Break-out session 3

Respiratory & Immunology: emerging pipeline

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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_mahGjExaRVlDh7sxI6zl0w
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Targeting diseases with great unmet medical need

Building on 50 years of respiratory care in immune-driven diseases

<table>
<thead>
<tr>
<th>Asthma</th>
<th>COPD(^4)</th>
<th>Immunology</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;50% patients remain uncontrolled(^1)</td>
<td>3rd leading cause of death worldwide(^5,6)</td>
<td>5-7% of people living with autoimmune diseases, ranging from ultra-rare to common(^8)</td>
</tr>
<tr>
<td>~30% patients considered refractory to inhaled corticosteroids(^2)</td>
<td>&gt;$100bn estimated annual global burden(^7)</td>
<td>70-90% of patients not in remission on current therapies for most autoimmune diseases</td>
</tr>
<tr>
<td>339m patients(^3)</td>
<td>0 treatments indicated to slow or stop progression</td>
<td>~3-7% annual increases in prevalence of many autoimmune diseases(^9,10)</td>
</tr>
<tr>
<td>broad access to treatment requires both biologic and novel non-biologic therapies</td>
<td>0 new treatment modalities for past 10 years</td>
<td>Opportunities to build franchises across many unmet needs</td>
</tr>
</tbody>
</table>

Respiratory & Immunology: strategy
Disease modification and clinical remission

Diseases with great unmet need
- Asthma
- COPD
- IPF
- Cough
- Rheumatological
- Dermatological
- Gastro-intestinal
- Osteoarthritis pain

Increased probability of success
- Differentiated and unbiased novel targets
- New modalities - nothing is undruggable
- Precision medicine from the start

Transformative endpoints
- Demonstrating disease modification: small airway function and imaging
- Digital health
- Patient-centricity

1. Idiopathic pulmonary fibrosis.
MEDI3506: IL33\textsuperscript{1} mAb\textsuperscript{2}

Targeting a broad-acting, damage-response epithelial cytokine

**Disease-modification potential**

![Diagram](Diagram of disease-modification potential)

**Reverting the epithelial phenotype**

![Diagram](Diagram of reverting the epithelial phenotype)

1. Interleukin 33  
2. monoclonal antibody  
3. Oxidised IL33  
4. Reduced IL33  
5. ST2 (also known as IL1RL1, DER4, T1 and FIT-1) is a member of the toll-like/interleukin-1 receptor superfamily. Source: AstraZeneca data on file.

Source: AstraZeneca data on file.
MEDI3506: IL33 mAb
Targeting a broad-acting, damage-response epithelial cytokine

Phase I: pharmacodynamic effects demonstrated in COPD

1. Mixed effect longitudinal modelling: MEDI3506 reduced serum IL5 and IL13 (p=0.0037 and 0.034, respectively). All plots show means +/- SEMs. 2. Interleukin 5 3. Interleukin 13. Source: AstraZeneca data on file.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Phase II n</th>
<th>Data Anticipated</th>
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<tbody>
<tr>
<td>COPD</td>
<td>322 FPCD</td>
<td>Q1 2021</td>
</tr>
<tr>
<td>Asthma</td>
<td>228 FPCD</td>
<td>Q4 2020</td>
</tr>
<tr>
<td>Atopic dermatitis</td>
<td>152 FPCD</td>
<td>Q4 2019</td>
</tr>
<tr>
<td>Diabetic kidney disease</td>
<td>565 FPCD</td>
<td>Q4 2019</td>
</tr>
<tr>
<td>COVID-19 ACCORD</td>
<td>120 FPCD</td>
<td>Q2 2020</td>
</tr>
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4. First patient commenced dosing 5. Sponsored by the UK Government’s Therapeutics Taskforce.
AZD1402\(^1\): IL4Ra\(^2\) and AZD0449: iJAK\(^3\)
Addressing unmet need in asthma


Targeted approach following preceded system biologic

AZD1402

Inhaled targeted biologics and inhaled broader spectrum small molecules

Opportunity for broader efficacy across asthma endotypes

AZD0449

FeNO\(^4\), a biomarker of type-2 pulmonary inflammation

Rapid inhibition of FeNO in mild asthmatic patients

Inhibition of phosphorylation of STAT3\(^5\) following OVA\(^6\) challenge

Source: AstraZeneca data on file.

Target engagement demonstrated in rodent models of asthma

Source: AstraZeneca data on file.
MEDI7352: bispecific fusion protein specific for NGF\(^1\) and TNF\(^2\)
Potential synergy between blocking NGF and TNF in pain

### Decreased daily pain scores in osteoarthritis patients

- **Graph:**
  - Chart showing pain score changes over study days.
  - Y-axis: Change in pain score (0-10).
  - X-axis: Study day (0-80).
  - Key lines:
    - Placebo
    - MEDI7352 150ug/kg IV
    - MEDI7352 450ug/kg IV

- **Legend:**
  - Standard of Care/low-dose anti NGF

- **Insights:**
  - Peak reduction of c.3 points on a numerical rating scale vs. placebo.

### Modelling suggests significant efficacy at <50% NGF suppression

- **Graph:**
  - Treatment effect (difference from oxycodone 40mg).
  - Key data points:
    - Average pain NRS
    - Observed average % NGF suppression

- **Insights:**
  - Lower levels of NGF suppression may be associated with a favourable safety profile.

### Phase I/II trials

- **Painful osteoarthritis of the knee**
  - Phase I n=132
  - FPCD: Q1 2016
  - Data anticipated: H1 2021

- **Painful diabetic neuropathy**
  - Phase II n=271
  - FPCD Q4 2018
  - Data anticipated: H2 2021

- **Painful osteoarthritis of the knee**
  - Phase IIb n=300
  - Initiating
  - Data anticipated: 2022

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Source: AstraZeneca data on file.
### Full pipeline and news flow

**Upcoming milestones and expanding pipeline**

#### Respiratory & Immunology: emerging pipeline

<table>
<thead>
<tr>
<th>Phase I</th>
<th>Phase II</th>
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<tr>
<td><strong>AZD0284</strong>&lt;sup&gt;1&lt;/sup&gt; RORgamma&lt;sup&gt;2&lt;/sup&gt; psoriasis / respiratory</td>
<td><strong>AZD1402</strong>&lt;sup&gt;7&lt;/sup&gt; inhaled IL4Ra asthma</td>
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<tr>
<td><strong>AZD0449</strong> inhaled JAK inhibitor asthma</td>
<td><strong>AZD7986</strong>&lt;sup&gt;10&lt;/sup&gt; DPP1&lt;sup&gt;10&lt;/sup&gt; COPD</td>
</tr>
<tr>
<td><strong>AZD4041</strong>&lt;sup&gt;3&lt;/sup&gt; orexin 1 receptor antagonist opioid use disorder</td>
<td><strong>AZD9567</strong> GPRM&lt;sup&gt;10&lt;/sup&gt; chronic inflammatory diseases</td>
</tr>
<tr>
<td><strong>AZD8154</strong> inhaled Pi3Kgd&lt;sup&gt;11&lt;/sup&gt; asthma</td>
<td><strong>MEDI3506</strong>&lt;sup&gt;10&lt;/sup&gt; IL33 COPD</td>
</tr>
<tr>
<td><strong>MEDI0618</strong> PAR2&lt;sup&gt;12&lt;/sup&gt; antagonist mAb osteoarthritis pain</td>
<td><strong>MEDI3506</strong>&lt;sup&gt;11&lt;/sup&gt; IL33 asthma</td>
</tr>
<tr>
<td><strong>MEDI1341</strong>&lt;sup&gt;5&lt;/sup&gt; alpha synuclein Parkinson’s disease</td>
<td><strong>MEDI3506</strong>&lt;sup&gt;11&lt;/sup&gt; IL33 COVID-19</td>
</tr>
<tr>
<td><strong>MEDI1814</strong>&lt;sup&gt;6&lt;/sup&gt; amyloid beta Alzheimer’s disease</td>
<td><strong>MEDI7352</strong>&lt;sup&gt;9&lt;/sup&gt; NGF/TNF osteoarthritis pain</td>
</tr>
<tr>
<td><strong>AZD4604</strong> inhaled JAK inhibitor asthma</td>
<td><strong>MEDI7352</strong>&lt;sup&gt;9&lt;/sup&gt; NGF/TNF painful diabetic neuropathy</td>
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#### Status as of 25 March 2021.


### Upcoming milestones

#### H1 2021
- **MEDI3506** - multiple indications: Phase I data, Phase II data
- **AZD1402** - asthma: Phase II start
- **AZD0449** - asthma: Phase II start
- **MEDI7352** - pain: Phase I data, Phase II start, Phase II data
- **AZD4604** - asthma: Phase I start

#### H2 2021
- **MEDI3506** - multiple indications: Phase II data
- **MEDI7352** - pain: Phase II data

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Highlighted in presentation

Other pipeline medicines
Questions & Answers

To ask a question

Webinar
Click ‘Raise Hand’ (preferred):

or type your question into the Q&A box (alternative)

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

<table>
<thead>
<tr>
<th>Trial</th>
<th>Congress/Journal</th>
<th>Title</th>
<th>Author</th>
<th>Citation</th>
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<tr>
<td>Pre-clinical</td>
<td>British Thoracic Society (BTS)</td>
<td>The pharma perspective – what can academia do (and do we need any new drugs)?</td>
<td>Belvisi, M.G.</td>
<td>Available at: <a href="https://btswinter.online-event.co/login">https://btswinter.online-event.co/login</a></td>
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<td>Winter Meeting 2021</td>
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<td>Pre-clinical</td>
<td>Keystone eSymposia 2020: Asthma</td>
<td>Asthma Therapeutics: Now and Future Directions</td>
<td>Belvisi, M.G.</td>
<td>Available at: <a href="https://virtual.keystonesymposia.org/ks/live/683/page/6431#sessionCollapse4773">https://virtual.keystonesymposia.org/ks/live/683/page/6431#sessionCollapse4773</a></td>
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<td>Therapies in the Age of COVID</td>
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<td>(ERS) 2020: European Respiratory Journal</td>
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