Full-year and Q4 2021 results

March 2022 Roadshow
Forward-looking statements

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Agenda

1. Opening remarks
2. Financial results
3. Oncology
4. BioPharmaceuticals, Emerging Markets
5. Rare Disease
6. Closing remarks and Q&A
Opening remarks
Pascal Soriot
Chief Executive Officer
Full year and Q4 2021: key updates
Continuing to deliver on our strategic objectives

Robust growth
Exceeded FY 2021 revenue guidance

• Total Revenue $37.4bn (+38%)
  – $33.4bn (+23%) excluding FY 2021 Vaxzevria\(^1\) revenue
  – $35.2bn (+30%) including Q4 2021 Vaxzevria\(^1\) revenue
• Core EPS $5.29 (+37%)

Broad-based performance
Delivering value to patients

• Oncology $13.7bn (+17%)
• BioPharmaceuticals:
  – CVRM $8.0bn (+9%)
  – Respiratory & Immunology $6.0bn (+9%)
  – Other medicines $2.5bn (-7%)
  – COVID-19 $4.1bn (n/m)
• Rare Disease\(^2\) $3.1bn (+9%)

Science-led innovation
Strong Q4 2021 performance

• Tezspire US approval
  – severe asthma
• Evusheld US EUA
  – COVID-19 prophylaxis
• Lynparza US Priority Review
  - adjuvant breast cancer
• Saphnelo EU CHMP recommendation
  - systemic lupus erythematosus
• Ultomiris US Priority Review
  - generalised myasthenia gravis

Absolute values at actual exchange rates; changes at constant exchange rates (CER) and for year-to-date (YTD) December 2021, unless stated otherwise. CVRM = Cardiovascular, Renal and Metabolism; COVID-19 = coronavirus disease 2019; CHMP = Committee for Medicinal Products for Human Use; EUA = Emergency Use Authorisation; n/m = growth rate not meaningful. 1. Vaxzevria Total Revenue` also includes Collaboration Revenue from sub-licensees that produce and supply the AstraZeneca COVID-19 Vaccine under their own trademarks. 2. FY 2021 revenues from date of acquisition closing, 21 July 2021 through 31 December 2021; pro forma growth rates calculated by comparison post-acquisition revenues with the corresponding prior year revenues adjusted pro-rata to match the post-acquisition period.
Full year and Q4 2021: performance
Oncology, CVRM, R&I and Rare Disease all delivered strong growth

<table>
<thead>
<tr>
<th>Disease Area</th>
<th>FY 2021 $m</th>
<th>CER growth %</th>
<th>Q4 2021 $m</th>
<th>CER growth %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oncology</td>
<td>13,663</td>
<td>17</td>
<td>3,919</td>
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<tr>
<td>CVRM</td>
<td>8,034</td>
<td>9</td>
<td>2,007</td>
<td>8</td>
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<tr>
<td>Respiratory &amp; Immunology</td>
<td>6,049</td>
<td>9</td>
<td>1,593</td>
<td>3</td>
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<tr>
<td>Rare Disease</td>
<td>3,071</td>
<td>9</td>
<td>1,760</td>
<td>11</td>
</tr>
<tr>
<td>Other medicines</td>
<td>2,484</td>
<td>(7)</td>
<td>835</td>
<td>14</td>
</tr>
<tr>
<td>Evusheld</td>
<td>135</td>
<td>n/m</td>
<td>135</td>
<td>n/m</td>
</tr>
<tr>
<td><strong>Total revenue excl. Vaxzevria</strong></td>
<td><strong>33,436</strong></td>
<td><strong>23</strong></td>
<td><strong>10,250</strong></td>
<td><strong>39</strong></td>
</tr>
<tr>
<td>Vaxzevria²</td>
<td>3,981</td>
<td>n/m</td>
<td>1,762</td>
<td>n/m</td>
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<td><strong>Total Revenue</strong></td>
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<table>
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<tr>
<th>Geographies</th>
<th>FY 2021 $m</th>
<th>CER growth %</th>
<th>Q4 2021 $m</th>
<th>CER growth %</th>
</tr>
</thead>
<tbody>
<tr>
<td>US</td>
<td>12,164</td>
<td>38</td>
<td>3,859</td>
<td>62</td>
</tr>
<tr>
<td>EM</td>
<td>9,977</td>
<td>10</td>
<td>2,498</td>
<td>10</td>
</tr>
<tr>
<td>- EM excl. China</td>
<td>3,977</td>
<td>21</td>
<td>1,197</td>
<td>38</td>
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<tr>
<td>- China</td>
<td>6,000</td>
<td>4</td>
<td>1,301</td>
<td>(9)</td>
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<tr>
<td>Europe</td>
<td>7,015</td>
<td>22</td>
<td>2,573</td>
<td>42</td>
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<tr>
<td>Established Rest of World</td>
<td>4,280</td>
<td>21</td>
<td>1,320</td>
<td>47</td>
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<tr>
<td><strong>Total revenue excl. Vaxzevria</strong></td>
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Total revenue at actual exchange rates; changes at CER. R&I = Respiratory and Immunology; EM = emerging markets. 1. FY 2021 revenues from date of acquisition closing, 21 July 2021 through 31 December 2021; growth rates calculated by comparison post-acquisition revenues with the corresponding prior year revenues adjusted pro-rata to match the post-acquisition. 2. Vaxzevria Total Revenue also includes Collaboration Revenue from sub-licensees that produce and supply the AstraZeneca COVID-19 Vaccine under their own trademarks.
AstraZeneca: 2022-2025

Industry leading double-digit growth

Durable growth drivers through 2025
including multiple blockbuster-medicines

**AstraZeneca: 2022-2025**

**Industry leading double-digit growth**

**Durable growth drivers through 2025**

including multiple blockbuster-medicines

**Oncology**

**CVRM**

**R&I**

**V&I**

**Rare Disease**

<table>
<thead>
<tr>
<th>Oncology</th>
<th>CVRM</th>
<th>R&amp;I</th>
<th>V&amp;I</th>
<th>Rare Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMFINZI</td>
<td>farxiga</td>
<td>IMFINZI</td>
<td>farxiga</td>
<td>rare disease</td>
</tr>
<tr>
<td>CALQUENCE</td>
<td>LOKELMA</td>
<td>CALQUENCE</td>
<td>LOKELMA</td>
<td>rare disease</td>
</tr>
<tr>
<td>Lynparza</td>
<td>Lynparza</td>
<td>Lynparza</td>
<td>Lynparza</td>
<td>rare disease</td>
</tr>
<tr>
<td>TAGRISSE</td>
<td>TAGRISSE</td>
<td>TAGRISSE</td>
<td>TAGRISSE</td>
<td>rare disease</td>
</tr>
<tr>
<td>ENHERTU</td>
<td>ENHERTU</td>
<td>ENHERTU</td>
<td>ENHERTU</td>
<td>rare disease</td>
</tr>
</tbody>
</table>

**Diversification**
of disease areas and geographies

Q4 2021 Total Revenue¹

- Oncology 38%
- CVRM 20%
- R&I 16%
- Rare 17%
- Other 9%

- US 38%
- Europe 25%
- Emerging Markets 24%
- Est. RoW 13%

¹ Total revenue excluding Vaxzevria. Evusheld is included in other. V&I = Vaccines and Immune Therapies. V&I will be a new reporting line within BioPharmaceuticals from Q1 2022, and will contain the following medicines, Vaxzevria, Evusheld, FluMist, Synagis and potential new medicine nirsevimab, which is being developed in collaboration with Sanofi.
AstraZeneca: 2025+
Delivering growth through innovation

Robust life-cycle management

Supports durable, growing revenue base

Innovative late-stage pipeline

Continued investment in clinical stage pipeline

15 NMEs in Phase III

128 NME or major LCM projects in Phase II and III

Across a number of areas of high unmet need, with first or best in class potential

Strategic business development

Recent clinical stage business development

• Rare Disease (Alexion)
• Dato-DXd (Daiichi Sankyo)
• Eplontersen (Ionis)
• CAEL-101 (Caelum Bio)
• NI006 (Neurimmune)

Attractive LoE profile

US LoE for selected medicines

LCM = life-cycle management; NME = new molecular entity; Dato-DXd = datopotamab deruxtecan; LoE = loss of exclusivity. *Amgen IPR settled to grant Amgen a non-exclusive, royalty-free license to sell an eculizumab product in the US from March 1, 2025.
## Late-stage pipeline delivery

### Important milestones since Q3 2021 update

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Indication / Event</th>
<th>Geography</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Regulatory approvals or other regulatory action</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saphnelo</td>
<td>systemic lupus erythematosus: CHMP positive opinion</td>
<td>EU</td>
</tr>
<tr>
<td>Tezspire</td>
<td>severe asthma</td>
<td>US</td>
</tr>
<tr>
<td>Evusheld</td>
<td>COVID-19 prophylaxis: emergency use authorisation</td>
<td>US</td>
</tr>
<tr>
<td><strong>Regulatory submissions or acceptances</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lynparza</td>
<td>breast cancer (adjuvant, BRCAm): priority review</td>
<td>US</td>
</tr>
<tr>
<td>Lynparza</td>
<td>breast cancer (adjuvant, BRCAm): regulatory submission</td>
<td>EU, JP</td>
</tr>
<tr>
<td>Lynparza</td>
<td>ovarian cancer (1st-line): regulatory submission</td>
<td>CN</td>
</tr>
<tr>
<td>Lynparza</td>
<td>prostate cancer (1st-line): regulatory submission</td>
<td>EU</td>
</tr>
<tr>
<td>Enhertu</td>
<td>HER2-positive breast cancer (2nd-line): priority review</td>
<td>US</td>
</tr>
<tr>
<td>Enhertu</td>
<td>HER2-positive breast cancer (2nd-line): regulatory submission</td>
<td>EU, JP</td>
</tr>
<tr>
<td>Imfinzi +/- tremelimumab</td>
<td>NSCLC (1st-line): regulatory submission</td>
<td>US, EU, JP</td>
</tr>
<tr>
<td>Koselugo</td>
<td>NF1-PN: regulatory submission</td>
<td>JP</td>
</tr>
<tr>
<td>Ultomiris</td>
<td>subcutaneous formulation in PNH and aHUS: regulatory submission</td>
<td>US</td>
</tr>
<tr>
<td>Ultomiris</td>
<td>generalised myasthenia gravis: priority review</td>
<td>US</td>
</tr>
<tr>
<td><strong>Major Phase III data readouts or other significant developments</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaxzevria / AZD2816</td>
<td>COVID-19: phase III primary endpoint met</td>
<td></td>
</tr>
<tr>
<td>Lynparza</td>
<td>breast cancer (adjuvant, BRCAm): orphan drug designation</td>
<td>JP</td>
</tr>
<tr>
<td>Lokelma</td>
<td>chronic haemodialysis with hyperkalaemia: fast track designation</td>
<td>US</td>
</tr>
<tr>
<td>Eplontersen</td>
<td>transthyretin amyloidosis: orphan drug designation</td>
<td>US</td>
</tr>
</tbody>
</table>

**HER2-positive = human epidermal growth factor 2 positive; BRCAm = breast cancer susceptibility gene 1/2 mutation; NSCLC = non-small cell lung cancer; NF1-PN = neurofibromatosis type 1 with plexiform neurofibromas; PNH = paroxysmal nocturnal haemoglobinuria; aHUS = atypical haemolytic uraemic syndrome. Status as of 10 February 2022.**
Reported profit and loss

<table>
<thead>
<tr>
<th></th>
<th>FY 2021 $m</th>
<th>CER change</th>
<th>% total revenue</th>
<th>Q4 2021 $m</th>
<th>CER change</th>
<th>% total revenue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Revenue</td>
<td>37,417</td>
<td>38</td>
<td>100</td>
<td>12,011</td>
<td>63</td>
<td>100</td>
</tr>
<tr>
<td>- Product Sales</td>
<td>36,541</td>
<td>38</td>
<td>98</td>
<td>11,498</td>
<td>65</td>
<td>96</td>
</tr>
<tr>
<td>- Collaboration Revenue</td>
<td>876</td>
<td>20</td>
<td>2</td>
<td>513</td>
<td>29</td>
<td>4</td>
</tr>
<tr>
<td>Gross margin</td>
<td>66.0%</td>
<td>(12.6) pp</td>
<td></td>
<td>59.8%</td>
<td>(16.0) pp</td>
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<tr>
<td>Operating expenses¹</td>
<td>25,416</td>
<td>40</td>
<td>68</td>
<td>7,825</td>
<td>55</td>
<td>65</td>
</tr>
<tr>
<td>- R&amp;D expenses</td>
<td>9,736</td>
<td>59</td>
<td>26</td>
<td>2,584</td>
<td>50</td>
<td>22</td>
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<tr>
<td>- SG&amp;A expenses</td>
<td>15,234</td>
<td>32</td>
<td>41</td>
<td>5,117</td>
<td>59</td>
<td>43</td>
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<tr>
<td>Other operating income</td>
<td>1,492</td>
<td>(4)</td>
<td>4</td>
<td>147</td>
<td>(78)</td>
<td>1</td>
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<tr>
<td>Operating profit</td>
<td>1,056</td>
<td>(70)</td>
<td>3</td>
<td>(292)</td>
<td>(105)</td>
<td>(2)</td>
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<tr>
<td>Tax rate</td>
<td>143.4%</td>
<td></td>
<td></td>
<td>45.6%</td>
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<tr>
<td>EPS</td>
<td>$0.08</td>
<td>(84)</td>
<td></td>
<td>($0.22)</td>
<td>(113)</td>
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</table>

Absolute values at actual exchange rates; changes at CER. Gross margin excludes the impact of collaboration revenue and any associated costs, thereby reflecting the underlying performance of product sales.

1. Includes distribution expenses. R&D = research and development; SG&A = sales, general and administration; pp = percentage points; n/m = growth rate not meaningful.
## Core profit and loss

### Core EPS above FY 2021 guidance

<table>
<thead>
<tr>
<th></th>
<th>FY 2021 $m</th>
<th>CER change %</th>
<th>% total revenue</th>
<th>Q4 2021 $m</th>
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<th>% total revenue</th>
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<td>96</td>
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<td>20</td>
<td>2</td>
<td>513</td>
<td>29</td>
<td>4</td>
</tr>
<tr>
<td><strong>Gross margin</strong></td>
<td>74.2%</td>
<td>(4.7) pp</td>
<td></td>
<td>74.3%</td>
<td>(1.9) pp</td>
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<tr>
<td><strong>Operating expenses</strong>¹</td>
<td>19,537</td>
<td>22</td>
<td>52</td>
<td>5,888</td>
<td>26</td>
<td>49</td>
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<tr>
<td>- <strong>R&amp;D expenses</strong></td>
<td>7,987</td>
<td>33</td>
<td>21</td>
<td>2,396</td>
<td>40</td>
<td>20</td>
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<tr>
<td>- <strong>SG&amp;A expenses</strong></td>
<td>11,104</td>
<td>15</td>
<td>30</td>
<td>3,368</td>
<td>18</td>
<td>28</td>
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<tr>
<td><strong>Other operating income</strong></td>
<td>1,492</td>
<td>(4)</td>
<td>4</td>
<td>146</td>
<td>(78)</td>
<td>1</td>
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<tr>
<td><strong>Operating profit</strong></td>
<td>9,928</td>
<td>41</td>
<td>27</td>
<td>3,318</td>
<td>94</td>
<td>28</td>
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<tr>
<td><strong>Tax rate</strong></td>
<td>16.6%</td>
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<td>16.2%</td>
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<td></td>
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<tr>
<td><strong>EPS</strong></td>
<td>$5.29</td>
<td>37</td>
<td></td>
<td>$1.67</td>
<td>74</td>
<td></td>
</tr>
</tbody>
</table>
**2022 Guidance**
Continuing to drive innovation and growth

**Total revenue guidance**

**Core EPS guidance**

**Headwinds**
- Ongoing pricing pressure in China, mid single-digit revenue decline anticipated
- COVID-19 still impacting diagnosis and treatment rates, particularly in Oncology
- Decline in COVID-19 therapies revenue expected in 2022
- Intensified competition for some legacy medicines
- Continued pricing pressure in many markets

**Tailwinds**
- First full year of Alexion ownership
- Strong ex-China Emerging markets growth
- Continued strong uptake for key medicines e.g. Farxiga, Tagrisso, Calquence and Enhertu
- Unique opportunity for Evusheld to provide protection against COVID-19 in vulnerable patients

**Growth supported by a diversified business model across key disease areas and geographies**

Growth rates at CER.
Financial results

Aradhana Sarin
Chief Financial Officer
Net debt and capital allocation priorities

FY 2021 dividend increased to $2.87 (intended annualised dividend increase of $0.10)

Net debt and capital allocation priorities

- Strong investment grade credit rating
- Reinvestment in the business
- Value-enhancing business development
- Progressive dividend policy

Net debt

Net debt: $24,322m; EBITDA: $7,586m

Net debt/EBITDA: 3.2x
Net debt/EBITDA adjusted for Alexion inventory fair value uplift: 2.5x

Capital allocation priorities

1. Earnings before interest, tax, depreciation and amortisation. 2. Comprises purchase and disposal of intangible assets, payment of contingent consideration from business combinations, purchase and disposal of non-current asset investments, movement in profit participation liability and disposal of investments in associates and joint ventures. 3. Comprises for Alexion acquisition: Upfront payment of ($13,349m), payments upon vesting of employee share awards ($211m) and movement in net debt related to acquisitions +$1,307m. AstraZeneca credit ratings: Moody’s: short-term rating P-2, long-term rating A3, outlook negative. S&P Global Ratings: short-term rating A-2, long-term rating A-, CreditWatch neutral. 4. EBITDA adding back the impact of $2,198m (FY 2020: $nil) unwind of inventory fair value uplift recognised on acquisition of Alexion. 5. Progressive dividend policy defined as either stable or increasing dividend per share in US dollar terms.
Oncology

Dave Fredrickson
EVP Oncology Business

Susan Galbraith
EVP Oncology R&D
Tagrisso and Imfinzi
Increased reimbursement and launches offsetting COVID-19 impact on diagnosis

**Tagrisso:** 13% growth to $5.0bn
Approvals/Reimbursements: 69/19 (adjuvant), 92/52 (1L), 92/68 (2L)

- **US +14%**
  FLAURA and ADAURA new patient starts and DoT growth
  2021 exit diagnosis rates for lung 10-15% below pre-pandemic levels
- **Europe +25% (Q4 +7%)**
  Increased reimbursement
- **ERoW +14%**
  Japan +8%
- **EM +6% (Q4 +23%)**
  China 1st-line volume growth continues after NRDL implementation

**Imfinzi:** 16% growth to $2.4bn
Approvals/Reimbursements: 75/35 (NSCLC), 67/9 (ES-SCLC)

- **US +5% (Q4 +10%)**
- **Europe +25%**
  Growth from PACIFIC and CASPIAN launches
- **ERoW +23%**
  Improving CRT rates and strong CASPIAN demand driving growth despite mandatory price adjustment in Japan in August
- **EM +68% (Q4 +44%)**
  Strong underlying demand China destocking in Q4 2021

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ERoW = established rest of world; EM = emerging markets; 1L = first line; 2L = second line; DoT = duration of treatment; ES-SCLC = extensive-stage small cell lung cancer; CRT = chemoradiation therapy; NRDL = national reimbursement drug list.
Lynparza

The globally leading PARP inhibitor across four tumour types

Product sales
30% growth to $2.3bn

Growth in all regions
Approvals: 86 (OC), 84 (mBC), 70 (mCRPC)

- US +24%
  Growth driven by ovarian, prostate and breast performance
  2021 exit diagnosis rates: 5-15% below baseline

- Europe +35%
  Increasing HRD testing, launches in new markets

- ERoW +28%
  Japan +21% driven by PAOLA-1 launch

- EM +41%
  Strong demand growth across EM, offsetting China NRDL renewal impact

Collaboration revenue
$3.5bn recorded, $4.2bn future potential
Calquence and Enhertu
Strong launch trajectories continue

**Calquence: 136% growth to $1.2bn**
Approvals/Reimbursements: 76/25 (CLL), 37/13 (MCL)

- Global $1,238m; US $1,089m
- US CLL
  Strong performance with 54% share of new patients starts
- Global CLL
  Continued launch performance in DE, UK, FR and International markets
- US MCL
  Preferred BTKi in relapsed refractory MCL

**Enhertu: 123% growth to $214m**
Approvals/Reimbursements: 9/4 (mBC), 4/2 (GC)

- Global $214m; US $169m
- Total in-market sales ex-Japan: $426m
- US
  #1 in 3rd-line HER2+ mBC, continuing launch in 2nd-line GC, NCCN and ESMO guidelines for 2nd-line mBC
- Global
  Strong launches in France and UK

CLL = chronic lymphocytic leukaemia; MCL = mantle cell lymphoma; BTKi = Bruton tyrosine kinase inhibitor; GC = gastric cancer; 3L = 3rd-line; NCCN = National Comprehensive Cancer Network; ESMO = European Society for Medical Oncology.
Oncology: R&D pipeline highlights

Strong congress presence; HIMALAYA and TOPAZ-1 support launch into GI cancers

**SABCS**

*Enhertu, Dato-DXd, Lynparza, Imfinzi and camizestrant*

- TROPION-PanTumor01: promising evidence of the anti-tumour activity of datopotamab deruxtecan in TNBC

**ASH**

*Calquence and capivasertib*

- ASCEND: durable efficacy for *Calquence* over three years in r/r CLL

**ASCO GI**

*Imfinzi, tremelimumab and Enhertu*

- Positive results in IO: HIMALAYA (HCC) and TOPAZ-1 (BTC)
- *Enhertu* gastric and colorectal trials

Wealth of new data reinforces leadership in Oncology, underscoring ambition to redefine cancer care
BioPharmaceuticals, Emerging Markets

Ruud Dobber
EVP, BioPharmaceuticals Business

Mene Pangalos
EVP, BioPharmaceuticals R&D
BioPharmaceuticals: Cardiovascular, Renal and Metabolism

Total Revenue $8.0bn; growth +9%

**Farxiga: 49% growth to $3.0bn**

Strong momentum continues, fastest growing SGLT2i globally

- US +29%, Europe +52% and EM +70%, boosted by HFrEF and CKD launches
- Volumes growing faster than the SGLT2i market in most major markets
- China NRDL status renewed
- #1 innovative anti-diabetic in China and Brazil

**Lokelma**

Global sales of $175m

- Continued strong growth in US and Japan. Expanding in new markets in Europe with new reimbursements achieved
- China NRDL listing from January 2022

---

SGLT2 = sodium-glucose transport protein 2 inhibitor; HFrEF = heart failure with reduced ejection fraction; CKD = chronic kidney disease; K+ = potassium; TRx = total prescriptions. 1. IQVIA US monthly total prescription share data
BioPharmaceuticals: Respiratory and Immunology

Total Revenue $6.0bn; growth +9%

**Fasenra**

- 31% growth to $1.3bn
- Leading biologic in eosinophilic asthma\(^1\)
- Global performance driven by new patient share
- Now a blockbuster medicine

**Breztri**

- COPD launch progressing; sales of $203m
- Global launch underway with 13% triple FDC branded market share in T8 countries, with 23% share in US, CN, JP
- Demand sales volume increase in China following NRDL inclusion

**Saphnelo**

- SLE launch progressing
  - Positive early market response, despite COVID-19 headwinds
  - US: $8m sales, with 35% NBRx share of i.v. market\(^3\)
  - Japan: formulary listing submissions are proceeding

---

\(^1\) Based on IQVIA MIDAS consolidated total patient top-7 market share (markets: US, JP, DE, FR, ES, IT, UK) in Q3 2021.

\(^2\) IQVIA MIDAS monthly days of therapy month end November 2021.

\(^3\) IQVIA LAAD claims data.

NBRx = new to brand prescriptions; COPD = chronic obstructive pulmonary disorder; FDC = fixed dose combinations; i.v. = intravenous.
**Tezspire** approved for severe asthma in the US

**First and only** biologic approved with no phenotype or biomarker limitation

### Addressing the unmet need in severe asthma

<table>
<thead>
<tr>
<th>c.2.5m of patients eligible for biologic treatment¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>c.83% patients not currently treated with biologics²</td>
</tr>
</tbody>
</table>

### Tezspire addresses the full spectrum of severe asthma patients

<table>
<thead>
<tr>
<th>Indicator</th>
<th>% Total Patient Population³-¹²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood eosinophils (≥ 300 cells/µL)</td>
<td>40-50%</td>
</tr>
<tr>
<td>Blood eosinophils (&lt;300 cells/µL)</td>
<td>50-60%</td>
</tr>
<tr>
<td>Blood eosinophils (&lt;150 cells/µL)</td>
<td>25-30%</td>
</tr>
<tr>
<td>With allergic features</td>
<td>c.65%</td>
</tr>
<tr>
<td>Inflammatory drivers overlap</td>
<td>c.60%</td>
</tr>
</tbody>
</table>

Only biologic proven to significantly reduce exacerbations in these patient populations

---

Emerging Markets
Total revenue $12.3bn (including Vaxzevria\textsuperscript{1} revenue)

Diversified growth across geographies
Launches in ex-China Emerging Markets progressing well

- **Oncology** $3.2bn, +6%; *Tagrisso* $1.3bn, up 6% continued impact from NRDL inclusion in China, offset by solid growth ex-China for *Lynparza, Imfinzi,* and *Tagrisso*

- **CVRM** $3.8bn, +12%; continued strong growth for *Forxiga* ($1.2bn, +70%) driven by HF and CKD launches

- **Respiratory & Immunology** $1.7bn, +4%; *Pulmicort* ($770m, -9%) due to VBP inclusion in October. *Symbicort* growth ($609m, +4%) mainly driven by ex-China

\textsuperscript{1} Vaxzevria Total Revenue\textsuperscript{1} also includes Collaboration Revenue from sub-licensees that produce and supply the AstraZeneca COVID-19 Vaccine under their own trademarks. 2. Growth number calculated excluding revenue of the Vaxzevria. Growth including Vaxzevria is as follows: Emerging Market total revenue growth +36%, China +4%; Other EMs +89%.
BioPharmaceuticals: R&D pipeline highlights

Four NMEs approved in 2021: Saphnelo, Tezspire, Evusheld and Vaxzevria

**Evusheld**

Only long-acting antibody combination shown to prevent and treat COVID-19

- Authorised in eight countries, including US EUA
- Retains neutralising activity against Omicron
- US agreements for 1.2m doses
  - Agreements include US Gov development funding

**Vaxzevria**

Clinical and real-world evidence supports use as booster

- 2.5bn doses supplied in 2021
- Boosts immune response against Omicron
- Retains neutralising activity after two-doses
- Vaxzevria and AZD2816 generated similar immune response to variants of concern

**eplontersen**

ATTR

Collaboration with Ionis Pharmaceuticals

- ATTR: misfolded protein and accumulation as amyloid fibrils
  - ATTR-CM (cardiomyopathy)
  - hATTR-PN (polyneuropathy, hereditary)

- Phase III trials:
  - CARDIO-TTRansform (data 2023+)
  - NEURO-TTRansform (data H2 2022)
Rare Disease

Marc Dunoyer
Chief Executive Officer, Alexion
Rare Disease

Total Revenue $3.1bn; +9% pro rata\textsuperscript{1} FY 2021

Growth across all regions

<table>
<thead>
<tr>
<th>Region</th>
<th>FY 2020\textsuperscript{2}</th>
<th>FY 2021</th>
</tr>
</thead>
<tbody>
<tr>
<td>US</td>
<td>+8%</td>
<td>+9%</td>
</tr>
<tr>
<td>EU</td>
<td>+11%</td>
<td></td>
</tr>
<tr>
<td>ERoW</td>
<td>+18%</td>
<td></td>
</tr>
<tr>
<td>EM</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Opportunity for geographic expansion leveraging AstraZeneca’s footprint

Rare Disease performance

C5 Franchise (\textit{Soliris} + \textit{Ultomiris}) +11% Q4; +8% pro rata FY 2021\textsuperscript{2}:

- \textbf{Soliris}: double-digit volume growth in Neurology; Q4 benefitted from tender market order timing
- \textbf{Ultomiris}: continued conversion in PNH, aHUS despite COVID-19 impact; 14 new country launches in FY 2021
- \textbf{Strensiq}: growth driven by increased demand in US
- \textbf{Kanuma}: strong revenue growth driven by ex-US demand
- \textbf{Andexxa}: strong revenue growth in EU, offset by COVID-related hospital access challenges in the US

1. FY 2021 revenues from date of acquisition closing, 21 July 2021 through 31 December 2021; pro forma growth rates calculated by comparison post-acquisition revenues with the corresponding prior year revenues adjusted pro-rata to match the post-acquisition period. 2. Inclusive of total revenues previously reported by Alexion and not adjusted for consistency with AstraZeneca’s accounting policies, not audited and not included in AstraZeneca’s FY 2021 results.
Expanding beyond heart failure in amyloidosis

Cohesive commercial and development strategy across Cardiovascular and Rare Disease

Leveraging strengths and expertise
across Cardiovascular, Rare Disease

Farxiga in Heart Failure (HFrEF, HFpEF)

Amyloidosis commonly misdiagnosed as HFpEF

TTR and AL represent majority of amyloidosis diagnoses

ATTR amyloidosis
AL amyloidosis

Ex. ATTR-CM ~400-500k patients WW1,2
~20k patients US, EU5

Complementary MOAs needed in ATTR
to address full spectrum of patient need

Building a strategic presence in amyloidosis

4. Internal epidemiological analysis: Mayo Stage III a + b
Investing in Rare Disease
Late-stage weighted pipeline, multiple long-term growth opportunities

Robust late-stage pipeline
breadth of LCM and NME opportunities

Expanding & diversifying
our Rare Disease portfolio; key events in Q4

- US FDA accepted *Ultomiris* in generalised myasthenia gravis for priority review, PDUFA date in Q2 2022

- Exclusive global license for NI006, novel depleter in development for ATTR amyloidosis

- Investing in complement capabilities with expansion of New Haven research facility, and establishment of European development hub in Barcelona

Diversified pipeline with multiple late-stage programmes beyond complement

FDA = Food and Drug Administration; PDUFA = Prescription Drug User Fee Act.
Closing remarks
and Q&A
### Pipeline catalysts for 2022 - 2023

**Industry leading news flow**

<table>
<thead>
<tr>
<th>Year</th>
<th>Regulatory decision</th>
<th>Regulatory submission and/or acceptance</th>
<th>Key Phase III data readouts</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>H1 2022</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymparza – breast cancer (adjuvant) (US)</td>
<td>Imfinzi +/- tremelimumab – liver cancer (1L) (HIMALAYA)</td>
<td>Imfinzi – NSCLC (1L) (PEARL)</td>
<td></td>
</tr>
<tr>
<td>Brilique – stroke (THALES) (CN)</td>
<td>Imfinzi – cervical cancer (EMERALD-1)</td>
<td>Imfinzi – cervical cancer (CALLA)</td>
<td></td>
</tr>
<tr>
<td>Farxiga – chronic kidney disease (CN)</td>
<td>Enhertu – HER2-low breast cancer (3L) (DESTINY-Breast04)</td>
<td>Enhertu – HER2+ breast cancer (3L) (DESTINY-Breast02)</td>
<td></td>
</tr>
<tr>
<td>Saphnelo – lupus (SLE) (EU)</td>
<td>Koselugo – NF1-PN (SPRINT) (CN)</td>
<td>Fasenra – NMOSD</td>
<td></td>
</tr>
<tr>
<td>Ultomiris – gMG (US)</td>
<td>eplontersen – hTTR-PN (NEURO-TTRTransform)</td>
<td>Imfinzi – NSCLC (unresectable, Stg. III) (PACIFIC-2)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ultomiris – subcutaneous, PNH and aHUS (EU)</td>
<td>Imfinzi – NSCLC (unresectable, Stg. III) (PACIFIC-2)</td>
<td></td>
</tr>
</tbody>
</table>

| **H2 2022** | | | |
| Tagrisso – EGFRm NSCLC (adjuvant) (JP) | Imfinzi +/- tremelimumab – NSCLC (1L) | Imfinzi – NSCLC (1L) (PEARL) |
| Tagrisso – EGFRm NSCLC (adjuvant) (JP) | Lymparza – ovarian cancer (1L) (CN) | Imfinzi – cervical cancer (CALLA) |
| Tagrisso – EGFRm NSCLC (1L) (FLAURA2) | Lymparza – prostate cancer (1L) (EU) | Enhertu – HER2+ breast cancer (3L) (DESTINY-Breast02) |
| | Enhertu – HER2+ breast cancer (2L) (EU, JP) | Koselugo – NF1-PN (SPRINT) (CN) |
| | Enhertu – HER2+ gastric cancer (2L) (EU) | Fasenra – NMOSD |
| | Urolitumab – gMG (US, JP) | ALXN1840 – Wilson disease |

| **2023** | | | |
| Tagrisso – EGFRm NSCLC (1L) (FLAURA2) | Imfinzi – NSCLC (1L) (PEARL) | Imfinzi – NSCLC (1L) (PEARL) |
| Tagrisso – EGFRm NSCLC (unresectable Stg. III) (LAURA) | Imfinzi – cervical cancer (EMERALD-1) | Imfinzi – cervical cancer (EMERALD-1) |
| Tagrisso – EGFRm NSCLC (unresectable Stg. III) (LAURA) | Enhertu – HER2+ breast cancer (3L) (DESTINY-Breast02) | Enhertu – HER2+ breast cancer (3L) (DESTINY-Breast02) |
| | Koselugo – NF1-PN (SPRINT) (CN) | Koselugo – NF1-PN (SPRINT) (CN) |
| | Fasenra – NMOSD | Fasenra – NMOSD |
| | ALXN1840 – Wilson disease | ALXN1840 – Wilson disease |

**Key Pharmacology**

- **EGFRm =** epidermal growth factor receptor mutated; HER2+ = human epidermal growth factor receptor 2 low; Her2 = heart failure with preserved ejection fraction; NMOSD = neuromyelitis optica spectrum disorder; MCL = mantle cell lymphoma; HES = hyper eosinophilic syndrome; EOE = eosinophilic oesophagitis; TNBC = triple negative breast cancer; adv = advanced; met = metastatic; HR+ = hormone receptor positive; HER2- neg = human epidermal growth factor receptor 2 low; HER2oe = human epidermal growth factor receptor over expressing; HER2m = human epidermal growth factor mutant; CrhNP = chronic rhinosinusitis with nasal polyps; EGPA = eosinophilic granulomatosis with polyangiitis.
AstraZeneca: the next chapter

Industry-leading growth, best-in-class innovative pipeline

Double-digit CAGR through 2025
 Longer-term growth fueled by existing portfolio and new innovative medicines

Differentiated, durable portfolio
 Attractive LOE profile, unrivalled R&D productivity and pipeline

Financial execution
 Continued focus on operating leverage and cash generation

Reinvestment in our main disease areas
 High-growth pipeline opportunities, value-enhancing business development
Q&A

Full-year and Q4 2021 Results
Appendix
Scope 1+2 emissions reduction targets

Absoulute Scope 1+2 emissions reduction targets

Target ranking

<table>
<thead>
<tr>
<th>Company</th>
<th>Target temperature alignment (°C)²</th>
<th>Rank</th>
</tr>
</thead>
<tbody>
<tr>
<td>AstraZeneca</td>
<td>&lt;1.1</td>
<td>1</td>
</tr>
<tr>
<td>Novo Nordisk</td>
<td>&lt;1.1</td>
<td>2</td>
</tr>
<tr>
<td>Takeda</td>
<td>&lt;1.1</td>
<td>3</td>
</tr>
<tr>
<td>Sanofi</td>
<td>1.15</td>
<td>4</td>
</tr>
<tr>
<td>Merck &amp; Co</td>
<td>1.15</td>
<td>5</td>
</tr>
<tr>
<td>Roche</td>
<td>1.24</td>
<td>6</td>
</tr>
<tr>
<td>Johnson &amp; Johnson</td>
<td>1.37</td>
<td>7</td>
</tr>
<tr>
<td>GSK</td>
<td>1.38</td>
<td>8</td>
</tr>
<tr>
<td>Biogen</td>
<td>1.39</td>
<td>9</td>
</tr>
<tr>
<td>Bayer</td>
<td>1.40</td>
<td>10</td>
</tr>
<tr>
<td>Pfizer</td>
<td>1.40</td>
<td>11</td>
</tr>
<tr>
<td>AbbVie</td>
<td>1.64</td>
<td>12</td>
</tr>
<tr>
<td>Lonza</td>
<td>2.52</td>
<td>13</td>
</tr>
</tbody>
</table>

Source: Pollination, using Company reports, CDP. Note: Target trajectory is plotted from base year to target year. Actual historical emissions profiles from 2015 – 2020 will differ. Bayer’s target is not displayed due to scale of chart. Lonza’s target is not displayed due to being an intensity target. 1. Novartis’ target is to be carbon neutral across Scope 1+2 by 2025 from 2016 base year, level of mitigation targeted is unknown. 2. Utilising the SBTi temperature rating methodology.

* For AstraZeneca Pollination graphed the SBT “reduce absolute scope 1 and 2 GHG emissions 98% by FY2026 from a FY2015 base year”
Early pipeline news flow (1/2)

Next key milestone by project

### Oncology

<table>
<thead>
<tr>
<th>Project</th>
<th>Target</th>
<th>Phase</th>
<th>Indication</th>
<th>Next milestone</th>
</tr>
</thead>
<tbody>
<tr>
<td>adavosertib</td>
<td>WEE1</td>
<td>II</td>
<td>uterine, pancreatic cancer</td>
<td>Phase III start</td>
</tr>
<tr>
<td>ceralasertib</td>
<td>ATR</td>
<td>II</td>
<td>solid tumours blood cancers</td>
<td>Phase II data, 2023+</td>
</tr>
<tr>
<td>oleclumab</td>
<td>CD73</td>
<td>II</td>
<td>solid tumours</td>
<td>Phase II data, 2023</td>
</tr>
<tr>
<td>MEDIS752</td>
<td>PD-1/CTLA4</td>
<td>I/II</td>
<td>solid tumours</td>
<td>Phase I/II data, 2023+</td>
</tr>
<tr>
<td>AZD5991</td>
<td>MCL1</td>
<td>I/II</td>
<td>blood cancers</td>
<td>Phase I/II data, 2023+</td>
</tr>
<tr>
<td>AZD0466</td>
<td>Bcl-2-xL</td>
<td>II</td>
<td>blood cancers</td>
<td>Phase II data, 2023+</td>
</tr>
<tr>
<td>AZD8205</td>
<td>B7H4 ADC</td>
<td>I/II</td>
<td>solid tumours</td>
<td>Phase I/II data, 2023+</td>
</tr>
<tr>
<td>AZD5305</td>
<td>PARP1 sel</td>
<td>I/II</td>
<td>solid tumours</td>
<td>Phase I/II data, 2023+</td>
</tr>
<tr>
<td>AZD0171 + Imfinzi</td>
<td>anti-LIF mAb</td>
<td>II</td>
<td>NSCLC</td>
<td>Phase II data, 2023+</td>
</tr>
<tr>
<td>AZD7789</td>
<td>PD-1/TIM3</td>
<td>I/II</td>
<td>NSCLC</td>
<td>Phase I/II data, 2023+</td>
</tr>
<tr>
<td>AZD2936</td>
<td>PD-1/TIGIT</td>
<td>I</td>
<td>NSCLC</td>
<td>Phase I data, 2023+</td>
</tr>
<tr>
<td>AZD4573</td>
<td>CDK9</td>
<td>II</td>
<td>blood cancers</td>
<td>Phase II data, 2023</td>
</tr>
</tbody>
</table>

### BioPharmaceuticals: CVRM

<table>
<thead>
<tr>
<th>Project</th>
<th>Target</th>
<th>Phase</th>
<th>Indication</th>
<th>Next milestone</th>
</tr>
</thead>
<tbody>
<tr>
<td>cotadutide</td>
<td>GLP-1/glucagon</td>
<td>II</td>
<td>NASH</td>
<td>Phase III start, H2 2022</td>
</tr>
<tr>
<td>cotadutide</td>
<td>GLP-1/glucagon</td>
<td>II</td>
<td>DKD</td>
<td>Phase II data, H1 2022</td>
</tr>
<tr>
<td>AZD4831</td>
<td>MPO</td>
<td>II/III</td>
<td>HFpEF</td>
<td>Phase II/III data, 2023+</td>
</tr>
<tr>
<td>AZDS718</td>
<td>FLAP</td>
<td>II</td>
<td>CKD</td>
<td>Phase II data, 2023</td>
</tr>
<tr>
<td>AZD9977 + Farxiga</td>
<td>MCR + SGLT2</td>
<td>II</td>
<td>HF with CKD</td>
<td>Phase II data, 2023</td>
</tr>
<tr>
<td>zibotentan + Farxiga</td>
<td>ETR + SGLT2</td>
<td>II</td>
<td>CKD</td>
<td>Phase II data, H2 2022</td>
</tr>
<tr>
<td>AZD2693</td>
<td>PNPLA3</td>
<td>I</td>
<td>NASH</td>
<td>Phase I data, H1 2022</td>
</tr>
<tr>
<td>AZD8233</td>
<td>PCSK9</td>
<td>II</td>
<td>dyslipidaemia</td>
<td>Phase II data, H2 2022</td>
</tr>
<tr>
<td>tozorakimab</td>
<td>IL-33</td>
<td>II</td>
<td>DKD</td>
<td>Phase II data, 2023</td>
</tr>
</tbody>
</table>
## Early pipeline news flow (2/2)
### Next key milestone by project

### BioPharmaceuticals: Respiratory and Immunology

<table>
<thead>
<tr>
<th>Project</th>
<th>Target</th>
<th>Phase</th>
<th>Indication</th>
<th>Next milestone</th>
</tr>
</thead>
<tbody>
<tr>
<td>tozorakimab</td>
<td>IL-33</td>
<td>II</td>
<td>asthma</td>
<td>Phase II data, H2 2022</td>
</tr>
<tr>
<td>tozorakimab</td>
<td>IL-33</td>
<td>II</td>
<td>COPD</td>
<td>Phase III start, 2022</td>
</tr>
<tr>
<td>tozorakimab</td>
<td>IL-33</td>
<td>II</td>
<td>AD</td>
<td>Phase II data, H2 2022</td>
</tr>
<tr>
<td>tozorakimab</td>
<td>IL-33</td>
<td>II</td>
<td>COVID-19</td>
<td>Phase II data, H1 2022</td>
</tr>
<tr>
<td>AZD1402</td>
<td>IL-4R alpha</td>
<td>II</td>
<td>asthma</td>
<td>Phase II data, H2 2022</td>
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<tr>
<td>AZD4604</td>
<td>inhaled JAK</td>
<td>I</td>
<td>asthma</td>
<td>Phase I data, 2023</td>
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<tr>
<td>MEDI7352</td>
<td>NGF TNF</td>
<td>II</td>
<td>painful diabetic neuropathy</td>
<td>Phase II data, 2023</td>
</tr>
<tr>
<td>MEDI7352</td>
<td>NGF TNF</td>
<td>II</td>
<td>osteoarthritic pain</td>
<td>Phase II data, 2023</td>
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</table>

### Rare Disease

<table>
<thead>
<tr>
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<th>Target</th>
<th>Phase</th>
<th>Indication</th>
<th>Next milestone</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALXN1720</td>
<td>3rd-gen CS</td>
<td>I</td>
<td>gMG</td>
<td>Phase I data, H1 2022</td>
</tr>
<tr>
<td>danicopan</td>
<td>Factor D</td>
<td>II</td>
<td>geographic atrophy</td>
<td>Phase II data, 2023</td>
</tr>
<tr>
<td>danicopan</td>
<td>Factor D</td>
<td>III</td>
<td>PNH with EVH</td>
<td>Phase III data, H1 2023</td>
</tr>
<tr>
<td>ALXN1820</td>
<td>anti-properdin</td>
<td>I</td>
<td>haematology</td>
<td>Phase I data, 2023</td>
</tr>
<tr>
<td>ALXN2050</td>
<td>Factor D</td>
<td>II</td>
<td>PNH monotherapy</td>
<td>Phase II data, H1 2022</td>
</tr>
<tr>
<td>ALXN2050</td>
<td>Factor D</td>
<td>II</td>
<td>gMG</td>
<td>Phase II data, H1 2022</td>
</tr>
<tr>
<td>ALXN2050</td>
<td>Factor D</td>
<td>II</td>
<td>renal indications</td>
<td>Phase II data, 203+</td>
</tr>
<tr>
<td>ALXN1850</td>
<td>next-gen asfotase alfa</td>
<td>I</td>
<td>hypophosphatasia</td>
<td>Phase I data, H2 2022</td>
</tr>
</tbody>
</table>
Commercial context: PROpel, HIMALAYA, TOPAZ-1 and DESTINY-Breast04
PROOpel
Prostate is the second most common cancer in male patients. mCRPC therapies are limited; mostly monotherapy, including in first line.

<table>
<thead>
<tr>
<th>NHA naïve at mCRPC</th>
<th>NHA experienced in mCRPC</th>
<th>Hormone sensitive</th>
<th>Castration resistant</th>
</tr>
</thead>
<tbody>
<tr>
<td>~50%</td>
<td>~50%</td>
<td>Urologist-led</td>
<td>Urologists and oncologists</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Biochemical</td>
<td>mHSPC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>recurrence</td>
<td>nm CRPC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Recurrent</td>
<td>1st-line metastatic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ADT +/- docetaxel</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>De-novo</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>ADT +/- docetaxel +/- RTx</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>NHA or docetaxel</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Lynparza (PROfound)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>cheomo/palliative care</td>
</tr>
<tr>
<td></td>
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<td></td>
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</tr>
</tbody>
</table>


ADT = androgen deprivation therapy; RTx = radiation therapy; nmCRPC = non-metastatic castration resistant prostate cancer
Outcomes remain poor
in advanced prostate cancer

40% of patients with prostate cancer will develop metastatic disease\(^1\)-\(^3\)

30% the 5-year survival rate for patients with metastatic disease\(^4\)

3 years median OS for mCRPC patients in the first-line setting\(^5\)-\(^9\)

50% of patients receive only one line of active therapy in mCRPC\(^1\)\(^0\)

PROpel - unprecedented clinical benefit without compromising quality of life - a potential new SoC in mCRPC

42

PROpel building on the success of PROfound

• Representative real-world population - simple trial design
• All-comers ITT population
• Retrospective HRR testing via tissue and ctDNA testing\(^1\)\(^1\)
• Primary endpoint: radiographic progression free survival
• Key secondary endpoints: Overall survival, time to first subsequent therapy, time to second progression or death

8.2-month median rPFS benefit over abiraterone alone


OS = overall survival; ITT = intent-to-treat.
PROpel: a new treatment approach in 1st-line mCRPC

A clear option for NHA-naïve patients regardless of HRRm status

The first combination trial to demonstrate consistent clinical benefit in 1st-line mCRPC

Source: AstraZeneca estimates. 1. Pending health authority authorisation. The PROpel trial data is not currently approved in any jurisdiction.
HIMALAYA & TOPAZ-1
TOPAZ-1 has the potential to become the first-ever IO therapy available for first-line, advanced biliary tract cancer patients

Lack of innovation in biliary tract cancer

10+ years
without innovation on top of standard of care

5% to 15%
of all patients with BTC surviving only five years

75%
of BTC patients present with advanced, unresectable BTC

TOPAZ-1 has practice-changing potential

• Trial stopped early at an interim analysis due to clear efficacy, with almost all patients alive at two years versus one in 10 on chemotherapy alone

• Potential new standard of care in this historically underserved cancer

• Safety: no AE-related increase in discontinuations

First IO therapy to demonstrate long-term survival in first-line advanced BTC

~ 50,000 people in the US, Europe and Japan and about 210,000 people worldwide are diagnosed with BTC each year

HIMALAYA – an innovative IO regimen delivering survival benefit to patients with advanced, unresectable hepatocellular carcinoma

Large unmet need in liver cancer

3rd
leading cause of cancer death worldwide

7%
five-year survival in advanced HCC

At least 40%
of treatment eligible first-line advanced HCC patients are at risk of bleeding

1 in 3 patients alive at three years on STRIDE regimen versus one in five on sorafenib

Innovative STRIDE regimen with tremelimumab

• First IO+IO combination in first-line advanced, unresectable HCC
• Only Phase III trial to show benefit of single, priming dose of CTLA-4
• Impressive three-year landmark OS data with almost

Clear efficacy, safety and simplicity for patients

• Imfinzi monotherapy non-inferior to sorafenib, with numerical advantage in OS
• No increased bleeding risk or severe liver toxicity seen in trials
• Exceptional safety profile

IO-only combination strategy simplifies patient management

Regulatory submissions in H1 2022

~80,000 people in the US, Europe and Japan and 260,000 people in China present with advanced, unresectable HCC each year

Liver cancer: HIMALAYA & TOPAZ-1 extending survival in hard-to-treat GI cancers

Presenting with liver cancer

Hepato-cellular cancer

Local/Locoregional stage diagnosis

Advanced Stage, Drug treated

BSC

Recurrent patients

HIMALAYA

Presenting with non-liver biliary tract carcinomas

Biliary tract carcinoma

Early Stage

Advanced Stage, Drug treated

BSC

TOPAZ-1

Source: SEER, WHO, World Bank population projections, Kantar Health, Data Monitor, DRG and AZ modelling. BSC = best supportive care
DESTINY-Breast04
**Enhertu in breast cancer and beyond**

Opportunities across treatment settings

<table>
<thead>
<tr>
<th>HER2-positive breast cancer</th>
<th>neo-adjuvant / adjuvant</th>
<th>1st-line metastatic</th>
<th>2nd-line metastatic</th>
<th>3rd-line metastatic</th>
</tr>
</thead>
<tbody>
<tr>
<td>neo-adjuvant</td>
<td>replace chemo + trastuzumab + pertuzumab</td>
<td>replace chemotherapy + trastuzumab + pertuzumab</td>
<td>replace T-DM1 and other standard of care</td>
<td></td>
</tr>
<tr>
<td>post neo-adjuvant</td>
<td>replace T-DM1</td>
<td>replace chemotherapy + trastuzumab + pertuzumab</td>
<td></td>
<td></td>
</tr>
<tr>
<td>adjuvant</td>
<td>replace chemotherapy + trastuzumab + pertuzumab</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**HER2-low breast cancer**

<table>
<thead>
<tr>
<th>HR+: chemotherapy ± endocrine therapy</th>
<th>endocrine ± CDK4/6i</th>
<th>replace/displace chemotherapy and endocrine combinations¹</th>
</tr>
</thead>
</table>

**Beyond breast cancer**

- **HR-**: chemotherapy +/- IO
- **broaden** in gastric cancer and **expand** into NSCLC, CRC and other cancers

---

1. in endocrine therapy refractory/resistant patients.

**HR** = hormone-receptor positive; **CDK4/6i** = cyclin-dependent kinase 4/6 inhibitor; **HR** = hormone-receptor negative; **IO** = immuno-oncology. **NSCLC** = non-small cell lung cancer; **CRC** = colorectal cancer.
Enhertu: an extensive clinical development programme
Focusing on HER2+ and HER2-low breast cancer and other cancers

**Breast cancer**
- **HER2+**
  - Post-neoadjuvant/Adjuvant: DESTINY-Breast05 Ph III
  - 1st line: DESTINY-Breast07 Ph ib/II (Part 2)
  - 2nd line: DESTINY-Breast03 Ph III
  - 3rd line+: DESTINY-Breast01 Ph II

- **HER2 Low**
  - Post-neoadjuvant/Adjuvant: DESTINY-Breast09 Ph III
  - 1st line: DESTINY-Breast06 Ph III
  - 2nd line: DESTINY-Breast04 Ph III

**Gastric cancer**
- **HER2+**
  - Post-neoadjuvant/Adjuvant: DESTINY-Gastric03 Ph ib/II
  - 1st line: DESTINY-Gastric02 Ph II
  - 2nd line: DESTINY-Gastric01 Ph II
  - 3rd line+: DESTINY-Gastric06 Ph II

**Lung, CRC and other cancers**
- **HER2 mutated**
  - 1st line: DESTINY-Lung02 Ph II
  - 2nd line: DESTINY-Lung01 Ph II
  - 3rd line+: DESTINY-CRC01 Ph II

- **HER2 expressing**
  - 1st line: DESTINY-Lung03 Ph Ib
  - 2nd line: DESTINY-PanTumor02 Ph II
  - 3rd line+: DESTINY-CRC02 Ph II

**DESTINY** trials:
- DESTINY-Breast01 Ph II
- DESTINY-Breast02 Ph III
- DESTINY-Breast07 Ph ib/II (Part 1)
- DESTINY-Gastric01 Ph II
- DESTINY-Gastric06 Ph II
- DESTINY-Lung01 Ph II
- DESTINY-PanTumor02 Ph II
- DESTINY-CRC02 Ph II

**Monotherapy** vs **Combination**
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+ c.20% of patients</th>
<th>HER2 low c.55% of patients that are not HER2+</th>
<th>Hormone-receptor positive (HR+) c.65% of patients</th>
<th>Triple-negative (TNBC) c.15% of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early/curative setting</td>
<td>Neo-adjuvant</td>
<td>Adjuvant</td>
<td>ADC&lt;sup&gt;2&lt;/sup&gt;-/- IO&lt;sup&gt;3&lt;/sup&gt;</td>
</tr>
<tr>
<td>Early/curative setting</td>
<td>Enhertu monotherapy and potential combos</td>
<td>1st line</td>
<td>neo-adjuvant</td>
</tr>
<tr>
<td>Early/curative setting</td>
<td>camizestrant</td>
<td>2nd line</td>
<td>capivasertib + CTx&lt;sup&gt;4&lt;/sup&gt;</td>
</tr>
<tr>
<td>Early/curative setting</td>
<td>Enhertu monotherapy and potential combos</td>
<td>3rd line</td>
<td></td>
</tr>
<tr>
<td>Early/curative setting</td>
<td>datopatamab deruxtecan</td>
<td>3rd line+</td>
<td></td>
</tr>
<tr>
<td>Metastatic setting</td>
<td>c.20% of patients</td>
<td>1st line</td>
<td></td>
</tr>
<tr>
<td>Metastatic setting</td>
<td>camizestrant</td>
<td>2nd line</td>
<td></td>
</tr>
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<td></td>
</tr>
<tr>
<td>Metastatic setting</td>
<td>Enhertu</td>
<td>3rd line+</td>
<td></td>
</tr>
<tr>
<td>Metastatic setting</td>
<td>Enhertu</td>
<td>datopatamab deruxtecan</td>
<td></td>
</tr>
</tbody>
</table>

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

Illustrative; includes trials planned.
**DESTINY-Breast04**

**3L HER2-low mBC in the US**
- Chemo naïve ~65%
- Prior Chemo ~35%

**4L+ HER2-low mBC in the US**
- Chemo naïve ~35%
- Prior Chemo ~65%

**DB04**

DB04 population equates to a treated patient population of around half all 3L+ patients.

DB06 includes chemo naïve patients in 2L/3L+

Source: Kantar Health Cancer Mpact 2021, literature for HER2-Low. Prior estimate of US 3L HER2 low mBC was ~12k Feb 2020 epi update as drug treatment rates increase and HR- patients are included.
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