Meet AZN management: Oncology

2021 ASCO Annual Meeting

Dave Fredrickson, Executive Vice President, Oncology Business Unit

7 June 2021

Interactive event for investors and analysts. This webinar is being recorded.
https://astrazeneca.zoom.us/s/99688625459
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AstraZeneca Oncology

We are leading a revolution in oncology to redefine cancer care
Our ambition is to provide cures for cancer in every form.
We are following the science to understand cancer and all its complexities to discover, develop and deliver life-changing treatments and increase the potential for cure.

1. Our clinical strategy is designed to help transform survival

2. With our portfolio and pipeline, we strive to revolutionise cancer care

3. Catalysing changes in the practice of medicine to transform the patient experience

4. We are driven by our people, our passion and our culture of innovation
# Oncology: a leading, diversified portfolio

## Lung cancer
- Stage IV NSCLC
  - EGFRm (1L<sup>4</sup>)
  - T790M (2L<sup>6</sup>)
- Adjuvant EGFRm NSCLC

## Multiple cancers
- Ovarian, breast, pancreatic, prostate cancers<sup>8</sup>
- Merck collaboration

## Multiple cancers
- Breast cancer (3L<sup>9</sup>, HER2+<sup>10</sup>) and gastric cancer (2L, HER2+)
- Daiichi Sankyo collab.

## Blood cancers
- Chronic lymphocytic leukaemia
- Mantle cell lymphoma

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**What’s next:**

a rich early to mid-stage pipeline, including combinations and several new Phase III medicines

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1. Approved medicines only  
2. Non-small cell lung cancer  
3. Epidermal growth factor receptor mutation  
4. 1st line  
5. Substitution of threonine (T) with methionine (M) at position 790 of exon 20 mutation  
6. 2nd line  
7. Small cell lung cancer  
8. Exact patient population varies by indication  
9. 3rd line  
10. Human epidermal growth factor receptor 2 positive.
Oncology: strong launch and commercial execution capabilities

US  Europe  Established Rest of World (RoW)  Emerging markets

Total revenue at actual exchange rates; product sales only for Lynparza.
90 abstracts with 74 presentations

- **One** plenary session (*Lynparza* OlympiA Phase III trial)
- **12** oral presentations
- **14** poster discussions
- **47** posters
- **16** abstracts (publication only)

**Data highlights**

- *Lynparza* OlympiA Phase III adjuvant breast cancer
- *Calquence* ELEVATE-TN Phase III 4-year follow-up ELEVATE-RR Phase III vs ibrutinib
- *Imfinzi* PACIFIC Phase III 5-year overall survival
- *Enhertu*, datopotamab deruxtecan, other potential new medicines from the pipeline

Source: ASCO 2021 accepted abstracts. 24 additional presentations at ASCO 2021 will feature AstraZeneca medicines and potential new medicines but were not supported by AstraZeneca.
Agenda

- Lung cancer
- Breast cancer
- Haematology
- ‘What’s next’
- Q&A
Lung cancer

Mohit Manrao, Global Franchise Head,
Tagrisso and lung cancer

Greg Rossi, Global Franchise Head,
Immuno-Oncology

For additional questions and IR support, please email tom.waldron@astra zeneca.com.
Transforming lung cancer by embracing entire patient journey
Translating science to evidence, and evidence to practice

Personalise treatment
- NSCLC and SCLC
- Tumour drivers and resistance mechanisms (TDR) and immunoncology (IO)
- Biomarker-driven treatments across EGFR, HER2, exon 14, others
- Digital pathology and ctDNA-based personalised interventions

Diagnose and treat early
- Increase screening and early diagnosis
- Opportunity for patients to get treatment in curative setting

Improve quality of care
- Integrated remote care
- Digital therapeutics and convenient dosing
- Healthcare equity and sustainability

Later diagnosis drives poor outcomes in NSCLC

1. Loss of exon 14 transcription in the mensenchymal-epithelial transition (MET) gene driving tumour growth 2. Circulating tumour DNA.

5-year survival

<table>
<thead>
<tr>
<th>Stage</th>
<th>Survival Rate</th>
<th>% at Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>68–92%</td>
<td>26%</td>
</tr>
<tr>
<td>Stage II</td>
<td>53–60%</td>
<td>9%</td>
</tr>
<tr>
<td>Stage III (locally advanced)</td>
<td>13–36%</td>
<td>25%</td>
</tr>
<tr>
<td>Stage IV (metastatic)</td>
<td>0–10%</td>
<td>40%</td>
</tr>
</tbody>
</table>


The LungAmbition Alliance
Accelerating advances for people with lung cancer.
**Tagrisso: changing treatment expectations in EGFRm NSCLC**

Continuing to push the boundaries of science and patient care

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**Reshaping the treatment paradigm**

by moving into earlier lines of NSCLC

- **2015**
  - 2L
  - First EGFR TKI to overcome T790M resistance
  - Best-in-class blood-brain barrier penetration
  - Excellent tolerability profile, convenient oral dosing

- **2017**
  - 1L
  - EGFR standard of care
  - Only EGFR TKI with OS > 3 years and unsurpassed PFS³
  - Best-in-class CNS⁴ risk reduction

- **2020**
  - Adjuvant
  - Unparalleled Stage IB-III A efficacy (80% relative risk)
    - Protection against distant recurrences, including in the CNS
    - Strongest-rated curative-intent therapy in NSCLC (ESMO-MCBS)

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**Enabling maximal patient benefit globally**

Globally-embedded access

- **2L**
  - 67
  - Including China NRDL

- **1L**
  - 44
  - 90

- **Adjuvant**
  - 8
  - 55

Strong momentum in patient reach

- **2016**
  - 3,812

- **2017**
  - 10,365

- **2018**
  - 29,466

- **2019**
  - 96,770

- **2020**
  - 210,274

- **2021 YTD**
  - > 250,000

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Source: AstraZeneca.
Tagrisso: building new EGFRm standard of care in NSCLC
Clinical trials across the NSCLC continuum

1. Further embed leadership position within earlier-stage curative-intent setting with the strongest potential for clinical and economic value creation.

2. Define and deliver innovative combinations with Tagrisso as a backbone in 1st line and beyond 1st-line Tagrisso monotherapy.
**Enhertu**, datopotamab deruxtecan: ADC\(^1\) portfolio

Significant activity across NSCLC

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**Enhertu - HER2 ADC (DESTINY-Lung01 trial)**

**HER2m\(^4\) NSCLC

\(~2\%\) prevalence

**HER2+ NSCLC

\(~15\%\) prevalence

Planned trial: DESTINY-Lung02: 2L+, Phase II in HER2m NSCLC, further evaluation of dose 5.4 mg/kg

DESTINY-Lung 03: 1L Enhertu + durvalumab + chemo Phase I

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**Datopotamab deruxtecan - TROP2\(^6\) ADC (TROPION-PanTumor01 trial)**

**2L+ NSCLC**

Planned trials: TROPION-Lung01: EGFR / ALK WT\(^7\) 2-3L, Phase III

TROPION-Lung02: 1L, Phase I pembrolizumab combo ± platinum chemo

TROPION-Lung04: 1L, Phase I Imfinzi combo ± platinum chemo

TROPION-Lung05: Driver positive after TKI and platinum chemo 3L, Phase II

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**Imfinzi: immuno-oncology**

Unique position in lung cancer

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**Comprehensive programme in early lung builds on PACIFIC**

- PACIFIC updated OS (ITT\(^1\))
- 43% of patients alive at five years
- 33% progression free at five years

**Strong launch in ES-SCLC\(^2\)**

- Only IO medicine with two-year OS published data
- 3-year exploratory data anticipated in H2 2021

**Novel combinations**

- Post-checkpoint inhibitor use - overcome immune checkpoint resistance through ceralasertib + Imfinzi combination

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**Ongoing Phase III trials:**

Unresectable: PACIFIC-2, PACIFIC-4, PACIFIC-5, PACIFIC-8
Resectable: AEGEAN, BR.31, MeRmaiD 1/2

**Ongoing Phase III trials:**

Limited stage: ADRIATIC

**Ongoing Phase II trials:**

HUDSON (advanced NSCLC post CPI\(^3\)), MAGELLAN (1L NSCLC), NeoCOAST (resectable NSCLC, neoadjuvant), COAST (Imfinzi + novel MoAs\(^4\))

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1. Intention to treat.

2. Extensive-stage small cell lung cancer.
Source: Journal of Clinical Oncology 38, no. 15_suppl (20 May 2020) 9002-9002.

Source: abstract OA07.08, WCLC 2020.
NSCLC: leadership across the spectrum
Potential to cover most patients across settings and lines of treatment

<table>
<thead>
<tr>
<th>Stage I-IIIB neo-adjuvant resectable/unresectable</th>
<th>Stage I-IIIB early/adjuvant resectable</th>
<th>Stage I-IIIB unresectable</th>
<th>Metastatic 1st line</th>
<th>Metastatic 2nd line+</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>EGFR</em></td>
<td><em>Tagrisso</em></td>
<td><em>Tagrisso</em> monotherapy and combinations</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>HER2</em></td>
<td></td>
<td><em>Enhertu</em> mono and combo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other tumour drivers and resistance</td>
<td></td>
<td>savolitinib</td>
<td></td>
<td>“What’s next”</td>
</tr>
<tr>
<td>Immuno-oncology and non-TDR</td>
<td><em>Imfinzi</em> monotherapy and combinations</td>
<td>datopotamab deruxtecan mono and combo</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Illustrative; not to scale.
Breast cancer

Cristian Massacesi, Senior Vice President, Oncology R&D, late-stage development

Sunil Verma, Vice President, Oncology R&D, late-stage development breast cancer

For additional questions and IR support, please email nick.stone@astrazeneca.com.
Breast cancer: AstraZeneca’s pioneering medicines have helped patients for more than four decades

- **Nolvadex**
  - **1970’s**: On the World Health Organization’s list of essential drugs for the treatment of breast cancer

- **Zoladex**
  - **1980’s**: Lutenising hormone-releasing agonist of choice for ovarian suppression in premenopausal women with breast cancer

- **Arimidex**
  - **1990’s**: One of the gold-standard medicines for postmenopausal HR+ breast cancer for years

- **Faslodex**
  - **2000’s**: The current endocrine therapy of choice in metastatic breast cancer

- **Lynparza**
  - **2010’s**: First targeted treatment option for patients with BRCA-mutated breast cancer both in the metastatic and early breast cancer setting

- **ENHERTU**
  - **2020’s**: Transformative HER2-directed medicine that has started to redefine the way physicians classify and treat HER2-expressing breast cancer
Breast cancer: AstraZeneca has a bold 10-year ambition to transform survival

**Smarter**
Redefine the treatment paradigm and enable a more personalised approach

**Earlier**
Bring impactful medicines where there is an opportunity for cure

**Harder**
Establish foundational medicines that set new benchmarks in outcomes

Lynparza: potential new standard of care
Now BRCAm adjuvant breast cancer

*Lynparza* demonstrated a sustainable and clinically relevant treatment effect versus placebo for patients\(^1\)

![Graph showing invasive disease-free survival over time](image)

Stratified hazard ratio 0.58 (99.5% CI, 0.41–0.82); P<0.0001

Difference: 3-year IDFS rate 8.8% (95% CI, 4.5–13.0%)

<table>
<thead>
<tr>
<th>No. at risk</th>
<th>0</th>
<th>6</th>
<th>12</th>
<th>18</th>
<th>24</th>
<th>30</th>
<th>36</th>
<th>42</th>
</tr>
</thead>
<tbody>
<tr>
<td>Olaparib</td>
<td>921</td>
<td>820</td>
<td>737</td>
<td>607</td>
<td>477</td>
<td>361</td>
<td>276</td>
<td>183</td>
</tr>
<tr>
<td>Placebo</td>
<td>915</td>
<td>807</td>
<td>732</td>
<td>585</td>
<td>452</td>
<td>353</td>
<td>256</td>
<td>173</td>
</tr>
</tbody>
</table>

1. With germline BRCA-mutated (gBRCAm) high-risk human epidermal growth factor receptor 2 (HER2)-negative early breast cancer.

Source: abstract LBA01, plenary session, ASCO 2021.

2.3 million women diagnosed with breast cancer in 2020

5% breast cancer patients with BRCA mutation

50% of women diagnosed with BRCAm breast cancer are younger than 55 years of age

Source: AstraZeneca.
**Enhertu**: transforming HER2+ and redefining HER2-low BC

Clinical development programme across multiple lines and subtypes

- **Launched in 3L, HER2+ mBC**
  - Total revenue $40m; US $35m in Q1 2021
  - $73m US in-market sales by Daiichi Sankyo
  - Strong patient share
    - Most prescribed medicine in HER2+ mBC; c.5,000 patients treated
  - EU regulatory approval
    - January 2021

- **ASCO 2021: data demonstrates Enhertu’s strong CNS activity**

- **BEGONIA: Imfinzi + Enhertu, HER2-low 1L mTNBC**
  - Benefit observed in HER2 1+ and HER2 2+/ISH3-ve by local test

- **Upcoming Enhertu breast cancer data readouts**
  - H2 2021
    - DESTINY-Breast03 (2L, HER2+)
  - 2022
    - DESTINY-Breast02 (3L, HER2+)
    - DESTINY-Breast04 (HER2 low)
  - 2022+
    - Multiple trials across HER2+, HER2 low and earlier disease

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1. Metastatic breast cancer.
   - Collaboration revenue at actual exchange rates.
3. In situ hybridisation.
**Enhertu: clinical development programme**

Opportunities across breast cancer, HER2-low and other tumours

<table>
<thead>
<tr>
<th>Neo-adjuvant / adjuvant</th>
<th>1L metastatic</th>
<th>2L metastatic</th>
<th>3L metastatic</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR$^+$: chemotherapy ± endocrine therapy</td>
<td>chemotherapy ± CDK4/6i</td>
<td>endocrine ± CDK4/6i</td>
<td>endocrine ± CDK4/6i</td>
</tr>
<tr>
<td>HR$^-$: chemotherapy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Post neo-adjuvant replace trastuzumab emtansine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>chemotherapy + trastuzumab + pertuzumab</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**HER2-low breast cancer**

**HER2-positive breast cancer**

**Beyond breast cancer**

Expand into other cancer types: gastric, NSCLC, CRC$^+$ and others

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1. Hormone-receptor positive  
2. Cyclin-dependent kinase 4/6 inhibitor  
3. Hormone-receptor negative  
Breast cancer: competitive late-stage breast cancer pipeline
Phase III trials underway and planned

**Capivasertib (AZD5363):** oral AKT inhibitor

**Breast Phase III trials underway**
- CAPItello-291, 2L breast cancer: capivasertib + Faslodex
- CAPItello-292, 1L advanced: capivasertib + Faslodex + CDK4/6i

**TNBC Phase III trial underway**
- CAPItello-290, metastatic TNBC: capivasertib + chemo

**Camizestrant (AZD9833):** next-generation oral SERD

Encouraging monotherapy efficacy and dose-dependent safety profile

16.3% overall response rate

42.3% clinical benefit rate

**Datopotamab deruxtecan (DS-1062):** TROP2 ADC

Promising preliminary activity in heavily pre-treated TNBC population; favourable profile vs. SoC


N.B. Faslodex provided ~5-10% ORR in similar setting. Source: abstract 1024, ASCO 2020.
Breast cancer: well-positioned with at least six medicines
Potential to cover most patients across settings and lines of treatment

<table>
<thead>
<tr>
<th>HER2+</th>
<th>c.20% of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Early/curative setting</strong></td>
<td>Neo-adjuvant</td>
</tr>
<tr>
<td><strong>HER2 low</strong></td>
<td>c.55%(^1) of patients that are not HER2+</td>
</tr>
<tr>
<td><strong>Hormone-receptor positive (HR+)</strong></td>
<td>c.65% of patients</td>
</tr>
<tr>
<td><strong>Triple-negative (TNBC)</strong></td>
<td>c.15% of patients</td>
</tr>
</tbody>
</table>

1. HER2-low prevalence is anticipated to be c.35-40% in TNBC
2. Antibody drug conjugates (Enhertu and datopotamab deruxtecan)
3. Immunotherapy
4. Chemotherapy

<table>
<thead>
<tr>
<th><strong>Neo-adjuvant</strong></th>
<th><strong>Adjuvant</strong></th>
<th><strong>1st line</strong></th>
<th><strong>2nd line</strong></th>
<th><strong>3rd line</strong></th>
<th><strong>3rd line+</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Enhertu monotherapy and potential combos</td>
<td>camizestrant</td>
<td>camizestrant</td>
<td>camizestrant</td>
<td>datopotamab deruxtecan</td>
<td></td>
</tr>
<tr>
<td>camivasertib combinations</td>
<td>capivasertib combinations</td>
<td>capivasertib combinations</td>
<td>Enhertu</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lynparza (BRCAm)</td>
<td>Lynparza (BRCAm)</td>
<td>Enhertu</td>
<td>datopotamab deruxtecan</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ADC +/- IO(^3)</td>
<td>neo-adjuvant</td>
<td>camivasertib + CTx(^4)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Haematology

Niko André, Global Franchise Head, Haematology and Calquence

Anas Younes, Senior Vice President, Oncology R&D, haematology

For additional questions and IR support, please email thomas.larsen@astrazeneca.com.
**Calquence: a standard of care in chronic lymphocytic leukaemia**

### Relapsed/refractory (R/R) ASCEND Phase III trial

- **HR, 0.31 (95% CI: 0.20, 0.49); P<0.0001**
- **Median follow-up, 16.1 mo (range, 0.5-22.4)**

<table>
<thead>
<tr>
<th>No. at risk</th>
<th>Months</th>
<th>Acala (N=155)</th>
<th>IdR/BR (N=155)</th>
</tr>
</thead>
<tbody>
<tr>
<td>177</td>
<td>27 (17)</td>
<td>88</td>
<td>68 (44)</td>
</tr>
</tbody>
</table>

**From a PFS HR of 0.31 in the R/R setting...**

1. Hazard ratio.
Other notes: IdR = idelalisib, BR = bendamustine and rituximab.

### Front line (FL) ELEVATE-TN Phase III trial

- **HR (95% CI)**
  - Calquence + obinutuzumab vs chlorambucil + obinutuzumab: **0.10 (0.06-0.17), p<0.0001**
  - Calquence vs chlorambucil + obinutuzumab: **0.20 (0.13-0.30), p<0.0001**

**...to a HR of 0.20 for mono and 0.1 for combinations in the FL setting**

**Calquence: launch trajectory confirms clinical value**

Inflection point from chronic lymphocytic leukaemia uptake

- **Solid launch trajectory**

- **US: high uptake in CLL**
  - CLL c.3/4 of all *Calquence* use
  - >10% growth in CLL patient starts on BTKi\(^1\) despite COVID-19 impact
  - 1st line: >40% **new-patient share** with BTKi use c.40% of all patients
  - Large opportunity in reducing chemotherapy use in front line

- **New-patient share in BTK class now more than 40%**

- **Ex-US: Europe launch and reimbursement underway**
  - **Approval**
    - 60 countries (CLL) and 27 (MCL\(^3\))
  - **Reimbursement**
    - 10 countries (CLL) and 9 (MCL)
  - **Sales in >25 countries**
    - Largest contribution from DE, UK, FR

**Product sales at actual exchange rates.**

1. Bruton’s tyrosine kinase inhibitor.
2. Chronic lymphocytic leukaemia.
   - Source: IQVIA market research.
Calquence: CLL launches
Global rollout in three waves

1st wave
Approval
US Q4 2019
93% of sales in Q1 2021

2nd wave
Approvals
EU Q4 2020
JP Q1 2021
Launch in DE, FR, UK with IT, ES in H2 2021
Sales in >25 countries

3rd wave
Regulatory submission
CN 2022
Calquence at ASCO: ELEVATE-TN Phase III trial
Sustained patient benefit at four years in a front-line setting

Overall population

Patients with del(17p) and/or mutated TP53

Hazard ratio was based on unstratified Cox-Proportional-Hazards model; P-value was based on unstratified log-rank test.

Notes: A = Calquence (acalabrutinib) O = obinutuzumab, a 2nd-generation CD20 monoclonal antibody Cb = chlorambucil, a standard-of-care chemotherapy.

Source: abstract 7509, ASCO 2021.
**Calquence at ASCO: ELEVATE-RR Phase III trial vs. ibrutinib**

Lower incidences of any-grade atrial fibrillation/flutter; solid safety overall

### Afib/Flutter

<table>
<thead>
<tr>
<th>Event</th>
<th>Acalabrutinib (n=266)</th>
<th>Ibrutinib (n=263)</th>
<th>Acalabrutinib (n=266)</th>
<th>Ibrutinib (n=263)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac events</td>
<td>64 (24.1)</td>
<td>79 (30.0)</td>
<td>23 (8.8)</td>
<td>25 (9.5)</td>
</tr>
<tr>
<td>Atrial fibrillation*</td>
<td>25 (9.4)</td>
<td>42 (16.0)</td>
<td>13 (4.9)</td>
<td>10 (3.8)</td>
</tr>
<tr>
<td>Ventricular arrhythmias</td>
<td>0</td>
<td>3 (1.1)</td>
<td>0</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Bleeding events*</td>
<td>101 (38.0)</td>
<td>119 (46.1)</td>
<td>10 (3.8)</td>
<td>12 (4.6)</td>
</tr>
<tr>
<td>Major bleeding events*</td>
<td>12 (4.5)</td>
<td>14 (5.3)</td>
<td>10 (3.8)</td>
<td>12 (4.6)</td>
</tr>
<tr>
<td>Hypertension*</td>
<td>25 (9.4)</td>
<td>61 (23.2)</td>
<td>11 (4.1)</td>
<td>34 (12.8)</td>
</tr>
<tr>
<td>Infections*</td>
<td>208 (78.2)</td>
<td>214 (81.4)</td>
<td>82 (30.8)</td>
<td>79 (30.0)</td>
</tr>
<tr>
<td>ILD/pneumonitis*</td>
<td>7 (2.6)</td>
<td>11 (4.6)</td>
<td>1 (0.4)</td>
<td>2 (0.8)</td>
</tr>
<tr>
<td>SPMs excluding NMSC</td>
<td>24 (9.0)</td>
<td>20 (7.6)</td>
<td>16 (6.0)</td>
<td>14 (5.3)</td>
</tr>
</tbody>
</table>

*Two-sided P-value for event comparisons <0.05 without multiplicity adjustment.

Notes: Afib = atrial fibrillation; irregular heartbeat (arrhythmia). CI = confidence interval.
Source: abstract 7500, ASCO 2021.
Haematology: projects in early development
Emerging pipeline in main haematology indications

### Broad portfolio in cell death

<table>
<thead>
<tr>
<th>Target/medicine</th>
<th>Bcl-2</th>
<th>Bcl-xL</th>
<th>BFL1</th>
<th>MCL1</th>
</tr>
</thead>
<tbody>
<tr>
<td>venetoclax</td>
<td>✓</td>
<td>✓</td>
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<tr>
<td>AZD0466 (Bcl-2/xL)</td>
<td>✓ ✓</td>
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<tr>
<td>AZD5991 (MCL1)</td>
<td>✓</td>
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<td>✓</td>
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<tr>
<td>AZD4573 (CDK9)</td>
<td>✓ ✓</td>
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**Potential in:**
- AML
- MDS
- NHL
- HL
- PTCL

### First immunotherapy bispecific antibody

- PD-1
- TIM3

**Potential in:**
- Hodgkin lymphoma

### Tumour drivers of resistance

- IDH1
- IDH2
- PD-1
- TIM3

**Potential in:**
- follicular lymphoma, MCL

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1. B-cell lymphoma
2. Induced myeloid leukaemia cell differentiation protein
3. Cyclin-dependent kinase
4. Acute myelogenous leukaemia
5. Myelodysplastic syndromes
6. Non-Hodgkin lymphoma
7. Hodgkin lymphoma
8. Peripheral T-cell lymphoma

9. Programmed cell death protein 1

Haematology: ‘What’s next’
Growing pipeline across medicines and indications

<table>
<thead>
<tr>
<th>Tumour drivers of resistance</th>
<th>CLL/SLL&lt;sup&gt;1&lt;/sup&gt;</th>
<th>MCL</th>
<th>DLBCL&lt;sup&gt;2&lt;/sup&gt;</th>
<th>FL/MZL&lt;sup&gt;3&lt;/sup&gt;</th>
<th>AML/MDS</th>
<th>MM&lt;sup&gt;4&lt;/sup&gt;</th>
<th>Other</th>
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<tr>
<td><strong>Calquence (BTK)</strong></td>
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<td><strong>capivasertib (AKT)</strong></td>
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<td><strong>New targets</strong></td>
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<tr>
<td><strong>Cell death</strong></td>
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<tr>
<td><strong>IO / bispecifics / cell therapy</strong></td>
<td><strong>New targets</strong></td>
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<td><strong>Epigenetics</strong></td>
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<td>AZD5153</td>
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<td><strong>ADCs</strong></td>
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</tbody>
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Launched  Current portfolio  Emerging portfolio
‘What’s next’

**Susan Galbraith**, Senior Vice President, Oncology R&D, early stage

**Andrew Mortlock**, Vice President, Oncology R&D, haematology projects

For additional questions and IR support, please email henry.wheeler@astrazeneca.com.
Comprehensive portfolio to combat cancer

Oncology ambition

Attained through diversity in portfolio

1. Tumour drivers and resistance
   - Oncogenic truncal drivers and mechanisms of resistance
   - Replacing standard of care (i.e. chemo) with targeted delivery of toxic molecules

2. DNA damage response
   - Synthetic lethality exploiting impaired DNA damage response

3. Antibody drug conjugates
   - Radioimmuno-conjugates
   - Nanomedicines

4. Epigenetics
   - Reprogramming tumour cells

- Cell therapy
  - Immune engagers
  - Redirect local immunity
  - Awaken dormant immune cells
  - Infuse with engineered T cells

- Oncolytic virus
  - Targeted delivery of medicines that recruit immunity
  - Build on PDx
  - Overcome immune suppression

- Immuno-oncology
  - Microenvironment
  - Build synthetic immunity

- Direct killing
  - Tumour
  - Radioimmuno-conjugates

- Microenvironment
  - Tumour

- Epigenetics
  - Reprogramming tumour cells

Diagnosis by ctDNA

Tumor burden

Time

Long-term survival and cure

Source: AstraZeneca.
What’s next?
Selectively expanding technologies and platforms

1. Tyrosine kinase WEE1 2. Ataxia telangiectasia and rad3-related kinase.

Source: AstraZeneca.


ADCs & RICs

PROTACs

Functional genomic capabilities
Advancing the DDR portfolio

Key data at ASCO and AACR

AZD5305
PARP-1 selective inhibitor
- Five abstracts at AACR
- Selective PARP1-DNA trapper
- More potent and efficacious than first-generation PARP inhibitors

EFFORT
Adavosertib Phase II trial
- Adavosertib monotherapy
- ORR: 23%
- DOR: 5.5 months
- PFS: 5.5 months
- Adavosertib and Lynparza
- ORR: 29%
- DOR: 5.5 months
- PFS: 6.4 months

HUDSON
Umbrella NSCLC platform post-IO
- ATR activity in combination with Imfinzi in IO-pretreated patients

1. American Association for Cancer Research.
2. Overall response rate
3. Duration of response.
Source: abstract 5505, ASCO 2021.
Source: abstract OA07.08, WCLC 2020.
Next-wave IO
Clinical-stage progress

Key Phase II *Imfinzi* combination trial readouts

*Imfinzi* + oleclumab (CD73<sup>1</sup>) or monalizumab (NKG2A<sup>2</sup>)
- COAST (Stage III unresectable NSCLC)
- NeoCOAST (early-stage NSCLC)

*Imfinzi* + ceralasertib (ATR)
- HUDSON (NSCLC)
- MONETTE (melanoma)

**COAST/NeoCOAST data presentation H2 2021**

**AZD7789**
PD1/TIM3 bispecific

- Humanised mouse model
- Potential to address patients who either don’t benefit from IO or benefit but still eventually progress
- May help to reverse resistance

**AZD8853**
Anti-GDF15

- Lewis lung (LL/2) syngeneic model (insensitive to PD1/L1) treated with anti-GDF15 Ab -5/12 mice had complete responses

**GDF15 regulates DC activation, T cell recruitment and monocyte/macrophage immunosuppression**

1. 5′-nucleotidase  2. NKG2-Atype II integral membrane protein.

Source: AstraZeneca.

Source: AstraZeneca.
Next-wave modalities
Innovative use of new modalities to deliver transformational change

ADCs & RICs
- Target density
- Internalisation kinetics
- Lysosomal trafficking vs. recycling
- Pharmacology, stability
- PK/PD, Kd, Tox, TI
- Warhead MOA
- Bystander kill activity

Targeted killing by targeting proteins immune to conventional approaches

PROTACS

Harnessing the cell’s natural waste disposal system

Genomics capabilities
CRISPR screens and DepMap-enhancing target identification

Selective targeting of the key resistance and survival pathways

Source: AstraZeneca.
# Early-stage oncology pipeline

<table>
<thead>
<tr>
<th>Phase I</th>
<th>Phase II</th>
</tr>
</thead>
<tbody>
<tr>
<td>MEDI1191 modIL-12</td>
<td>oleclumab CD73</td>
</tr>
<tr>
<td>IPHS201 CD39</td>
<td>imaradenant AZAR(^1)</td>
</tr>
<tr>
<td>AZD5069 CXCR2-ESR</td>
<td>MEDI5752 PD-1/CTLA4(^2)</td>
</tr>
<tr>
<td>AZD0171 LIF1</td>
<td>MEDI0457 HPV Vax</td>
</tr>
<tr>
<td>AZD8701 FOXP3 ASO</td>
<td>camizestrant SERD</td>
</tr>
<tr>
<td>MEDI3395 rNDV GMCSF</td>
<td>AZD4573 CDK9</td>
</tr>
<tr>
<td>MEDI9253 rNDV IL-12</td>
<td>ceralasertib ATR</td>
</tr>
<tr>
<td>AZD5153 BRD4-ESR</td>
<td>AZD2811 AURN</td>
</tr>
</tbody>
</table>

1. Adenosine A2A receptor  
‘What’s next’
Phase I/II new medicines, selected

<table>
<thead>
<tr>
<th>What’s now</th>
<th>Phase III new medicines</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>datopotamab deruxtecan</strong> lung cancer</td>
<td><strong>camizestrant</strong> breast cancer</td>
</tr>
<tr>
<td><strong>monalizumab</strong> head &amp; neck cancer</td>
<td><strong>capivasertib</strong> breast, prostate cancer</td>
</tr>
<tr>
<td><strong>savolitinib</strong> NSCLC&lt;sup&gt;1&lt;/sup&gt;</td>
<td><strong>tremelimumab</strong> multiple cancers</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>adavosertib (WEE1 inhibitor) uterine, ovarian cancer</th>
<th>ceralasertib (ATR inhibitor) solid tumours, blood cancers</th>
</tr>
</thead>
<tbody>
<tr>
<td>oleclumab (CD73 mAb) solid tumours</td>
<td>imardenant (A2AR inhibitor) solid tumours</td>
</tr>
<tr>
<td>AZD5305 (PARP1 inhibitor) solid tumours</td>
<td>MEDI5752 (PD-1/CTLA4 mAb) solid tumours</td>
</tr>
<tr>
<td>AZD4573 (CDK9 inhibitor) blood cancers</td>
<td>AZD2811 (Aurora B inhibitor) blood cancers</td>
</tr>
<tr>
<td>AZD5991 (MCL1 inhibitor) blood cancers</td>
<td>AZD0466 (Bcl-2/xL) solid tumours, blood cancers</td>
</tr>
</tbody>
</table>

**Phase III lifecycle management, major**

<table>
<thead>
<tr>
<th>Lynparza multiple cancers</th>
<th>Tagrisso NSCLC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enhertu multiple cancers</td>
<td>Imfinzi multiple cancers</td>
</tr>
<tr>
<td>Calquence multiple cancers</td>
<td></td>
</tr>
</tbody>
</table>

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<sup>1</sup> Potentially pivotal Phase II.
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
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