor portal

Sales and Marketing Practices

- US voluntarily commits to making HCP payments public
- First report made public of HCP payments in US
- US adoptions strict guidelines for quality CME grants
- New sales compensation model in the US
- Australia starts reporting HCP aggregate spend
- UK ends rewarding reps on sales targets and starts disclosing aggregate HCP payments
- Global announcement to remove individual sales targets and phase out payments for external speakers/ HCP convention travel from 2016
- China adopts strict HCP engagement rules and ends rewarding reps on sales targets
- European EFPIA Code named HCP disclosure begins 2015
- All GSK markets on new Global Sales Compensation Model
- No more payments to external speakers
Patient Involvement Through Drug Discovery and Development

**Commit to target**
- Target validation
- Lead discovery
- Lead optimisation

**Commit to candidate**
- Pre-clinical evaluation

**First time to human**
- Phase I
- Phase IIA

**Commit to Medicine Development**
- Phase IIIB
- Phase III

**Commit to Phase III**
- Registration and launch

**Commit to File and launch**
- Phase IV
- Post-marketing Surveillance

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**Device design (e.g. Ellipta)**

**PRO development**
**PRO validation and implementation**

**Disease area understanding**
- Exit interviews
- FoTP seminars

**Epidemiology, Observational studies and patient registries**

**Plain language summaries**

**End of trial questionnaire**
- Patients in Med. Vision Workshops

**Protocol input**
- Patient feedback on PRO messages/labels

**Greater disease area understanding, especially earlier in discovery and development:**
(pre-C2C, e.g. unmet need, current treatment, effectiveness/sub-populations)

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**Informed consent**

**Inform patient recruitment & patient engagement plans**

**Patient preference assessment**

**Patient input on patient counselling information, package inserts, med guides, instructions, devices**

**Protocol input on study design: patients views on potential barriers for study participation; feedback on endpoints**
- Patients on ad-comms, contributing to Benefit-Risk assessment

**Patient input on governance decisions at lifecycle transition points**

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Key enabler: Patient access via strategic partnerships with patient advocacy group

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**Area of established patient involvement**
**Area of recent patient involvement**
**Opportunity for greater patient involvement**
Patient Involvement Through Drug Discovery and Development

Benefits

- Identification of patient need and value drivers, enabling more informed decisions on target choices and required asset profiles for go/no go decisions
- Shorter trial cycle time & quicker to regulatory submission
- Patient preference demonstrated and communicated in label
- Better decision making & prioritization – reducing risk for development plans
- More products of value, greater access for patients
- Improved adherence & outcomes
- More relevant study designs & endpoints, improved recruitment & retention
Capturing the Patient Experience in R&D

GSK Examples

- **Real-World Clinical Studies** – *capturing real-world effectiveness*

- **PROs** – *understanding what and how to measure what is important to patients*

- **Focus on the Patient Seminars** – *capturing patient needs into medicine development*

- **End of trial questionnaires** - *capturing patient feedback on the design and execution of our trials*

- **Digital Health** – *reducing patient burden and capturing improved patient insights*
Capturing the Patient Experience in R&D

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- **Digital Health** – reducing patient burden and capturing improved patient insights
The Salford Lung Study is the world's first pragmatic, real-world study initiated on what was, at the time, a pre-licence medicine. The study aims to:

- Compare, in a real-world setting, the safety and efficacy of Relvar Ellipta, with existing maintenance therapy for COPD and asthma in a general practice setting in the UK
- Provide relevant and important information for clinicians, healthcare providers, payers and patients

<table>
<thead>
<tr>
<th>Salford Lung Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evidence representing medicines in the real world</td>
</tr>
<tr>
<td>Real world study</td>
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<tr>
<td>Real-time integrated data</td>
</tr>
<tr>
<td>Effectiveness</td>
</tr>
<tr>
<td>Broad population – age, comorbidities, disease definition</td>
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<tr>
<td>Close monitoring</td>
</tr>
<tr>
<td>Open label</td>
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<tr>
<td>Drugs prescribed and collected in usual way</td>
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<tr>
<td>Set in normal care</td>
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<tr>
<td>Health Outcome and Utilisation Endpoints i.e. Real life</td>
</tr>
<tr>
<td>Unique collaboration</td>
</tr>
<tr>
<td>Minimal intrusion</td>
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<tr>
<td>One geographical location</td>
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</table>

<table>
<thead>
<tr>
<th>RCTs</th>
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<tbody>
<tr>
<td>Efficacy</td>
</tr>
<tr>
<td>Double dummy</td>
</tr>
<tr>
<td>Double blind</td>
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<tr>
<td>Strict inclusion criteria</td>
</tr>
<tr>
<td>Exclusions</td>
</tr>
<tr>
<td>Adherence encouraged</td>
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</tbody>
</table>

Science to answer specific questions

Traditional Efficacy Endpoints
Traditional clinical trial

Both types of randomised control trials (RCTs) are a robust and rigorous way of studying a COPD medicine, with many studies falling somewhere on their spectrum. Both are equally important and serve distinct scientific purposes, answering different questions.

<table>
<thead>
<tr>
<th><strong>Focus on Efficacy</strong></th>
<th><strong>Focus on Effectiveness</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>by measuring a medicine’s impact under controlled conditions</td>
<td>by measuring a medicine’s impact under close to normal conditions</td>
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</table>

<table>
<thead>
<tr>
<th><strong>Medication compared with</strong></th>
<th><strong>Medication compared with</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>placebo or standard treatment</td>
<td>patients’ usual care</td>
</tr>
</tbody>
</table>

**Standardised patient experience**

- tightly controlled
  - Doctor and patient ‘blinded’ to study medication
  - Closely monitored with little ability for usual doctor to interfere with treatment
  - Adherence to medicine closely monitored

**Patient experience**

- reflects near normal life
  - Usual doctor and pharmacist manages the patient’s condition
  - Potential for doctor to influence patient’s outcome
  - Normal adherence rate, which can often be low

**Selected population**

- population – likely to respond to the medication

**Non-selective**

- population - broad and inclusive group with varied lifestyles and comorbidities

**Set amount of standardised data allows quick comparison with other efficacy trials**

**Traditionally gold standard of clinical research**

**Large volume of non-standard data captured in patients closely reflecting those treated in everyday clinical practice**

**New pioneering approach to clinical trials, additive to findings from randomised control trials**

Required by **drug approval** regulators

Provides highly relevant data for **healthcare community, prescribers and decision makers**

Salford Lung Study

**Traditionally gold standard of clinical research**

Focus on **Efficacy** by measuring a medicine’s impact under controlled conditions

Focus on **Effectiveness** by measuring a medicine’s impact under close to normal conditions

Medication compared with placebo or standard treatment vs medication compared with patients’ usual care

Standardised patient experience tightly controlled

- Doctor and patient ‘blinded’ to study medication
- Closely monitored with little ability for usual doctor to interfere with treatment
- Adherence to medicine closely monitored

Patient experience reflects near normal life

- Usual doctor and pharmacist manages the patient’s condition
- Potential for doctor to influence patient’s outcome
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Selected population population – likely to respond to the medication

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RF/FFT/0029/16a Date of preparation: April 2016
COPD Salford Lung study in numbers

The COPD Relvar/Breo® Salford Lung Study is an RCT conducted in everyday clinical practice

- 2,802 COPD patients
- 130 pharmacies involved
- >235 million rows of data
- 80 GP practices
- 1 electronic health medical record system
- 3,000 people trained as part of study
Primary endpoint: Moderate/severe exacerbation (defined by oral steroid (and/or antibiotic use) +/− hospitalisations)
Secondary endpoints: Serious Pneumonias, Healthcare utilisation, COPD Assessment Test (CAT)

2800 patients
- Patients in primary care, aged 40+
- GP diagnosis of COPD
- Taking ICS, LABA, LAMA alone or in combination
- Exacerbation in last 3 years
- Consented

Randomised

New Rx open label

Visit 2
Routine respiratory review
Device instruction
CAT

Visit 6
Routine respiratory review
CAT

12 months of normal care

Existing maintenance Rx, ICS, LABA, LAMA

Constant real-time data collection of all HC interventions/safety monitoring
Relvar/Breo Salford Lung study in COPD

Headline Results

• The Relvar/Breo SLS met its primary end point and demonstrated superior reduction of 8.41% (CI 1.12, 15.17) in the rate of moderate/severe exacerbations compared to usual care (p=0.025). 86% of the patients were on an ICS-containing regimen as part of their usual care.

• Incidence of SAEs were similar between groups (29% FF/VI, 27% usual care) and non-inferiority was confirmed for FF/VI vs usual care on SAEs of pneumonia (7% vs 6%) 5.

• FF/VI is the only ICS/LABA which provides 24hr continuous efficacy in a once daily dose, combined with a patient preferred device.

• These attributes of FF/VI deliver meaningful patient benefits in everyday clinical practice when compared to other COPD treatments, including BD ICS/LABAs.

Capturing the Patient Experience in R&D

GSK Examples

– Real-World Clinical Studies – capturing real-world effectiveness

– PROs – understanding what and how to measure what is important to patients

– Focus on the Patient Seminars – capturing patient needs into medicine development

– Digital Health – reducing patient burden and capturing improved patient insights

– End of trial questionnaires - capturing patient feedback on the design and execution of our trials
Patient Focused Outcomes: Where We Obtain Patient Input to Show We Help Patients Do more and Feel Better

**Phase I**
- Qualitative Research with target patients
- Select or develop new or adapt existing measures

**Phase II**
- Pilot PFOs
- Exit Interviews

**Phase III**
- Include PFOs in pivotal studies

**Example PFO Activities**
- What is important from patient perspective and how & what to measure
- Potential areas of unmet need and differentiation possibilities
- Informed, credible input into target product profile, asset development/ study designs

**VALUE**
- Preliminary evidence of impact & potential for differentiation from patient perspective
- Possible publications
- Updated input into target product profile & development plans

- Documented evidence of impact / differentiation from patient perspective to substantiate
- PRO claims possibly in labels
- Publications
- Evidence for value dossiers, payers and HTAs
**Danirixin (GSK1325756): an oral CXCR2 antagonist**

*ER-S™:COPD is a daily digital diary which allows data interrogation in real time*

- Blocks chemokine receptor on neutrophils and other cell types (CXCR2)
- Target engagement demonstrated with danirixin (neutrophil activation biomarker, CD11b)
- Competitor compounds produced clinical effects, but with reduction in blood neutrophils
- In the clinic, danirixin has efficacy at a dose not associated with reduced blood neutrophils
- Influenza infection Phase IIa study ongoing

1. Am J Respir Crit Care Med 2015;191:1001–1011

**Status:** Phase IIa  
**Indication:** Symptomatic COPD  
**Planned Filing:** 2021-2025

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**Real-time digital data demonstrate improvement of symptoms with danirixin in symptomatic COPD (frequent exacerbators)**

![Graph showing Total Symptom Score (ERS™:COPD) over days for placebo and danirixin 75mg](image)

- Placebo (n=35 in study)  
- danirixin 75mg (n=35 in study)

GSK, data on file (study 200163)
PROs: Measuring what Matters to Patients

Development of an RA Symptom and Impact Daily Diary

- Response to treatment in rheumatoid arthritis traditionally evaluated with outcome measures comprising the RA core set:
  - Pain, disease activity (Patient Global Assessment), physical function (HAQ-DI)
  - Fatigue and health-related quality of life (HRQL) may additionally be assessed
- Holistic assessment of response to treatment and optimised ongoing disease management require consideration of all outcomes of relevance to RA patients
- A review of the literature identified 42 PROs, as well the following key symptoms and impacts:

<table>
<thead>
<tr>
<th>Pain</th>
<th>Mobility</th>
<th>Loss of balance</th>
<th>Physical function</th>
<th>Emotional impact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>Swelling</td>
<td>Visible signs</td>
<td>Everyday activities</td>
<td>Fear of the future</td>
</tr>
<tr>
<td>Sleep</td>
<td>Tender joints</td>
<td>Deformity</td>
<td>Independence</td>
<td>Relationships</td>
</tr>
<tr>
<td>Lack of energy</td>
<td>Grip force</td>
<td>Recovery</td>
<td>Leisure activities</td>
<td>Wellbeing</td>
</tr>
<tr>
<td>Stiffness</td>
<td>Muscle strength</td>
<td>Disease stability</td>
<td>Participation</td>
<td>Return to normality</td>
</tr>
</tbody>
</table>

- Despite numerous existing PRO instruments, there remains an unmet need for a comprehensive PRO to assess key symptoms and impacts in RA:
  - Developed with significant patient input
  - With a short recall period (past 24 hours) to capture symptom variability
  - Developed according to best practice as described in the FDA PRO Guidance (2009)
PROs: Measuring what Matters to Patients

Development and Application

Objectives
- Identify patient-relevant concepts related to the symptoms and impacts of rheumatoid arthritis
- Develop or modify an existing PRO instrument to measure the concepts identified.
- PRO to be developed according to best practice, as described in the FDA PRO Guidance (2009)

PRO Development
- Targeted literature review of RA PRO instruments and qualitative research conducted with RA patients
- Develop draft item pool of concepts related to symptoms and impacts of RA
- Clinician review and input on draft item pool
- Patient input: Concept elicitation and cognitive debriefing of draft RA instrument
- Final PRO instrument: 13 items assessing symptoms (joint pain, joint stiffness, energy and physical tiredness), and 3 items that measure the impact of symptoms

Application
- Use as an endpoint in clinical research as complementary evidence of treatment benefit to other clinical and patient-reported outcomes
- Draft RA PRO currently being piloted in global ph2b RA to explore correlations between changes in physical activity (measured using actigraphy) and changes in RA symptoms and other clinical outcomes
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Focus On The Patient Seminars: Cutaneous Lupus

Research Goal:

• To understand how patients view their current status
• To seek insight around whether they would take a new topical treatment, and how it would fit into current treatment regimes
• To seek insight into development of experimental medicine research studies and clinical trials
Focus On The Patient Seminars:
Cutaneous lupus

“My doctor says it’s not only my skin but whole body you are as sick as someone with SLE”

“The worse thing is having to give up my job, I was raised to be independent and successful.. now dependent on my boyfriend”

“I am now disabled in Netherlands for work. They didn’t understand in my office, they thought I was contagious, they would walk around me give me wide berth because they were scared of the spots on my arm”

“I feel upset sometimes. I didn’t speak about lupus with anybody with work, with my friends, only with my family.

“Spots are always there - have been taking medicines for the last 30 years”

“I react very strongly to sunlight but I do manage to protect myself, I don’t go out in the sun unless I have to.”

“I always have to think can I go outside or not?”

Patient Input into Clinical Trial
• Most willing to do biopsy
• UV photosensitivity test is OK
• Applying cream for 28 days is like routine so would not be a problem.
• Patients are looking for something that will cure the itch associated with CLE and enable them to not think about going out and the impact UV from the sun
**Focus On The Patient Seminars: Primary Sjögren’s Syndrome**

**Aim was to:**

- Understand how patients view their current states (i.e., treating symptoms with eye drops) vs their level of knowledge about disease progression.
- Seek insight around whether they would take medicines or just want to continue self-management.
- Potential insight to inform Ph2 study design.
Focus On The Patient Seminars:
Primary Sjögren’s Syndrome

“I’m concerned it’s is going to get worse and affect my organs”

“my mind is not as sharp as it once was”

7 teeth extracted as a result

“I can’t play football with my grandchildren, now can only be goalkeeper”

“The physical and mental effects meant I stopped work”

“Most challenging is thirst, dryness and fatigue”

“I’ve stopped walking my dogs, due to the fatigue”

“it interferes with normal life, I get angry and down”

“affects ability to work due to fatigue... could no longer work in an office environment”

“I’ve had to adapt my life around it”

“I’m concerned it’s is going to get worse and affect my organs”

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“affects ability to work due to fatigue... could no longer work in an office environment”

“I’ve had to adapt my life around it”

• Many other symptoms and broader impact was revealed
• Uncertainty about disease progression caused concern
• Current symptom relief (oral / ocular drops/gels) don’t work well or aren’t long lasting
• “Ask us more, ask us sooner”
Capturing the Patient Experience in R&D

GSK Examples

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- **End of trial questionnaires** - capturing patient feedback on the design and execution of our trials

- Digital Health – reducing patient burden and capturing improved patient insights
GSK’s End of Trial Questionnaire
Capturing patient feedback on the design and execution of our trials

- What exactly can we do to make our studies more patient-centric?
- Why can’t we just ask the patient directly what they thought of the experience of being in one of our clinical trials?
- To make our trials more patient centric, we wanted to ask patients directly what they felt about participating in our studies and how the experience could be improved.
- To do this, we developed a formal questionnaire about the trial process that can be applied across a variety of trial and disease settings
- Topics covered include the process of joining the trial, the convenience of the study schedule, site interactions and trial termination.
Capturing the Patient Experience in R&D

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Clinical Innovation and Digital Platforms - 2015

Initiated & supported several pilots: eConsent, sensors & use of Apple Research Kit

Using sensors and algorithms to digitize gait assessment

- Comparison of traditional clinic assessments vs. actigraphy via sensor
- Strong correlation which may permit reduced clinic visits and in home monitoring

Novel endpoint development

- ALS biotelemetry study
- Comparison of activity vs. ALS Functional Rating Score (FRS)

Multi-parametric remote data collection via Medidata Patient Cloud

- Activity and Vital signs data collected at a clinical pharmacology unit for 5 days

Apple ResearchKit Pilot

- Testing Apple RK platform capability in a virtual, E2E, observational study in the US Rheumatoid Arthritis population
Patient-Centric Drug Development: patient-friendly technology

- eDiary (daily) and tablet devices to record responses to RA Symptom and Impact Diary

- Accelerometer to record real-time physical activity (and inactivity) for up to 14 days
In partnership with Propeller Health we are developing a custom sensor for the Ellipta® inhaler.

Sensor will automatically collect and record data on the inhaler’s usage (i.e. date and time of each use), wirelessly transmitting the information to a central data repository for analysis by GSK’s clinical researchers.

The sensor technology will be used to provide greater insights into adherence patterns across patient populations and may allow for more precise correlation of adherence with safety, efficacy and economic outcomes.
Capturing the Patient Experience in R&D: Summary

- Use of patient insights throughout the drug discovery and development lifecycle supports development of new treatments with benefits that matter most to patients
- Traditional endpoints may not capture all patient-relevant outcomes
- Holistic assessment of treatment response requires determination of outcomes that matter most to patients, and use of ‘fit for purpose’ instruments to assess those outcomes
- Real world evidence that reflects real patient experience promises to help get medicines to patients sooner by providing highly relevant data for healthcare community, prescribers and decision makers.