Break-out session 4

Respiratory & Immunology: near-term opportunities

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25 March 2021

Interactive event for investors and analysts. This webinar is being recorded.
https://astrazeneca.zoom.us/webinar/register/WN_WkP2lbwaRWlCoa9ROqIkUQ
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Respiratory diseases
Under recognised and under treated

Asthma

339m patients worldwide
176m attacks each year
>50% remain uncontrolled
~34m with severe disease
50% of asthma healthcare costs from severe disease

COPD¹

384m patients worldwide
3rd cause of death in 2020, more deaths than cancer each year
20% will die within one year after 1st hospitalisation
One COPD exacerbation can more than double the rate of lung function decline

Evidence to transform care

• ICS²/formoterol preferred anti-inflammatory reliever in asthma [Symbicort]
• Biologics standard of care for severe asthma and to reduce need for OCS³ [Fasenra]
• Beneficial effects on mortality from triple therapy in COPD [Breztri]


¹ Evidence to transform care


**Breztri and PT027: strength in inhaled medicines**

Next-generation medicines for mild and moderate disease

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**Breztri: poised to be a strong competitor in the fastest-growing COPD class**

- **COPD patients, millions**
- **Pack units sold, FY 2020, China**
- **Launch aligned TRx volume (24wks), US**

**Encouraging performance seen in China and US**

**Asthma programme in progress, data readout 2022+**

**PT027: first ICS/SABA\(^1\) rescue medicine for the US**

- **Replace traditional SABA rescue approach with ‘as needed’ ICS/SABA to treat underlying inflammation**
- **Phase III results in H2 2021**

  "Concomitant ICS and SABA taken as needed is a preferred option at Step 2"

**71m**

Rescue inhalers used in the US per year

**Rescue medicines valued at $2.5bn**

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**Fixed triple  Open triple  Breztri  Competitor**

Source: IQVIA China hospital sales Jan-Dec 2020; IQVIA weekly data - week ending 12/03/21, Breztri week one = week ending 02/10/20, Competitor week one = week ending 03/11/17. TB markets are US, EUS, China and Japan.

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Sources: NIH, NAEPP report: 2020 focused updates to the asthma management guidelines [online]. IQVIA, MAT sales 2020, Rescue defined as SABA only.

1. Short-acting beta agonist.
Greater use of biologics anticipated in severe asthma

Tezepelumab\(^5\): positive NAVIGATOR Phase III data in broad population

The first and only biologic to demonstrate AAER\(^6\) reduction irrespective of baseline blood EOS, FeNO\(^7\), and allergic status

**Tezepelumab** versus **placebo**

<table>
<thead>
<tr>
<th>AAER ratio over 52 weeks</th>
<th>Overall population</th>
<th>EOS&lt;300</th>
<th>EOS&lt;150</th>
<th>EOS ≥300</th>
<th>FeNO ≤25</th>
<th>FeNO &gt;25</th>
<th>IgE – any FEIA positive</th>
<th>IgE – any FEIA negative</th>
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</thead>
<tbody>
<tr>
<td>↓56%* ((95% CI: 47, 63))</td>
<td>2.10</td>
<td>1.73</td>
<td>1.04</td>
<td>2.66</td>
<td>2.52</td>
<td>2.03</td>
<td>2.21</td>
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<tr>
<td>↓41%* ((95% CI: 25, 54))</td>
<td>0.93</td>
<td>1.02</td>
<td>0.79</td>
<td>1.07</td>
<td>0.82</td>
<td>0.85</td>
<td>1.09</td>
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<tr>
<td>↓39% ((95% CI: 12, 58))</td>
<td>1.73</td>
<td>0.79</td>
<td>1.57</td>
<td>1.07</td>
<td>0.82</td>
<td>0.85</td>
<td>1.09</td>
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<tr>
<td>↓70% ((95% CI: 60, 78))</td>
<td>2.66</td>
<td>1.57</td>
<td>1.07</td>
<td>1.07</td>
<td>0.82</td>
<td>0.85</td>
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<tr>
<td>↓68% ((95% CI: 58, 75))</td>
<td>2.52</td>
<td>1.57</td>
<td>1.07</td>
<td>1.07</td>
<td>0.82</td>
<td>0.85</td>
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<tr>
<td>↓58% ((95% CI: 47, 67))</td>
<td>2.03</td>
<td>0.82</td>
<td>0.85</td>
<td>1.07</td>
<td>0.82</td>
<td>0.85</td>
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<tr>
<td>↓51% ((95% CI: 33, 64))</td>
<td>2.21</td>
<td>1.09</td>
<td>1.09</td>
<td>1.09</td>
<td>0.82</td>
<td>0.85</td>
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**Fasenra** and tezepelumab: asthma leadership

Significant opportunity to grow biopenetration in severe asthma

**Fasenra** remains key choice for high EOS\(^1\) patients

TRx\(^2\) 23% | NBRx\(^3\) 28%

New PONENTE data in OCS

Only 15% of eligible patients have access to a biologic (RA\(^4\) ~45% in US)


References:

1. Eosinophil
2. Total prescriptions, exit share Dec 2020
3. New-to-brand prescriptions, YTD Dec 2020
4. Rheumatoid arthritis.
Increasing presence in immunology
Pursuing leadership, starting with lupus

Adaptive Immunity
- T regulatory cell induction
- B-cell humoral responses
- T effector cell dysfunction

Innate Immunity
- Inflammatory myeloid cell responses
- Nucleic acid signaling/Inflammasome
- Eosinophil/mast cell activation
- Th2-cell responses

Tissue Mechanisms
- Tissue damage/barrier
- Stromal-immune axis
- Fibrosis

In clinical development
- anifrolumab
- brazikumab
- tezepelumab
- MEDI3506 (IL33)
- AZD9567 (oSGRM)

Early-stage and emerging projects
- Four preclinical projects in adaptive immunity
- Two preclinical projects in innate immunity
- Two preclinical projects addressing tissue mechanisms

Near term
- Enter rheumatology with anifrolumab in systemic lupus erythematosus

Medium term
- Expand anifrolumab in interferon diseases
- Launch Fasenra and tezepelumab LCM\textsuperscript{3} indications
- Enter Crohn’s disease and ulcerative colitis with brazikumab

Long term
- Novel pathways with disruptive potential

Anifrolumab: first new SLE\(^1\) treatment in 10 years
Potential first-in-class MOA\(^2\) with robust efficacy. LCM plans include LN\(^3\), CLE\(^4\), myositis

**TULIP 2 Phase III trial BICLA\(^5\)**
scores, overall responders

- Early and sustained reduction in overall disease activity

**Pooled TULIP 1/2 Phase III trials**
Skin CLAS\(^6\)I response

- Improves key organs of interest, including reduction in skin activity

**Pooled TULIP 1/2 Phase III trials**
OCS sparing without flares

- Prevents flares while also allowing patients to taper OCS


Week 52 treatment difference: 16.3
95% CI: 6.3%, 26.3%
p value: 0.001

Subset of patients ≥ 10 CLASI-A score at baseline,
≥50% CLASI-A response at Week 12
Treatment difference: 21.0% (95% CI: 8.1%, 34.0%); nominal p<0.001

Subset of patients taking ≥ 10mg OCS per day at baseline.
**Upcoming milestones and key readouts**

**Respiratory and Immunology: near-term opportunities**

**Upcoming milestones**

**H1 2021**
- **tezepelumab** - severe asthma: regulatory submission
- **Fasenra** – nasal polyps: regulatory submission

**H2 2021**
- **anifrolumab** - lupus: regulatory decision
- **Fasenra** - eosinophilic oesophagitis, hypereosinophilic syndrome: Phase III data readout

**2022**
- **Fasenra** - eosinophilic oesophagitis, hypereosinophilic syndrome: Phase III data readout
Questions & Answers

To ask a question

*Webinar*
Click ‘Raise Hand’ (preferred):

*Phone*
*6 - Toggle mute/unmute
*9 - Raise hand

* or type your question into the Q&A box (alternative)*
Appendix
## Publications

### anifrolumab

<table>
<thead>
<tr>
<th>Trial</th>
<th>Congress/journal</th>
<th>Title</th>
<th>Author</th>
<th>Citation</th>
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</table>

### Breztri

| ETHOS          | ERS 2020, European Respiratory Journal               | Poster: *COPD exacerbation rates by month in the ETHOS trial with budesonide/glycopyrronium/formoterol metered dose inhaler (BGF MDI) at two ICS dose levels* | Rabe KF, Martinez FJ, Ferguson GT, et al.            | 2020;56(suppl. 64):977.      |
## Publications, continued

### Fasenra

<table>
<thead>
<tr>
<th>Trial</th>
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<tbody>
<tr>
<td>ANDHI</td>
<td>European Academy of Allergy and Clinical Immunology (EAACI), Allergy</td>
<td>Oral Presentation: Benralizumab Efficacy for Severe, Eosinophilic Asthma with a Diagnosis of Nasal Polyposis: Results from the Phase IIIb ANDHI Trial</td>
<td>Canonica GW, Harrison TW, Chanez P, et al.</td>
<td>2020;75(suppl. 109):114</td>
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<tr>
<td>PT027</td>
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<td>MANDALA</td>
<td>ATS 2020, American Journal of Respiratory and Critical Care Medicine</td>
<td>Poster: Evaluation of the Efficacy and Safety of As-needed PT027 (budesonide/albuterol MDI) Compared to As-needed Albuterol MDI in Adults and Children 4 Years of Age or Older with Uncontrolled Moderate to Severe Asthma: Design of the MANDALA Study</td>
<td>Chipps BE, Albers FC, Reilly L, et al.</td>
<td>2020;201(suppl.):A3015.</td>
</tr>
<tr>
<td>tezepelumab</td>
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<tr>
<td>NAVIGATOR</td>
<td>AAAAI 2021, The Journal of Allergy and Clinical Immunology</td>
<td>Poster: Efficacy and safety of tezepelumab in adults and adolescents with severe, uncontrolled asthma: results from the phase 3 NAVIGATOR study</td>
<td>Menzies-Gow A, Corren J, Bourdin A, et al.</td>
<td>2021;147(2 suppl.):AB249.</td>
</tr>
<tr>
<td>PATHWAY</td>
<td>AAAAI 2021, The Journal of Allergy and Clinical Immunology</td>
<td>Poster: Treatment with tezepelumab reduces serum interleukin (IL)-5 and IL-13 in patients with severe, uncontrolled asthma to levels approaching those observed in healthy individuals</td>
<td>Pham T-H, Cook B, Colice G, et al.</td>
<td>2021;147(2 suppl.):AB57.</td>
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<tr>
<td>PATHWAY</td>
<td>American College of Chest Physicians (CHEST) 2020, Allergy and Airway</td>
<td>Oral Presentation: The effect of tezepelumab on exacerbations in patients with severe, uncontrolled asthma according to baseline inhaled corticosteroid dose: results from the phase 2b PATHWAY study</td>
<td>Corren J, Ambrose CS, Salapa K, et al.</td>
<td>2020;158(4(suppl)):A30-A31.</td>
</tr>
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