Meet AZN management: ASCO 2019
Forward-looking statements

In order, among other things, to utilise the ‘safe harbour’ provisions of the US Private Securities Litigation Reform Act 1995, we are providing the following cautionary statement: this document contains certain forward-looking statements with respect to the operations, performance and financial condition of the Group, including, among other things, statements about expected revenues, margins, earnings per share or other financial or other measures. Although we believe our expectations are based on reasonable assumptions, any forward-looking statements, by their very nature, involve risks and uncertainties and may be influenced by factors that could cause actual outcomes and results to be materially different from those predicted. The forward-looking statements reflect knowledge and information available at the date of preparation of this document and AstraZeneca undertakes no obligation to update these forward-looking statements. We identify the forward-looking statements by using the words 'anticipates', 'believes', 'expects', 'intends' and similar expressions in such statements. Important factors that could cause actual results to differ materially from those contained in forward-looking statements, certain of which are beyond our control, include, among other things: the loss or expiration of, or limitations to, patents, marketing exclusivity or trademarks, or the risk of failure to obtain and enforce patent protection; effects of patent litigation in respect of IP rights; the impact of any delays in the manufacturing, distribution and sale of any of our products; the impact of any failure by third parties to supply materials or services; the risk of failure of outsourcing; the risks associated with manufacturing biologics; the risk that R&D will not yield new products that achieve commercial success; the risk of delay to new product launches; the risk that new products do not perform as we expect; the risk that strategic alliances and acquisitions, including licensing and collaborations, will be unsuccessful; the risks from pressures resulting from generic competition; the impact of competition, price controls and price reductions; the risks associated with developing our business in emerging markets; the risk of illegal trade in our products; the difficulties of obtaining and maintaining regulatory approvals for products; the risk that regulatory approval processes for biosimilars could have an adverse effect on future commercial prospects; the risk of failure to successfully implement cost reduction measures through productivity initiatives and restructuring programmes; the risk of failure of critical processes affecting business continuity; economic, regulatory and political pressures to limit or reduce the cost of our products; failure to achieve strategic priorities or to meet targets or expectations; the risk of substantial adverse litigation/government investigation claims and insufficient insurance coverage; the risk of substantial product liability claims; the risk of failure to adhere to applicable laws, rules and regulations; the risk of failure to adhere to applicable laws, rules and regulations relating to anti-competitive behaviour; the impact of increasing implementation and enforcement of more stringent anti-bribery and anti-corruption legislation; taxation risks; exchange rate fluctuations; the risk of an adverse impact of a sustained economic downturn; political and socio-economic conditions; the risk of environmental liabilities; the risk of occupational health and safety liabilities; the risk associated with pensions liabilities; the impact of failing to attract and retain key personnel and to successfully engage with our employees; the risk of misuse of social medial platforms and new technology; and the risk of failure of information technology and cybercrime. Nothing in this presentation / webcast should be construed as a profit forecast.
Meet AZN management: ASCO 2019
Opening session
Agenda

Strategy and business

ASCO 2019 highlights

- *Lynparza* pancreatic cancer (POLO trial)
- *Lynparza* 3rd-line ovarian cancer (SOLO3 trial)
- Other highlights

Breakout sessions
Cancer is still a growing burden

<table>
<thead>
<tr>
<th>Year</th>
<th>New Patients</th>
<th>Deaths</th>
<th>Living with Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>2018</td>
<td>18.1 million</td>
<td>9.6 million</td>
<td>43 million</td>
</tr>
<tr>
<td>2030 estimate</td>
<td>26.4 million</td>
<td>17 million</td>
<td>82 million</td>
</tr>
</tbody>
</table>

Source: International Agency for Research on Cancer.
# Oncology: strategy

A leading, diversified oncology business

<table>
<thead>
<tr>
<th>Lung cancer</th>
<th>Multiple cancers</th>
<th>Multiple cancers</th>
<th>Haematology</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Stage IV NSCLC&lt;sup&gt;1&lt;/sup&gt; T790Mm&lt;sup&gt;2&lt;/sup&gt; / EGFRm&lt;sup&gt;3&lt;/sup&gt;</td>
<td>• Unresectable, Stage III NSCLC</td>
<td>• Ovarian, breast cancers</td>
<td>• First medicine in haematology</td>
</tr>
<tr>
<td>• Next: adjuvant, Stage III</td>
<td>• Next: early / advanced stages in several cancers</td>
<td>• MRK collaboration</td>
<td>• MCL&lt;sup&gt;6&lt;/sup&gt; launched</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Next: pancreatic, prostate cancers</td>
<td>• CLL&lt;sup&gt;7&lt;/sup&gt; data started</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Next: combos</td>
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</tbody>
</table>

**‘What’s next’: rich early to mid-stage pipeline, including combinations**

Lung cancer: *Tagrisso*
Realising global opportunity in patients with 1st-line EGFRm disease

**Strong performance in all markets: +92% in Q1 2019**

**1st-line opportunity is moving global**

- **Phase IIIs in early-stage disease**
  - Adjuvant (ADAURA trial)
  - Locally-advanced (LAURA trial)

- **Phase IIls in post-*Tagrisso* progression**
  - Savolitinib/MET combination (SAVANNAH trial)
  - EGFR, PD-L1, MET, A2aR, CD73, dual EGFR (ORCHARD trial)

**Final overall survival data anticipated in H2 2019**

Source: European Society for Medical Oncology meeting 2017.

Source: AstraZeneca data on file.
Lung cancer: Imfinzi
Global adoption underway; lifecycle trials will expand to more patients

Ex-US now 22% of total, up from 18% in Q4 2018

Major ongoing Phase III trials with Imfinzi used as backbone

- AEGEAN (2020)
- ADJUVANT (2020+)
- NIAGARA (2020+)
- PACIFIC-5 (2020+)
- ADRIATIC (2020+)
- EMERALD-1 (2020+)
- POTOMAC (2020+)
- PACIFIC-2 (2020+)
- PACIFIC-4 (2020+)
- EMERALD-2 (-)
- PACIFIC-5 (2020+)
- NILE (2020+)
- PEARL (2020+)
- CASPIAN (H2 2019)
- DANUBE (H2 2019)
- POSEIDON (H2 2019)
- NEPTUNE (H2 2019)
- HIMALAYA (2020+)
- KESTREL (H2 2019)
- TOPAZ-1 (-)
- CALLA (2020+)

Cancer type
- Bladder
- Lung
- Liver
- H&N
- Cervical
- Biliary

( ) denote anticipated timeline for data readout. The staging above does not apply to small-cell lung cancer (CASPIAN and ADRIATIC trials). Source: AstraZeneca Q1 2019 results announcement. Excludes combination trials where Lynparza is considered the backbone medicine.
Lynparza
Strong performance; industry-leading development programme

Seven quarters of strong growth: +105% in Q1 2019
Ex-US now 50% of total

Extensive, strategic development programme underway

Earlier lines of treatment

1st-line ovarian SOLO-1
2nd-line ovarian SOLO-2
3rd-line ovarian SOLO3
adjuvant breast OlympiA
Ovarian with cediranib
Ovarian with bevacizumab
Ovarian with Imfinzi
Ovarian with abiraterone

New cancer types

Ovarian Study 19
Breast OlympiAD
Pancreas POLO
Prostate PROfound

US Europe Established RoW Emerging markets
Absolute values at actual exchange rates; changes at CER and for Q1 2019, unless otherwise stated.

In collaboration with Merck.
Source: AstraZeneca data on file.
Important future platforms with significant growth

Trastuzumab deruxtecan and *Calquence*

Trastuzumab deruxtecan: unprecedented efficacy in heavily-pretreated HER2+ metastatic breast cancer

- **59.5%** confirmed objective response rate
- **20.7 months** median duration of response
- **Seven** median lines of prior treatment

**US regulatory submission in H2 2019**

**Regulatory decision anticipated in 2020**

Haematology taking shape: *Calquence* on track to benefit patients globally

**CLL**
- Study ‘309’ in relapsed/refractory (r/r) patients met primary endpoint; presentation at meeting in June 2019
- Study ‘007’ in front-line patients on track for H2 2019 data readout

**MCL**
- Launched in US and a few global markets
- Sales of $94m since launch

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1. Not estimable.

Source: based on Phase I data, *The Lancet Oncology*, April 2019. Phase II DESTINY-Breast01 data have not been presented yet; trial met primary endpoint in May 2019 and will form the basis for the US regulatory submission.

Source: AstraZeneca data on file.

Absolute values at actual exchange rates.

Source: AstraZeneca data on file.
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Breakout sessions
### ASCO 2019 highlights

**Solid AstraZeneca presence at ASCO 2019**

- 93 abstracts accepted, including **12 orals** and **11 poster discussions**
- Externally-sponsored ~45% of total

**Data highlights from select mid-to-late stage trials**

- **Lynparza**
  - Phase III POLO - BRCAm pancreatic cancer
  - Phase III SOLO3 - BRCAm ovarian cancer
  - Phase II TOPARP-B - prostate cancer HRRm\(^1\)
- **Imfinzi**
  - Phase III PACIFIC - unresectable, Stage III NSCLC (three-year landmark OS data)
- **Calquence**
  - Phase II ACE-CL-208/ACE-CL-003 - CLL
- **capivasertib (AKT inhibitor)**
  - Phase II FAKTION - ER\(^+\) breast cancer

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1. Homologous recombination repair.
2. Eestrogen-receptor positive.

Source: AstraZeneca data on file based on submitted and accepted ASCO 2019 Annual Meeting abstracts.

Source: ASCO 2019.
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Breakout sessions
**Lynparza**
Pancreatic cancer - POLO trial

**Metastatic pancreatic cancer**

4–7% harbor a germline BRCA1 and/or BRCA2 mutation (gBRCAm)\(^4\,5\)

Increased benefit from platinum-based chemotherapy\(^6\,7\)

Maintenance treatments aim to delay disease progression following chemotherapy without compromising HRQoL

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Lynparza
Pancreatic cancer - POLO trial

Key eligibility criteria
Metastatic pancreatic cancer
Deleterious or suspected deleterious germline BRCA1 or BRCA2 mutation
≥16 weeks first-line platinum-based chemotherapy with no limit to duration, without progression (CR, PR or SD)*

Randomized 3:2
No stratification factors

Olaparib tablets 300 mg bid
or
Placebo

Until investigator-assessed disease progression or unacceptable toxicity

38% of gBRCAm patients had disease progression, were ineligible, or declined randomization

*There was no maximum limit to the duration of first-line chemotherapy. bid, twice daily; CR, complete response; PR, partial response; SD, stable disease
Lynparza
Pancreatic cancer - POLO trial
**Lynparza**
Pancreatic cancer - POLO trial

**OS: interim analysis, 46% maturity***

- **Median OS, months**
  - Olaparib (N=92): 18.9
  - Placebo (N=62): 18.1
  - HR 0.91
  - 95% CI 0.56, 1.46; P=0.68

- **Final OS analysis planned at 106 events**

**Subsequent treatment with a PARP inhibitor:**
1 olaparib patient (1.1%)
9 placebo patients (14.5%)

**No. at risk**
- Olaparib: 92, 87, 80, 71, 61, 51, 46, 39, 31, 28, 20, 16, 14, 12, 9, 6, 5, 4, 4, 4, 2, 1, 1, 0
- Placebo: 62, 60, 56, 50, 44, 32, 29, 27, 20, 18, 14, 10, 8, 6, 6, 4, 1, 1, 1, 1, 1, 1, 0

*Dots indicate censorship. Crossover to olaparib was not permitted during this study; subsequent therapies were given at the investigators’ discretion.*
**Lynparza**
Pancreatic cancer - POLO trial

**Objective response** in patients with measurable disease by blinded independent central review

- **Two olaparib arm patients had a complete response**
  - Both complete responses were ongoing at the data cut-off

<table>
<thead>
<tr>
<th></th>
<th>Olaparib</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Objective response</strong></td>
<td>23.1%</td>
<td>11.5%</td>
</tr>
<tr>
<td><strong>n</strong></td>
<td>n=18</td>
<td>n=6</td>
</tr>
<tr>
<td><strong>Median time to onset of response</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Olaparib</td>
<td>5.4 months</td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>3.6 months</td>
<td></td>
</tr>
<tr>
<td><strong>Median duration of response</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Olaparib</td>
<td>24.9 months</td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>3.7 months</td>
<td></td>
</tr>
</tbody>
</table>

*By modified RECIST v1.1. †January 15, 2019*
**Lynparza**
Pancreatic cancer - POLO trial

<table>
<thead>
<tr>
<th>Event</th>
<th>Olaparib (N=91)</th>
<th>Placebo (N=60)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any grade, n (%)</td>
<td>87 (95.6)</td>
<td>56 (93.3)</td>
</tr>
<tr>
<td>Grade ≥3, n (%)</td>
<td>36 (39.6)</td>
<td>14 (23.3)</td>
</tr>
<tr>
<td>AEs leading to dose interruption, n (%)</td>
<td>32 (35.2)</td>
<td>3 (5.0)</td>
</tr>
<tr>
<td>AEs leading to dose reduction, n (%)</td>
<td>15 (16.5)</td>
<td>2 (3.3)</td>
</tr>
<tr>
<td>AEs leading to treatment discontinuation, n (%)</td>
<td>5 (5.5)</td>
<td>1 (1.7)</td>
</tr>
<tr>
<td>Median duration of treatment, months (range)</td>
<td>6.0 (0.8–45.3)</td>
<td>3.7 (0.1–30.1)</td>
</tr>
</tbody>
</table>

AE, adverse event
**Conclusions**

- Maintenance olaparib provided a statistically significant and clinically meaningful improvement in PFS to patients with a gBRCAm and metastatic pancreatic cancer whose disease had not progressed during platinum-based chemotherapy.
- Interim OS data (at 46% maturity) showed no difference between arms. Final OS results will be evaluated at 69% data maturity.
- Maintenance olaparib was well tolerated, with an AE profile similar to that seen in other tumor types.
- HRQoL was preserved with olaparib treatment and showed no difference between arms.
- Our results are the first from a Phase III trial to validate a targeted treatment in a biomarker-selected population of pancreatic cancer patients, highlighting the importance of gBRCAm testing in this setting.

Simultaneous publication in *The New England Journal of Medicine*
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Breakout sessions
**Lynparza**

Ovarian cancer - SOLO3 trial

**Study Design**

- Relapsed, high-grade serous or endometrioid ovarian, primary peritoneal, and/or fallopian tube cancer
- Germline BRCAm
- ECOG performance status 0–2
- ≥2 previous lines of platinum-based chemotherapy
- Platinum sensitive

Study treatment administered until disease progression

**Open-label**

- 2:1 randomization
- Stratified by:
  - Selected chemotherapy
  - Number of prior lines of chemotherapy
  - Time to progression after previous platinum-based chemotherapy

**Primary endpoint**

- ORR by BICR (RECIST v1.1)

**Secondary endpoints**

- PFS
- PFS2
- OS
- TFST
- TSST
- HRQoL
- Safety

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*Prior treatment with a PARP inhibitor was not permitted; Full platinum sensitive: progression >12 months after platinum-based chemotherapy; partially platinum sensitive: progression 6-12 months after platinum-based chemotherapy; for each patient, the investigator declared their choice of non-platinum chemotherapy before randomization; PLD, 50 mg/m² on day 1 q4w; paclitaxel, 80 mg/m² on days 1, 8, 15, and 22 q4w; gemcitabine, 1000 mg/m² on days 1, 8, and 15 q4w; topotecan, 4 mg/m² on days 1, 8, and 15 q4w; BICR, blinded independent central review; BRCAm, BRCA1 or BRCA2 mutation; ECOG, Eastern Cooperative Oncology Group; HRQoL, health related quality of life; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PFS2, second progression-free survival; PLD, pegylated liposomal doxorubicin; q4w, every 4 weeks; RECIST, response evaluation criteria in solid tumors; TFST, time to first subsequent therapy or death; TSST, time to second subsequent therapy or death*
Lynparza
Ovarian cancer - SOLO3 trial

**Primary Endpoint: ORR by BICR**

- **ORR 72%**
  - Olaparib: 63%
  - Chemotherapy: 49%
- **ORR 85%**
  - Olaparib: 73%
  - Chemotherapy: 56%
- **ORR 59%**
  - Olaparib: 52%
  - Chemotherapy: 39%

**All patients***

- OR 2.53 (1.40, 4.58) P=0.002

**Patients with 2 prior lines of chemotherapy***

- OR 3.44 (1.42, 8.54)

**Patients with ≥3 prior lines of chemotherapy***

- OR 2.21 (0.96, 5.20)

*Patients with measurable disease at baseline
Lynparza
Ovarian cancer - SOLO3 trial

Investigator-Assessed Best Response for Target Lesions by Patient

Chemotherapy (n=78)*
Olaparib (n=160)†

*19 patients were not evaluable for investigator-assessed best response; †11 patients were not evaluable for investigator-assessed best response
**Lynparza**

Ovarian cancer - SOLO3 trial

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**PFS (Intention-To-Treat Population)**

### BICR

- **Olaparib (n=178)**
  - No. at risk:
    - Olaparib: 178
    - Chemotherapy: 178
  - PFS events, n (%): 110 (62) vs. 49 (56)
  - Median PFS, months: 13.4 vs. 9.2
  - HR (95% CI), P value: 0.62 (0.43, 0.91); *P*<0.013

- **Chemotherapy (n=88)**
  - No. at risk:
    - Olaparib: 88
    - Chemotherapy: 88
  - PFS events, n (%): 63 (72)
  - Median PFS, months: 8.5

### Investigator-Assessed

- **Olaparib (n=178)**
  - No. at risk:
    - Olaparib: 178
    - Chemotherapy: 178
  - PFS events, n (%): 123 (69)
  - Median PFS, months: 13.2
  - HR (95% CI), P value: 0.49 (0.35, 0.70); *P*<0.001

- **Chemotherapy (n=88)**
  - No. at risk:
    - Olaparib: 88
    - Chemotherapy: 88
  - PFS events, n (%): 63 (72)
  - Median PFS, months: 8.5
### Safety Overview

<table>
<thead>
<tr>
<th>Event</th>
<th>Olaparib (n=178)</th>
<th>Chemotherapy (n=76)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-grade AEs, n (%)</td>
<td>174 (98)</td>
<td>73 (96)</td>
</tr>
<tr>
<td>Grade ≥3 AEs, n (%)</td>
<td>89 (50)</td>
<td>36 (47)</td>
</tr>
<tr>
<td>Serious AEs, n (%)*</td>
<td>42 (24)</td>
<td>14 (18)</td>
</tr>
<tr>
<td>AEs leading to dose interruption, n (%)</td>
<td>85 (48)</td>
<td>32 (42)</td>
</tr>
<tr>
<td>AEs leading to dose reduction, n (%)</td>
<td>48 (27)</td>
<td>25 (33)</td>
</tr>
<tr>
<td>AEs leading to treatment discontinuation, n (%)†</td>
<td>13 (7)</td>
<td>15 (20)</td>
</tr>
</tbody>
</table>

**Median total treatment duration (range), months**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Olaparib</th>
<th>Chemotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Olaparib</td>
<td>11.3 (0.1–39.5)</td>
<td>–</td>
</tr>
<tr>
<td>PLD</td>
<td>–</td>
<td>6.0 (0.9–15.4)</td>
</tr>
<tr>
<td>Paclitaxel</td>
<td>–</td>
<td>5.1 (1.8–18.2)</td>
</tr>
<tr>
<td>Gemcitabine</td>
<td>–</td>
<td>3.3 (0.7–14.3)</td>
</tr>
<tr>
<td>Topotecan</td>
<td>–</td>
<td>6.2 (2.3–9.7)</td>
</tr>
</tbody>
</table>

*Most common serious AE in the olaparib arm was anemia (3%) and in the chemotherapy arm was vomiting (4%); †Most common AEs leading to treatment discontinuation in the olaparib arm were vomiting, anemia, and thrombocytopenia (all 1%), and in the chemotherapy arm were PPE (9%), mucosal inflammation, peripheral neuropathy, and neutropenia (all 3%)
PPE, palmar-plantar erythrodysesthesia
Lynparza
Ovarian cancer - SOLO3 trial

Conclusions

- SOLO3 is the first Phase III randomized trial of a PARP inhibitor versus non-platinum-based chemotherapy in women with PSR gBRCA-mutated ovarian cancer
- A statistically significant and clinically relevant improvement in ORR and PFS was observed with olaparib versus non-platinum-based chemotherapy
- The tolerability profiles of olaparib and chemotherapy were consistent with previous data
  - Patients in the chemotherapy arm were more than twice as likely to discontinue study treatment because of an AE
- SOLO3 provides important prospective data on the efficacy of these treatment options for women with heavily pre-treated PSR gBRCA-mutated ovarian cancer
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Breakout sessions
Other highlights
AstraZeneca continues to redefine cancer treatment

<table>
<thead>
<tr>
<th>Breaking treatment boundaries</th>
<th>Treating patients earlier in their disease</th>
<th>Raising the bar for better outcomes</th>
<th>Advancing presence in haematology</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lynparza</strong> prostate cancer</td>
<td><strong>Imfinzi</strong> NSCLC Phase III PACIFIC three-year OS</td>
<td><strong>Tagrisso</strong> NSCLC Phase III FLAURA Additional data</td>
<td><strong>Calquence</strong> CLL Phase I/II ACE-CL-003</td>
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<tr>
<td>Neo-adjuvant breast cancer</td>
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<td><strong>Calquence</strong> CLL r/r Phase II ACE-CL-208</td>
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<td>Phase II GeparOLA</td>
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<tr>
<td><strong>Lynparza</strong> neo-adjuvant</td>
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<tr>
<td>breast cancer</td>
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<td>Phase II GeparOLA</td>
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<td><strong>Capivasertib</strong> breast cancer</td>
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<td>Phase II FAKTION</td>
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</tbody>
</table>

Other highlights

AstraZeneca continues to redefine cancer treatment

- **Lynparza** prostate cancer Phase II TOPARP-B
- **Lynparza** neo-adjuvant breast cancer Phase II GeparOLA
- **Capivasertib** breast cancer Phase II FAKTION
- **Imfinzi** NSCLC Phase III PACIFIC three-year OS
- **Tagrisso** NSCLC Phase III FLAURA Additional data
- **Calquence** CLL Phase I/II ACE-CL-003
- **Calquence** CLL r/r Phase II ACE-CL-208
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Meet AZN management: ASCO 2019
Breakout 1: sales and marketing
AstraZeneca’s commercial strategy in Oncology: providing the right treatment, for the right patient, at the right time, in the key franchises.

**Focused franchises**
- Lung cancer
- *Lynparza/DDR*\(^1\)
- *HER2*\(^2\)
- Haematology

**Global presence**
- **US** 81% sales growth
- **EU** 34% sales growth
- **Japan** #2 oncology company
- **China** #2 oncology company\(^3\)

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1. DNA damage response
2. Human epidermal growth factor receptor 2
3. Includes multinational and domestic companies. Sales growth at constant exchange rates and for Q1 2019.
Lung cancer: Tagrisso
Worldwide 1st-line rollout underway following strong initial launches

Underlying demand continues in the US

• 1st-line EGFRm\(^1\) new-patient starts currently at >60%

• Plans underway to increase EGFRm testing rates

• Quarterly total prescriptions volume continues to increase

Asian patients are especially in focus due to higher prevalence of the EGFR mutation

Western patients

\~10-15\% EGFRm

Asian patients

\~35-40\% EGFRm

• US
  >2/3 of sales in 1st line

• Europe
  <1/2 of sales in 1st line
  Reimbursement underway;
  \~10 countries so far

• Japan
  \~2/3 of sales in 1st line

• China
  NRDL\(^2\) in 2nd-line use ensures broader access, growth; 1st-line regulatory decision in mid 2019

Anticipated overall survival data readout in H2 2019

1. Epidermal growth factor receptor, mutated.
Source: internal specialty pharmacy and specialty distributor data.

Lung cancer: *Imfinzi*
US market uptake strong; greater opportunity worldwide

**Initiatives to further increase benefits to patients in the US**

- Emphasise use of *Imfinzi* immediately following cCRT\(^1\) for curative intent
- Increase HCP\(^2\) education for use of 52 weeks treatment to achieve full clinical benefit

**OS\(^3\) label anticipated in H2 2019**

**More patient need ex-US; EU reimbursement ongoing**

- Japan
  12% of sales
- Europe
  8% of sales
  Reimbursement in France and Germany

- **only ~1/5 of sales are ex-US**
  Compared to around half for *Lynparza*
- **but ~4/5 of potential patients are ex-US**

**Europe, cont.**
- UK, Italy and Spain reimbursement underway
- China
  Regulatory decision in H2 2019

---

3. Overall survival.
Lynparza
Continuing success in a competitive market

Cementing leadership in ovarian cancer

GY004/GY005
Combo w/cediranib
PSR\(^1\) and PRR\(^2\) in ‘all comers’

PAOLA-1
Combo w/bevacizumab
1st-line maintenance PSR ‘all comers’

SOLO-1
1st-line maintenance PSR:
only PARPi\(^3\) with 1st-line data

SOLO-2/Study 19
PSR maintenance: class leader
in 2nd line, with broad label

SOLO3
First PARPi to show
efficacy vs. chemotherapy

SOLO-1 data boosting US
2nd-line maintenance starts

Lynparza moving fast beyond ovarian cancer

~80%
US market share of
BRCAm\(^4\) breast cancer

News flow

- Pancreatic cancer
  Regulatory submission (H2 2019)
- Prostate cancer, data readouts
  Phase III PROfound (H2 2019)
  Phase III PROpel (2020+)
- Adjuvant breast cancer
  Data readout (2020+)

Source: Flatiron Health, 3-month rolling data; sample has low numbers.

1. Platinum sensitive recurrent.
2. Platinum relapsed recurrent.
3. Poly ADP-ribose polymerase inhibitor.
## Trastuzumab deruxtecan in breast cancer and beyond

Opportunities across treatment settings in breast cancer

<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>chemotherapy + trastuzumab + pertuzumab</td>
<td>Post neo-adjuvant Replace trastuzumab emtansine</td>
<td>Replace chemotherapy + trastuzumab + pertuzumab</td>
<td>Replace trastuzumab emtansine</td>
<td>Post trastuzumab emtansine</td>
</tr>
<tr>
<td>HR+¹: chemotherapy ± endocrine therapy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TNBC³: chemotherapy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| HER2-low breast cancer | | | | |
|------------------------| | | | |
| HR+¹: chemotherapy ± endocrine therapy | | | | |
| TNBC³: chemotherapy | | | | |

| Beyond breast cancer | | | | |
|---------------------| | | | |
| | | | Expand into other cancer types: gastric, NSCLC⁴, CRC⁵ and others | |

---

1. Hormone-receptor positive  
2. Cyclin-dependent kinase 4/6 inhibitor  
3. Triple-negative breast cancer  
4. Non-small cell lung cancer  
5. Colorectal cancer.
Haematology

*Calquence* Phase III data readout in CLL\(^1\) provides momentum

$94m worldwide *Calquence* sales since launch

11,000 patients in relapsed/refractory CLL, US and EU\(^2\)

17,000 patients in front-line CLL, US and EU5

<table>
<thead>
<tr>
<th>Trial/milestone</th>
<th>Phase</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE-CL-309 ASCEND in relapsed/refractory CLL</td>
<td>III</td>
<td>Positive top-line results announced</td>
</tr>
<tr>
<td>ACE-CL-007 ELEVATE-TN in previously-untreated CLL</td>
<td>III</td>
<td>Data anticipated H2 2019</td>
</tr>
<tr>
<td><em>Calquence</em> regulatory submissions in CLL</td>
<td>-</td>
<td>Anticipated H2 2019</td>
</tr>
<tr>
<td>ACE-CL-006 ELEVATE-RR in relapsed/refractory high-risk CLL</td>
<td>III</td>
<td>Data anticipated 2020+</td>
</tr>
<tr>
<td>ACE CL-311 in previously-untreated CLL (w/venetoclax)</td>
<td>III</td>
<td>Data anticipated 2020+</td>
</tr>
</tbody>
</table>

Commercial capabilities established in MCL\(^3\) a solid base for the launch in CLL

---

1. Chronic lymphocytic leukaemia.
2. EU5 defined as France, Germany, Italy, Spain and UK.
Meet AZN management: ASCO 2019
Breakout 2: late-stage pipeline
**Lynparza: ovarian cancer**

Leading development programme across lines of treatment

---

**Study 19: overall survival in ‘all-comer’ 3rd-line+ patients**

**SOLO-2: progression-free survival in BRACm 2nd line**

**SOLO-1: progression-free survival in BRACm 1st line**

**PAOLA-1: 1st-line ‘all-comer’ ovarian cancer**

1. Chemotherapy.
   Source: Study 19, abstract 5501, ASCO 2016; and SOLO3, abstract 5506, ASCO 2019.

2. Secondary endpoints.
   Source: AstraZeneca data on file.

---

1L (complete response; partial response; or non-evidence of disease)

Randomisation (1:2)

Bevacizumab + placebo (two years)

Bevacizumab + Lynparza

Progression-free survival (PFS1)

Follow up for second progression (PFS2) or death

Overall survival

H2 2019: Phase III data readout

2020: regulatory submission
**Lynparza: pancreatic and prostate cancers**

Extending benefit of PARP inhibition\(^1\) into new cancer types

---

**POLO: first positive Phase III trial of a PARPi in gBRCAm metastatic pancreatic cancer**

PROfound: Phase III in mCRPC\(^2\) HRRm\(^3\) (post abiraterone/enzalutamide)

PROpel: Phase III combination of *Lynparza* and abiraterone in ‘all comer’ 1L mCRPC

---

Hazard ratio 0.53

1. Poly (ADP-ribose) polymerase inhibitor.

   Source: AstraZeneca data on file.

3. Homologous recombination repair mutation.
   Source: AstraZeneca data on file.
Breast cancer: Lynparza and capivasertib
Going into early disease and new mode of action

OlympiAD: first PARP inhibitor approved in the EU for patients with gBRCAm HER2-negative advanced breast cancer

OlympiA: gBRCAm adjuvant breast cancer

Completed definitive local treatment and neoadjuvant or adjuvant chemotherapy

Randomisation (1:1)

Placebo

Lynparza

Treatment for up to a maximum of 12 months

Invasive disease free survival (IDFS)

42% reduction in the risk of disease progression or death vs. standard of care

52% objective response rate (ORR) was double that in the chemotherapy arm

OlympiAD approved in EU during H1 2019 - OlympiA Phase III data anticipated in 2020+

Capivasertib (AZD5363): novel, oral selective AKT inhibitor Potential in breast, prostate

Phase III start in Q2 2019


Source: AstraZeneca data on file.

Source: AstraZeneca data on file.
Tagrisso: non-small cell lung cancer
Focus on early-stage disease and resistance

**ADAURA: adjuvant EGFRm¹ NSCLC²**
- Stratification: Stage (Iba vs. II vs. IIIa); EGFRm; and race
- Randomisation (1:1)
- Placebo
- Tagrisso
- Treatment for three years from first dose; end of treatment assessment 4 weeks after last dose
- Investigator-assessed disease-free survival

**SAVANNAH: EGFRm, MET+ locally-advanced/metastatic NSCLC**
- Screening
- Disease progression following treatment with Tagrisso and MET+ tumour
- Tagrisso + savolitinib
- Treatment until disease progression
- ORR⁴ by investigator assessment in accordance with RECIST 1.1

**ORCHARD: identifying resistance / progression factors**
- Patients with NSCLC who progressed on 1st-line Tagrisso
- Non-randomised
- Carboplatin + pemetrexed + Imfinzi
- Tagrisso + savolitinib or Iressa or necitumumab
- ORR

**Phase III data anticipated 2020+³**
1. Epidermal growth factor receptor mutation
2. Non-small cell lung cancer
3. Based on current expectations and event rates, data from the ADAURA trial can be expected in 2022.
Source: AstraZeneca data on file.

**SAVANNAH Phase II data anticipated in 2020+**
4. Objective response rate.
Source: AstraZeneca data on file.

Source: AstraZeneca data on file.
**Imfinzi**: standard of care in unresectable, Stage III NSCLC

Differentially investing to focus on early-stage disease

Unprecedented 11.2 months improvement in median progression-free survival

>50% of patients receiving Imfinzi were alive at 36 months

Early-stage NSCLC trials

<table>
<thead>
<tr>
<th>Name</th>
<th>Phase</th>
<th>Population</th>
<th>Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>AEGEAN</td>
<td>III</td>
<td>Neo-adjuvant (before surgery)</td>
<td>2020</td>
</tr>
<tr>
<td>ADJUVANT.31</td>
<td>III</td>
<td>Stage Ib-IIia</td>
<td>2020+</td>
</tr>
<tr>
<td>PACIFIC-2</td>
<td>III</td>
<td>Unresectable, Stage III NSCLC</td>
<td>2020+</td>
</tr>
<tr>
<td>PACIFIC-4</td>
<td>III</td>
<td>Unresectable, Stage III NSCLC</td>
<td>2020+</td>
</tr>
<tr>
<td>PACIFIC-5</td>
<td>III</td>
<td>Unresectable, Stage III NSCLC (Asia predominant)</td>
<td>2020+</td>
</tr>
</tbody>
</table>


Source: AstraZeneca data on file.
Late-stage Immuno-Oncology strategy

Replace
Create a new treatment paradigm for patients that replaces CTx

Add
Generate additional benefits for patients through additive or combination treatment with CTx

Early
Provide earlier treatment for patients and replace standard of care

Source: AstraZeneca Q1 2019 results announcement.
Meet AZN management: ASCO 2019
Breakout 3: early-stage pipeline
Rich early to mid-stage pipeline

**Tumour drivers and resistance**

- **capivasertib** (AKT\(^1\) inhibitor)
  - breast, prostate cancers, Phase III to start
- **AZD9833** (SERD\(^2\), oral)
  - breast cancer, Phase I
- **AZD5991** (MCL\(^1\) inhibitor)
  - haematologic cancers, Phase I
- **savolitinib** (cMET\(^4\))
  - NSCLC, Phase II

**DNA damage response (DDR)**

- **adavosertib** (WEE\(^5\) inhibitor)
  - solid cancers, Phase II
- **ceralasertib** (ATR\(^6\) inhibitor)
  - solid cancers, Phase II
- **AZD2811** (aurora kinase B inhibitor)
  - solid cancers, Phase II
- **AZD1390** (ATM\(^7\) inhibitor)
  - solid cancers, Phase I
- **AZD7468** (DNA-PK\(^8\))
  - solid cancers

**Immuno-oncology (IO)**

- **monalizumab** (NKG2A\(^9\) mAb\(^10\))
  - head & neck, colorectal, Phase II ongoing
- **MEDI5752** (PD-1/CTLA-4 bispecific mAb)
  - solid cancers, Phase I
- **olecumab** (CD73\(^11\) mAb)
  - lung, pancreatic cancers, Phase I/II
- **AZD4635** (A2aR\(^12\) inhibitor)
  - solid cancers, Phase II
- **AZD9150** (STAT3\(^13\) inhibitor)
  - solid cancers, Phase II

---

Tumour drivers and resistance: early breast
Building on an established franchise

Early evidence of enhanced benefit with capivasertib + paclitaxel in altered metastatic TNBC

ASCO 2019 data on Tuesday 4 June 2019, abstract #1005:

- OS² HR⁵ 0.57 in the ITT⁶ population

Phase III to initiate

1. Phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha
2. Phosphatase and tensin homolog.
3. Triple-negative breast cancer
4. Overall survival
5. Hazard ratio
6. Intention to treat.

Source: ASCO 2018.
Tumour drivers and resistance: cell death
Haematologic cancers the next wave of innovation

Targeting distinct nodes of cell death

AZD5991 (MCL1): novel macrocyclic chemistry
AZD4573 (CDK9): distinct mechanism of targeting MCL1
AZD0466 (Bcl2\textsuperscript{2xL4}): nanomedicine to improve therapeutic margin

AZD5991 (MCL1 inhibitor)

Single dose of AZD5991 achieves tumour regression in haematological cancer preclinical models


AZD5991 in Phase I

1. Inhibitor.
2. Cyclin-dependent kinase 9.
DNA damage response: *Lynparza* and beyond

Developing chemo-free regimens, extending survival

- Launch adavosertib (WEE1) / ceralasertib (ATR) *Lynparza* combinations
- Expand *Lynparza* beyond BRCA (prostate cancer, ovarian cancer)
- Deliver next-generation DDR medicines: AZD1390 (ATM inhibitor), AZD2811 (aurora kinase B inhibitor), AZD7648 (DNA-PK)
- Establish *Lynparza* leadership as monotherapy
- Launch *Lynparza* combinations (VEGF¹, IO)

Scientific leadership in DDR

|-------------|-------------|-------------|

¹. Vascular endothelial growth factor.
DNA damage response: pipeline
The next wave of potential DDR medicines

A broad pipeline targeting complementary aspects of DNA damage repair and cell cycle regulation

AZD2811: targeting Aurora Kinase B

Monotherapy activity in SCLC\(^1\) model *in vivo*

Phase I ongoing
Phase II start in planning

---

1. Poly (ADP-ribose) polymerase.

---

# Broad IO pipeline: enhancement of antitumour immunity

Fully harnessing immune system to eliminate tumours

<table>
<thead>
<tr>
<th>No effective antitumour immunity</th>
<th>Suboptimal or exhausted antitumour immunity</th>
<th>Antitumour immunity suppressed by TME</th>
<th>Goal: highly-active antitumour immunity</th>
</tr>
</thead>
<tbody>
<tr>
<td>'Cold' tumour</td>
<td>Example: PD-L1+ tumour</td>
<td>Example: CD73+ tumour</td>
<td></td>
</tr>
</tbody>
</table>

- **Prime new response**
  - PD-L1/CD40L
  - IL-12 mRNA
  - NDV-GMCSF
  - HPV Vaccine

- **Potentiate existing response**
  - PD-L1
  - CTLA-4
  - PD-1/CTLA-4
  - NKG2A

- **Reverse tumour immunosuppression**
  - CD73
  - A2aR
  - CD39
  - STAT3

- **Eliminate tumour**

---

Developing an adenosine franchise
Reversing tumour immunosuppression

Targeting adenosine pathway

\[
\text{Cancer therapy} \quad \Rightarrow \quad \text{Cell death} \quad \Rightarrow \quad \text{A2A} \Rightarrow \text{Adenosine} \quad \Rightarrow \text{AMP} \quad \Rightarrow \text{AMP}\]

\[
\text{ATP} \quad \Rightarrow \text{CD39} \quad \Rightarrow \text{CD73} \quad \Rightarrow \text{AMP} \quad \Rightarrow \text{Adenosine}
\]

AZD4635: targeting A2aR

Phase I ongoing

Phase II in planning

Phase I ongoing

Multiple projects aimed at full suppression


RCC: renal cell carcinoma.
H&N: head and neck cancer.
Next-generation checkpoints
Utilising the innate and adaptive immune system

Monalizumab: targeting NKG2A

- Progressive Disease
- Partial Response
- Complete Response

Duration of treatment (weeks)

Tumour size change

N = 39 evaluable patients excluding 1 early death

Phase II ongoing
Phase III in planning

MEDI5752: PD-1/CTLA-4 bispecific

Tumour: increased efficacy
Periphery: increased safety

Internalisation and degradation of PD-1 leads to complete and durable blockade of PD-1 and CTLA-4 in the TME
Mitigated toxicity due to reduced binding to CTLA-4+ peripheral T cells

Phase I ongoing
Phase II in planning

Source: Cohen et al ESMO 2018.
Oncolytic viruses offer multiple mechanisms of action
Leveraging internal and external expertise

MEDI5395: NDV-GMCSF
Not a select agent; suitable for world-wide development

Collaboration with Transgene
1. IFN\(^{\gamma}\) production, Th\(^{2}\)1 education
2. T cell memory and homeostasis
3. Activation of APC\(^{3}\)s
4. Immune priming and APC activation
5. Increase lysis & Type I IFN response

Intracerebral pathogenicity index scale (ICPI): <0.4 is non-pathogenic

Collaboration of five oncolytic viruses

Meet AZN management: ASCO 2019
Breakout 4: trastuzumab deruxtecan
Trastuzumab deruxtecan
A state-of-the-art HER2\(^1\)-targeted, second-generation ADC\(^2\)

Differentiated ADC

- Higher-intensity chemotherapy (more payload on each antibody)
- Membrane permeability (potential HER2-low applicability)
- Selective protease-cleavable linker
- Short half-life of free payload reduces systemic toxicities

Potential best-in-class ADC for HER2-positive breast cancer

Potential first-in-class ADC for HER2-low cancers

1. Human epidermal growth factor receptor 2.
Trastuzumab deruxtecan
Unprecedented Phase I/II data

**Differentiated ADC**

- **59.5%** confirmed objective response rate
- **93.7%** confirmed disease control rate
- **20.7 months** median duration of response

**Unprecedented data in advanced HER2-positive breast cancer**


**Phase II primary endpoint met**

AstraZeneca and Daiichi Sankyo Company, Limited (Daiichi Sankyo) today announced positive top-line results for the pivotal Phase II DESTINY-Breast01 trial of trastuzumab deruxtecan (D9-8201). The HER2-targeting antibody drug conjugate (ADC) and potential new medicine was evaluated in patients with HER2-positive, unresectable and/or metastatic breast cancer previously treated with trastuzumab emtansine.

The response rate in DESTINY-Breast01, as assessed by an independent review committee, confirms in a heavily-pre-treated, global patient population the unprecedented clinical activity in the recently-published Phase I trial. The safety and tolerability profile of trastuzumab deruxtecan was also consistent with previous experience. These results are expected to support planned global regulatory submissions, including a Biologics License Application with the US Food and Drug Administration (FDA) anticipated in the second half of 2019.

DESTINY-Breast01 is a pivotal Phase II, open-label, global, multicentre, two-part trial of trastuzumab deruxtecan. The optimal dose of 5.4mg/kg was previously identified in part one of the trial. Today’s results from part two evaluated the efficacy and safety of that dose in patients who have failed or discontinued previous treatment with trastuzumab emtansine.

---

1. Disease control was calculated as the proportion of patients demonstrating complete response, partial response, or stable disease for a minimum of five weeks from the first dosing date
2. 95% confidence interval not estimable.
<table>
<thead>
<tr>
<th>HER2-positive breast cancer</th>
<th>Neo-adjuvant / adjuvant</th>
<th>1st-line metastatic</th>
<th>2nd-line metastatic</th>
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</thead>
<tbody>
<tr>
<td>Post neo-adjuvant</td>
<td>Replace trastuzumab emtansine</td>
<td>Replace chemotherapy + trastuzumab + pertuzumab</td>
<td>Replace trastuzumab emtansine</td>
<td>Post trastuzumab emtansine</td>
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<td>chemotherapy + trastuzumab + pertuzumab</td>
<td>HR+¹: chemotherapy ± endocrine therapy</td>
<td>endocrine ± CDK4/6i²</td>
<td></td>
<td>Post CDK4/6i</td>
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<tr>
<td>TNBC³: chemotherapy</td>
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</table>

| HER2-low breast cancer | | | | |
|-----------------------| | | | |
| HR+¹: chemotherapy ± endocrine therapy | | | | |

| Beyond breast cancer | | | | |
|----------------------| | | | |
| TNBC³: chemotherapy | | | | |
| Expand into other cancer types: gastric, NSCLC⁴, CRC⁵ and others | | | | |

1. Hormone-receptor positive  
2. Cyclin-dependent kinase 4/6 inhibitor  
3. Triple-negative breast cancer  
4. Non-small cell lung cancer  
5. Colorectal cancer.
Trastuzumab deruxtecan

Encouraging efficacy in HER2-low breast cancer

HER2-low breast cancer efficacy

44.2% objective response rate

9.4 months DoR\(^2\), 7.6 months median PFS\(^3\)

HR: hormone receptor.
IHC: immunohistochemistry.

Source: poster # p6-17-02, SABCS 2018 (based on 12 October 2018 data cut off).

2. Duration of response.
3. Progression-free survival.
Trastuzumab deruxtecan
Compelling efficacy in other cancer types

HER2-positive gastric cancer

Three average lines of prior treatment

43% ORR
5.6 months median PFS

Source: Phase I, Shitara et al., The Lancet Oncology.

HER2-positive and HER2-mutated NSCLC

N=11 HER2mut

73% ORR¹
14.1 months median PFS¹

¹ HER2-mutated NSCLC only.

Data cutoff, August 10, 2018.
Exon 20 insertion
Single base pair substitution
Not examined/missing
Trastuzumab deruxtecan
Development plans and news flow

Extensive Phase II/III programme underway

<table>
<thead>
<tr>
<th>2L DESTINY-Breast03 (2020+)</th>
<th>3L+ DESTINY-Breast02 (2020+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>To be communicated</td>
<td>To be communicated</td>
</tr>
<tr>
<td>HER2+ neoadjuv. breast cancer</td>
<td>HER2+ adjuvant breast cancer</td>
</tr>
<tr>
<td>HER2+ advanced breast cancer</td>
<td>HER2 low breast cancer</td>
</tr>
<tr>
<td>HER2+ Gastric cancer</td>
<td>HER2+ CRC</td>
</tr>
<tr>
<td>HER2+ NSCLC</td>
<td>bladder cancer</td>
</tr>
<tr>
<td>Other cancer</td>
<td>To be communicated</td>
</tr>
</tbody>
</table>

DESTINY-Breast01 (Phase II)

DESTINY-Breast04 (2020+)

DESTINY-Gastric01 (2020)

Phase II

Phase II combo with PD-1

News flow

- US FDA BTD\(^2\) granted in Aug 2017
- DESTINY-Breast01 data presentation in H2 2019
- Regulatory decision anticipated in 2020
- Further Phase III starts anticipated in 2019-2020
- US regulatory submission anticipated in H2 2019

Source: AstraZeneca data on file.
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