AstraZeneca
What science can do

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

Forward-looking statements

In order, among other things, to utilise the 'safe harbour' provisions of the US Private Securities Litigation Reform Act of 1995, AstraZeneca (hereafter 'the Group') provides 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 the Group believes its 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 the Group undertakes no obligation to update these forward-looking statements. The Group identifies 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 the Group's control, include, among other things: the risk of failure or delay in delivery of pipeline or launch of new medicines; the risk of failure to meet regulatory or ethical requirements for medicine development or approval; the risk of failure to obtain, defend and enforce effective intellectual property (IP) protection and IP challenges by third parties; the impact of competitive pressures including expiry or loss of IP rights, and generic competition; the impact of price controls and reductions; the impact of economic, regulatory and political pressures; the impact of uncertainty and volatility in relation to the UK's exit from the EU; the risk of failures or delays in the quality or execution of the Group's commercial strategies; the risk of failure to maintain supply of compliant, quality medicines; the risk of illegal trade in the Group's medicines; the impact of reliance on third-party goods and services; the risk of failure in information technology, data protection or cybercrime; the risk of failure of critical processes; any expected gains from productivity initiatives are uncertain; the risk of failure to attract, develop, engage and retain a diverse, talented and capable workforce; the risk of failure to adhere to applicable laws, rules and regulations; the risk of the safety and efficacy of marketed medicines being questioned; the risk of adverse outcome of litigation and/or governmental investigations; the risk of failure to adhere to increasingly stringent anti-bribery and anti-corruption legislation; the risk of failure to achieve strategic plans or meet targets or expectations; the risk of failure in financial control or the occurrence of fraud; the risk of unexpected deterioration in the Group's financial position; and the impact that the COVID-19 global pandemic may have or continue to have on these risks, on the Group's ability to continue to mitigate these risks, and on the Group's operations, financial results or financial condition. Nothing in this document, or any related presentation/webcast, should be construed as a profit forecast.

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 revolutionalise 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[1]

Lung cancer

TAGRISSO® osimertinib

- Stage IV NSCLC[2]
  - EGFRm[3] (1L[4])
  - T790M[5] (2L[6])
- Adjuvant EGFRm NSCLC

Next
- Neo-adjuvant and Stage III, unresectable EGFRm NSCLC and new combinations

IMFINZI® durvalumab Injection for Intravenous Use 50 mg/mL

- Stage III, unresectable NSCLC
- Extensive-stage SCLC[7]

Next
- Early / advanced stages of several cancers, combinations

Multiple cancers

Lynparza™ olaparib

- Ovarian, breast, pancreatic, prostate cancers[8]
- Merck collaboration

Next
- Adjuvant breast, earlier use in prostate cancer, combinations

Multiple cancers

ENHERTU® fam-trastuzumab deruxtecan-nxki 20 mg/mL INJECTION FOR INTRAVENOUS USE

- Breast cancer (3L[9], HER2+[10]) and gastric cancer (2L, HER2+)
- Daiichi Sankyo collab.

Next
- Earlier use, HER2 low and other cancers (lung, colorectal)

Blood cancers

CALQUENCE® (acalabrutinib) 100 mg capsules

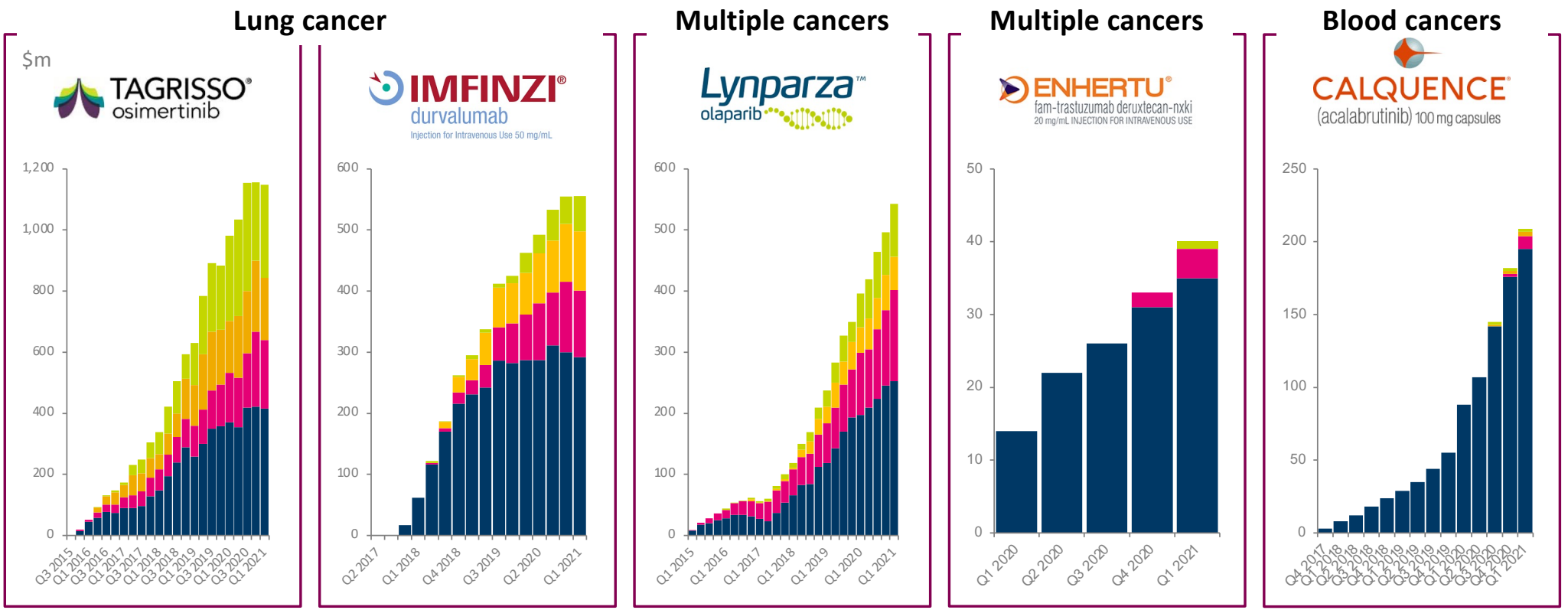
- Chronic lymphocytic leukaemia
- Mantle cell lymphoma

Next
- Combinations, other blood cancers

What's next:
a rich early to mid-stage pipeline, including combinations and several new Phase III medicines

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



Total revenue at actual exchange rates; product sales only for *Lynparza*.

ASCO 2021

Another strong presence

3rd plenary session in a row

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

AstraZeneca
What science can do

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@astrazeneca.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 immuno-oncology (IO)
- Biomarker-driven treatments across EGFR, HER2, exon 14[1], others
- Digital pathology and ctDNA[2]-based personalised interventions

Now

TAGRISSO® osimertinib

IMFINZI®

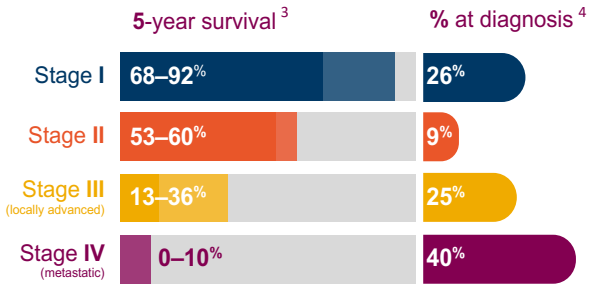
ENHERTU® fam-trastuzumab deruxtecan-nxki

Next

tremelimumab
savolitinib
ceralasertib
datopotamab deruxtecan

Diagnose and treat early

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



Later diagnosis drives poor outcomes in NSCLC

Improve quality of care

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

The LungAmbition Alliance

Accelerating advances for people with lung cancer.

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

3. Goldstraw et al., *J Thorac Oncol.* 2016; 11(1):39–51 4. EpiCast Report: NSCLC Epidemiology Forecast to 2025, GlobalData, 2016.

Tagrisso: changing treatment expectations in EGFRm NSCLC

Continuing to push the boundaries of science and patient care

Reshaping the treatment paradigm by moving into earlier lines of NSCLC

2015 — 2L

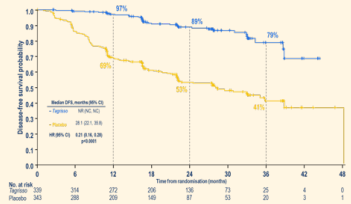
- First EGFR TKI[1] to overcome **T790M resistance**
- Best-in-class **blood-brain barrier penetration**
- Excellent tolerability profile, convenient oral dosing

2017 — 1L

- **1L EGFR standard of care**
- **Only EGFR TKI with OS[2] > 3 years** and unsurpassed PFS[3]
- Best-in-class CNS[4] risk reduction

2020 — Adjuvant

Unparalleled Stage IB-IIIA efficacy (80% relative risk)

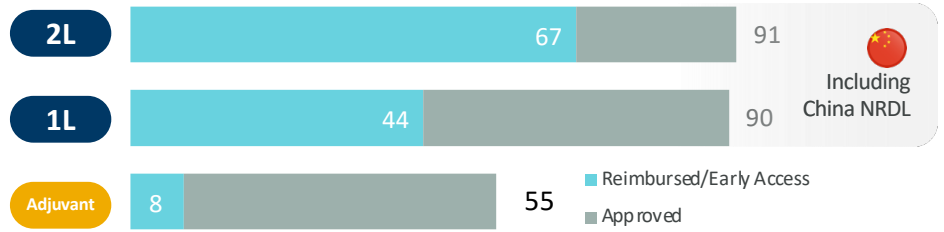


- **Protection against distant recurrences, including in the CNS**
- **Strongest-rated curative-intent therapy in NSCLC** (ESMO-MCBS)

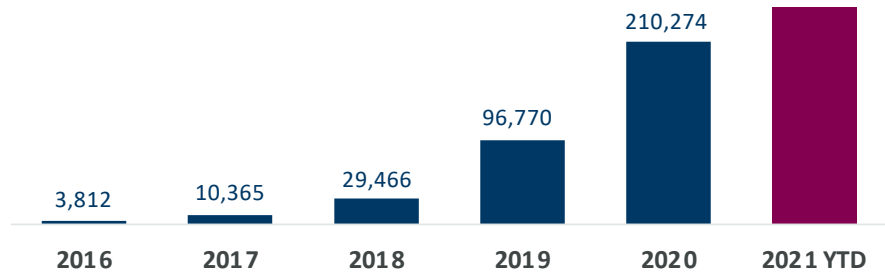
Established clinical leadership

Enabling maximal patient benefit globally

Globally-embedded access



Strong momentum in patient reach



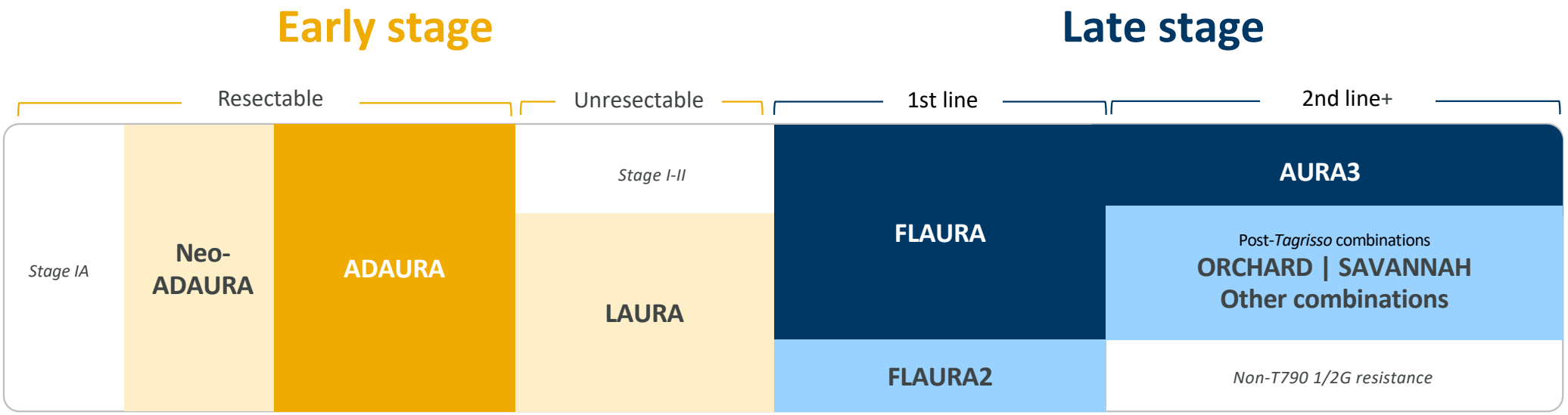
Bench to bedside excellence

1. Tyrosine kinase inhibitor 2. Overall survival 3. Progression-free survival 4. Central nervous system.
Source: abstract LBA5, ASCO 2020.

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

Approved indications Ongoing trials

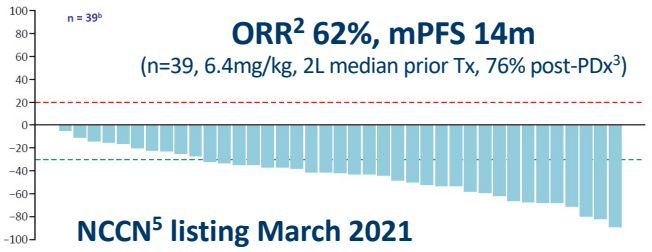
2 Define and deliver **innovative combinations** with *Tagrisso* as a backbone in 1st line and beyond 1st-line *Tagrisso* monotherapy

Approved indications Ongoing trials

Enhertu, datopotamab deruxtecan: ADC[1] portfolio

Significant activity across NSCLC

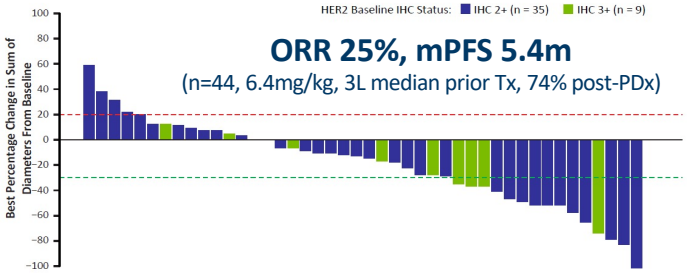
Enhertu - HER2 ADC (DESTINY-Lung01 trial)



ORR[2] 62%, mPFS 14m
(n=39, 6.4mg/kg, 2L median prior Tx, 76% post-PDx[3])

NCCN[5] listing March 2021

HER2m[4] NSCLC
~2% prevalence



ORR 25%, mPFS 5.4m
(n=44, 6.4mg/kg, 3L median prior Tx, 74% post-PDx)

HER2+ NSCLC
~15% prevalence

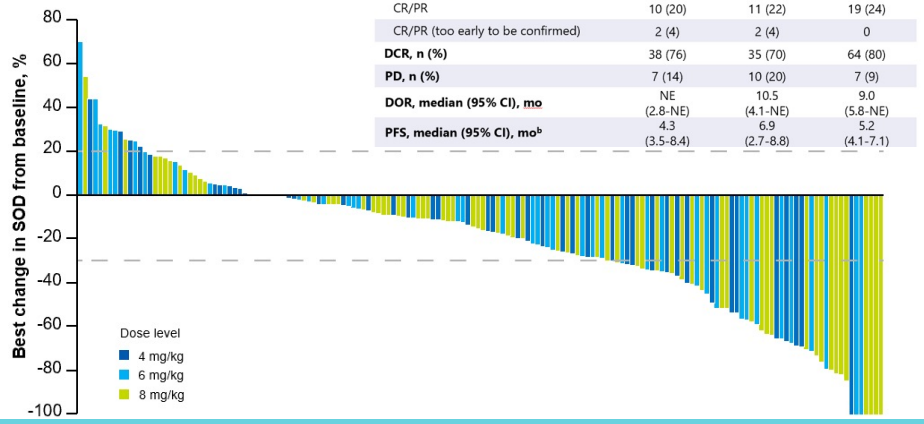
Planned trial: DESTINY-Lung02: 2L+, Phase II in HER2m NSCLC, further evaluation of dose 5.4 mg/kg
DESTINY-Lung 03: 1L *Enhertu* + durvalumab + chemo Phase I

Datopotamab deruxtecan - TROP2[6] ADC (TROPION-PanTumor01 trial)

2L+ NSCLC

Best Overall Response (BICR)

Patients[a]	Dato-DXd Dose 4 mg/kg (n=50)	6 mg/kg (n=50)	8 mg/kg (n=80)
ORR, n (%)	12 (24)	13 (26)	19 (24)
CR/PR	10 (20)	11 (22)	19 (24)
CR/PR (too early to be confirmed)	2 (4)	2 (4)	0
DCR, n (%)	38 (76)	35 (70)	64 (80)
PD, n (%)	7 (14)	10 (20)	7 (9)
DOR, median (95% CI), mo	NE (2.8-NE)	10.5 (4.1-NE)	9.0 (5.8-NE)
PFS, median (95% CI), mo[b]	4.3 (3.5-8.4)	6.9 (2.7-8.8)	5.2 (4.1-7.1)



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

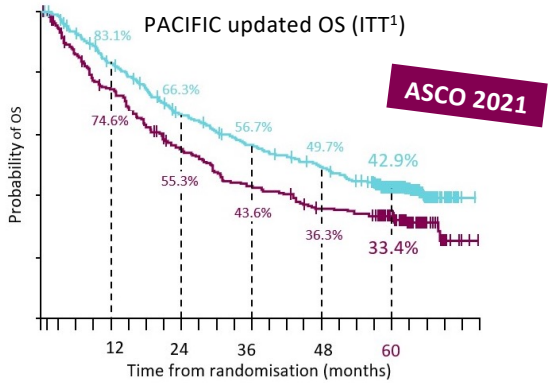
1. Antibody drug conjugate 2. Objective response rate 3. Post PD-1 or PD-L1 checkpoint inhibitor 4. HER2 mutated 5. National Comprehensive Cancer Network. Source: abstract OA04.05, World Conference on Lung Cancer (WCLC) 2020; HER2m and HER2+ (IHC2+/3+) prevalence, AstraZeneca data and Miller et al., Syst 2015, Oh and Bang et al., *Nature Oncology Reviews*, 2017.

6. Trophoblast cell-surface antigen 2, a transmembrane glycoprotein that is overexpressed in many cancers 7. Anaplastic lymphoma kinase wild type.
Source: abstract 9085, ASCO 2021.

Imfinzi: immuno-oncology

Unique position in lung cancer

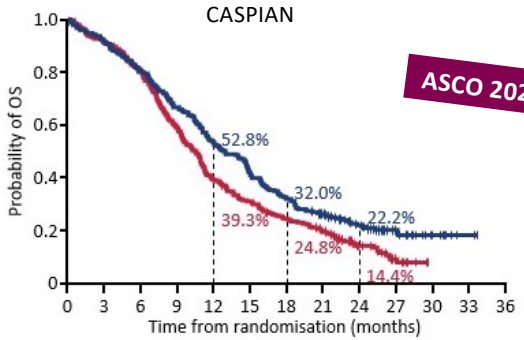
Comprehensive programme in early lung builds on PACIFIC



- 43% of patients alive at five years
- 33% progression free at five years

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

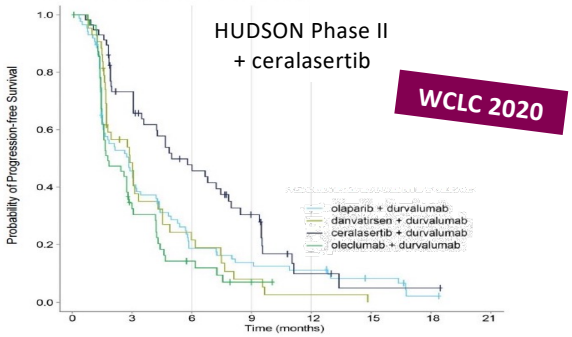
Strong launch in ES-SCLC[2]



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

Ongoing Phase III trials:
Limited stage: ADRIATIC

Novel combinations



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

Ongoing Phase II trials:
HUDSON (advanced NSCLC post CPI[3]), MAGELLAN (1L NSCLC), NeoCOAST (resectable NSCLC, neoadjuvant), COAST (*Imfinzi* + novel MoAs[4])

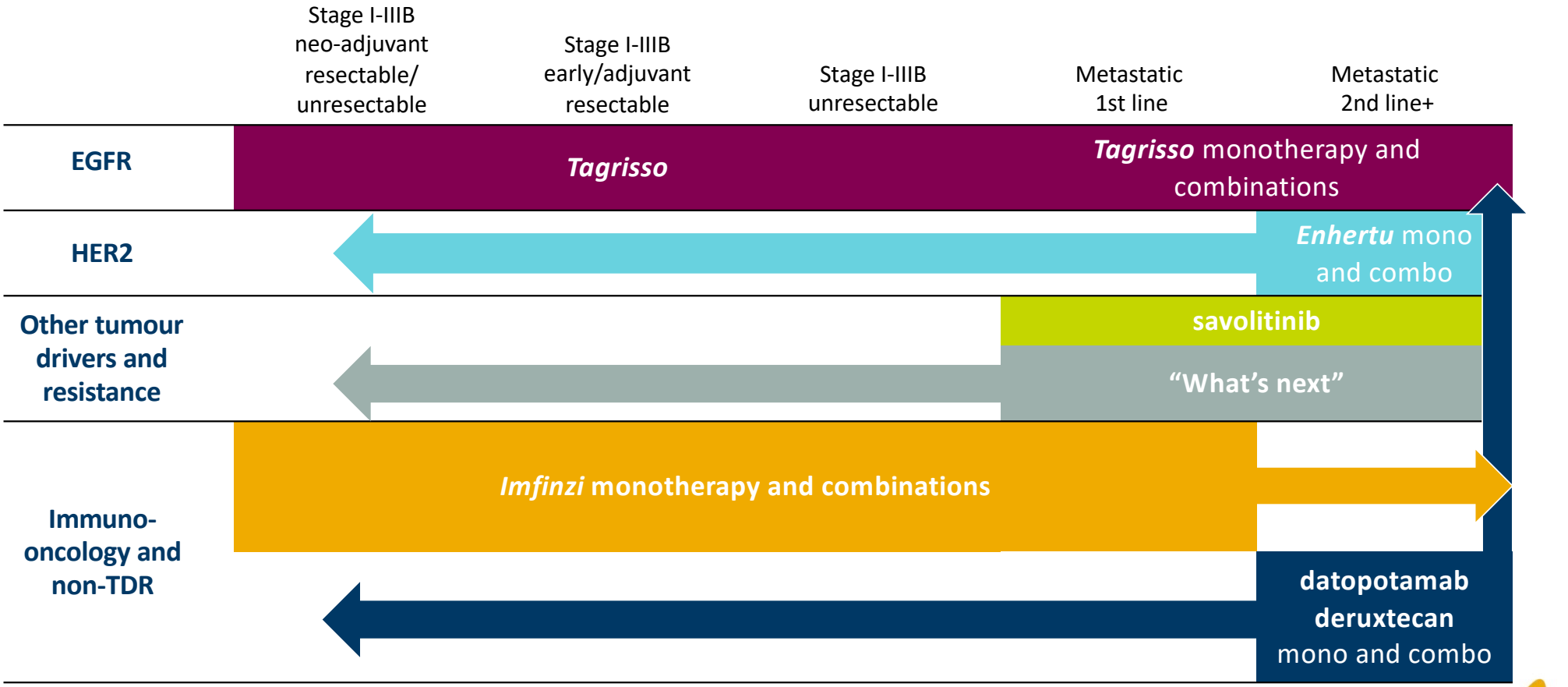
1.Intention to treat.
Source: abstract 8511, ASCO 2021.

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

3. Checkpoint inhibitors 4. Mode of action.
Source: abstract OA07.08, WCLC 2020.

NSCLC: leadership across the spectrum

Potential to cover most patients across settings and lines of treatment



Illustrative; not to scale.

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What science can do

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® goserelin acetate implant

1980's

Lutenising hormone-releasing agonist of choice for ovarian suppression in premenopausal women with breast cancer

Arimidex® anastrozole 1 mg tablets

1990's

One of the gold-standard medicines for postmenopausal HR+ breast cancer for years

FASLODEX® fulvestrant Injection

2000's

The current endocrine therapy of choice in metastatic breast cancer

Lynparza™ olaparib capsules 50 mg

2010's

First targeted treatment option for patients with BRCA-mutated breast cancer both in the metastatic and early breast cancer setting

ENHERTU® fam-trastuzumab deruxtecan-nxki 20 mg/mL INJECTION FOR INTRAVENOUS USE

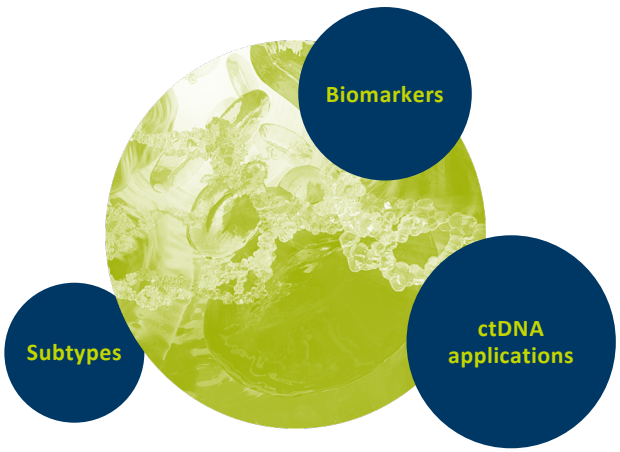
2020's

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

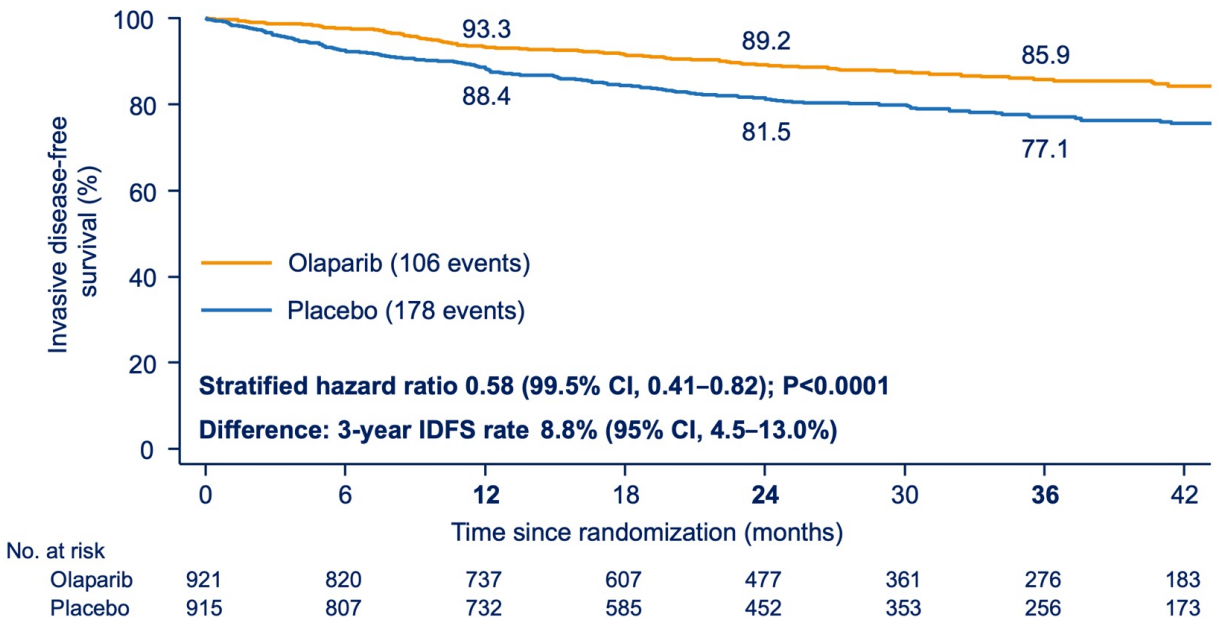
Establish foundational medicines that set new benchmarks in outcomes

1. Standard of care.

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]



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

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.

Source: AstraZeneca.

Enhertu: transforming HER2+ and redefining HER2-low BC

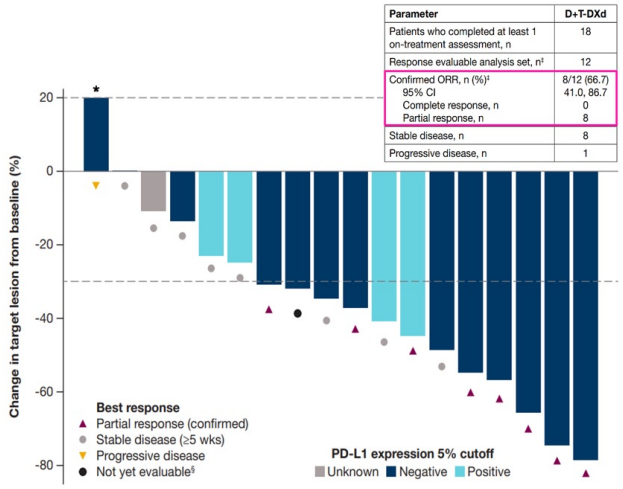
Clinical development programme across multiple lines and subtypes

Launched in 3L, HER2+ mBC[1]

- **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[2]



Benefit observed in HER2 1+ and HER2 2+/ISH[3]-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

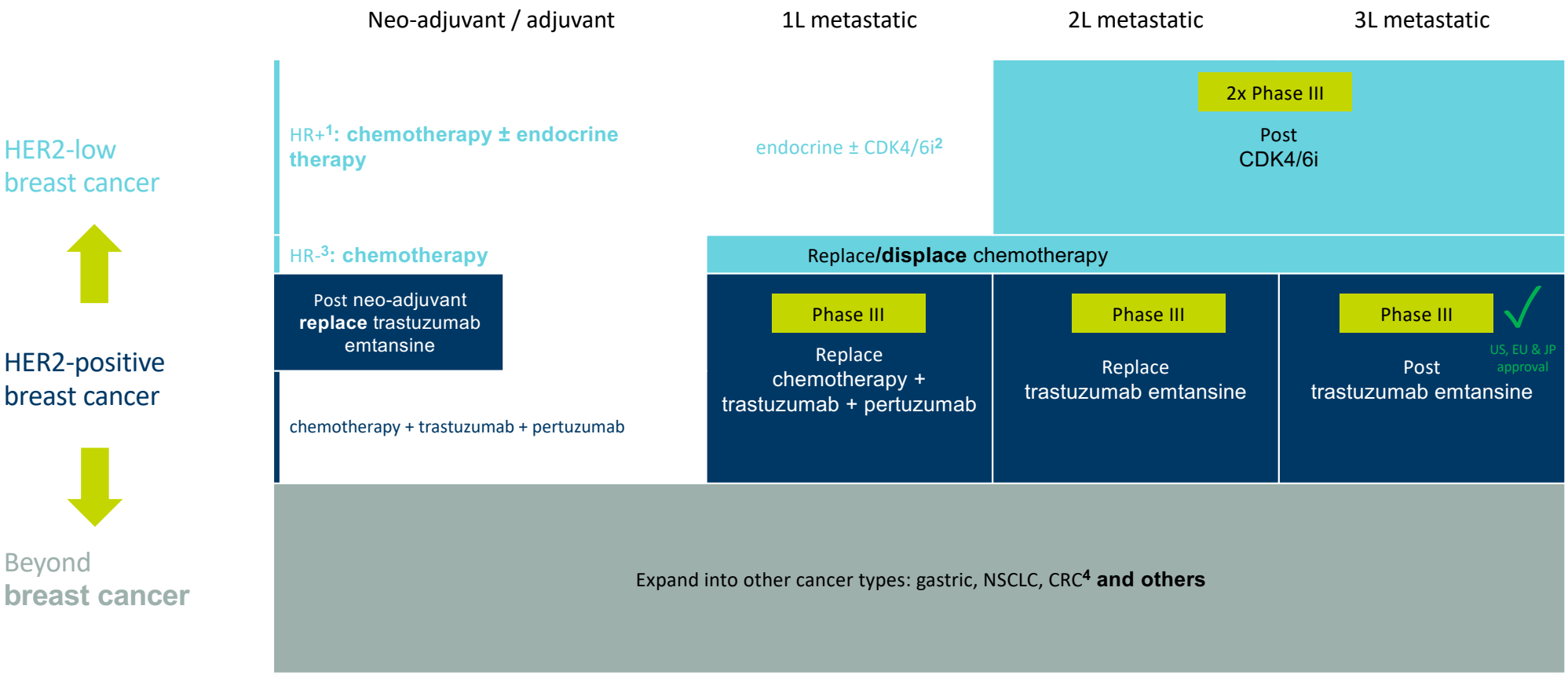
Multiple Phase III trials underway

1. Metastatic breast cancer.
Collaboration revenue at actual exchange rates.

2. Metastatic triple-negative breast cancer.
3. In situ hybridisation.
Source: poster 1023, ASCO 2021.

Enhertu: clinical development programme

Opportunities across breast cancer, HER2-low and other tumours



1. Hormone-receptor positive 2. Cyclin-dependent kinase 4/6 inhibitor 3. Hormone-receptor negative 4. Colorectal cancer.

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

Address endocrine resistance; evaluate different endocrine combinations

Camizestrant (AZD9833): next-generation oral SERD

Encouraging monotherapy efficacy and dose-dependent safety profile

16.3%

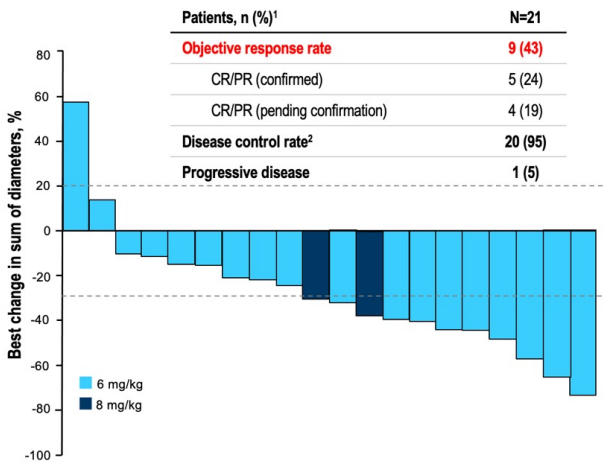
overall response rate

42.3%

clinical benefit rate

Phase III trials underway and planned SERENA-4 data anticipated 2022+

Datopotamab deruxtecan (DS-1062): TROP2 ADC



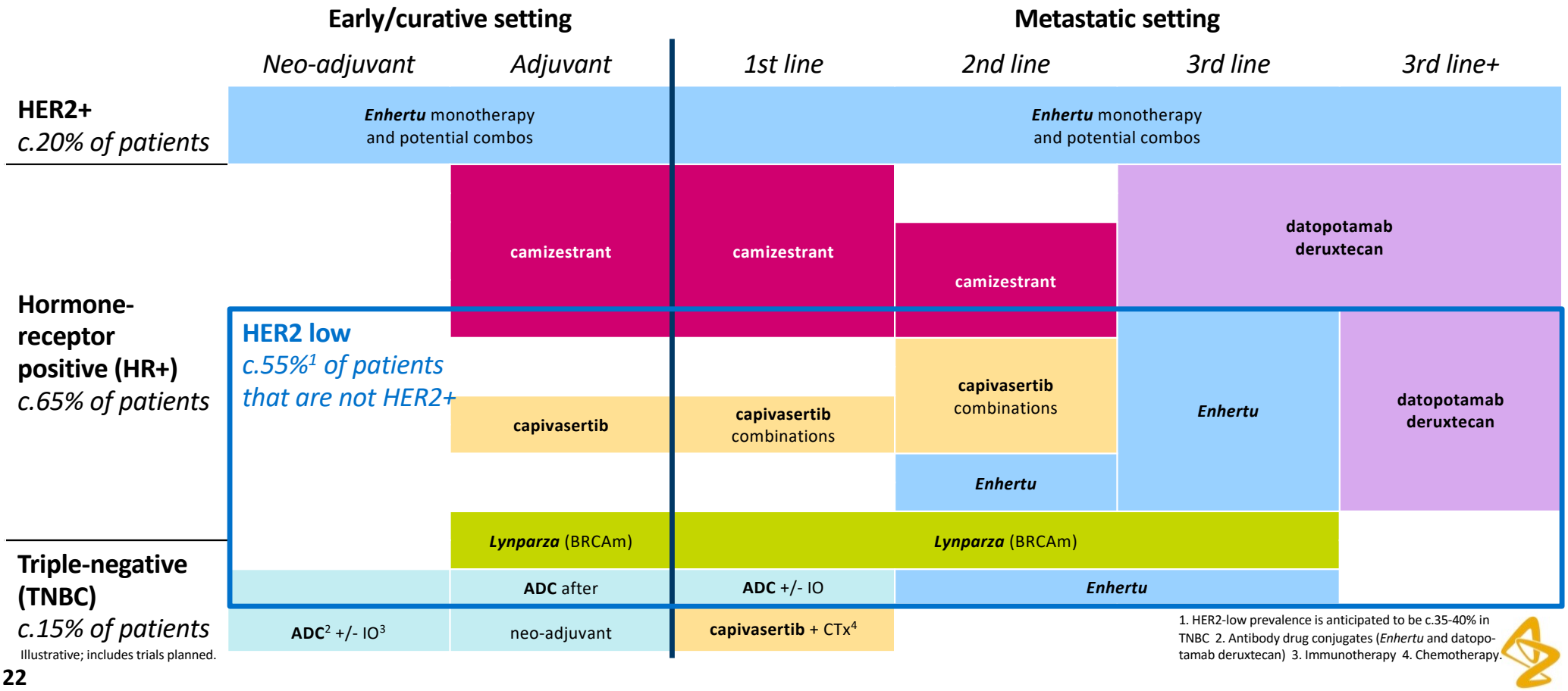
Promising preliminary activity in heavily pre-treated TNBC population; favourable profile vs. SoC

Source: abstract 1005, ASCO 2019; abstract 1007, ASCO 2018.

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



Illustrative; includes trials planned.

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.

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Haematology

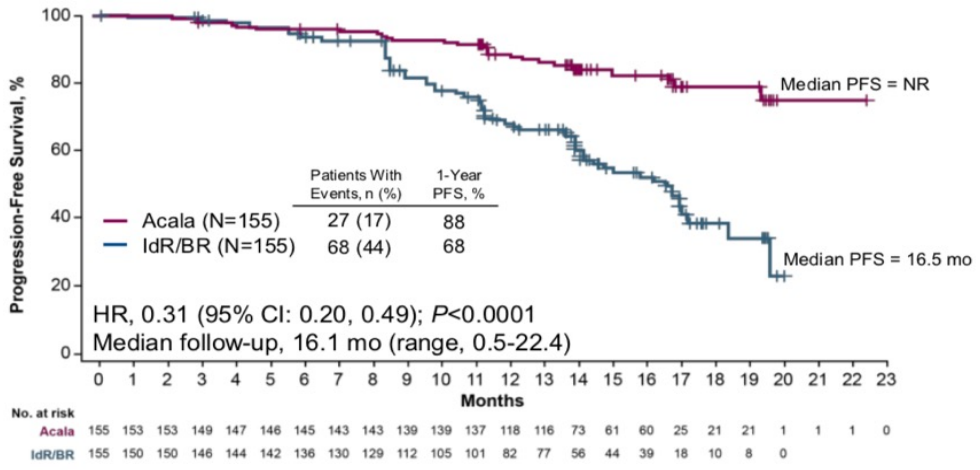
Niko André, Global Franchise Head, Haematology and *Calquence*

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

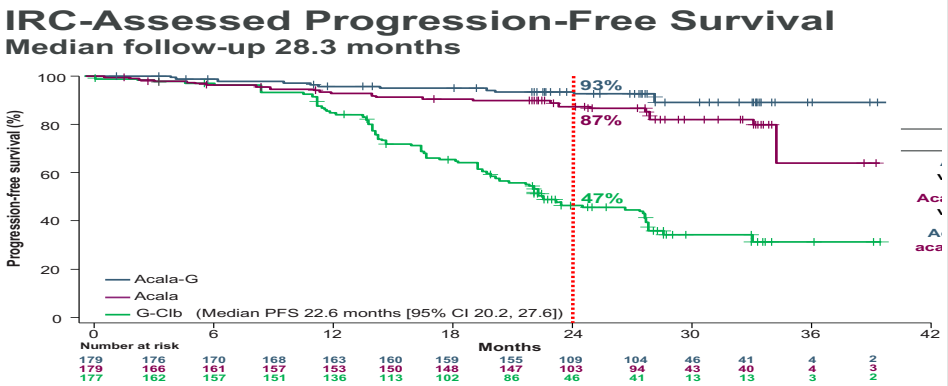
Relapsed/refractory (R/R)
ASCEND Phase III trial



HR[1] (95% CI)	
Calquence vs IdR/BR	**0.31** (0.20-0.49), p<0.0001

From a PFS HR of 0.31 in the R/R setting…

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

1. Hazard ratio.

Other notes: IdR = idelalisib BR = bendamustine and rituximab.

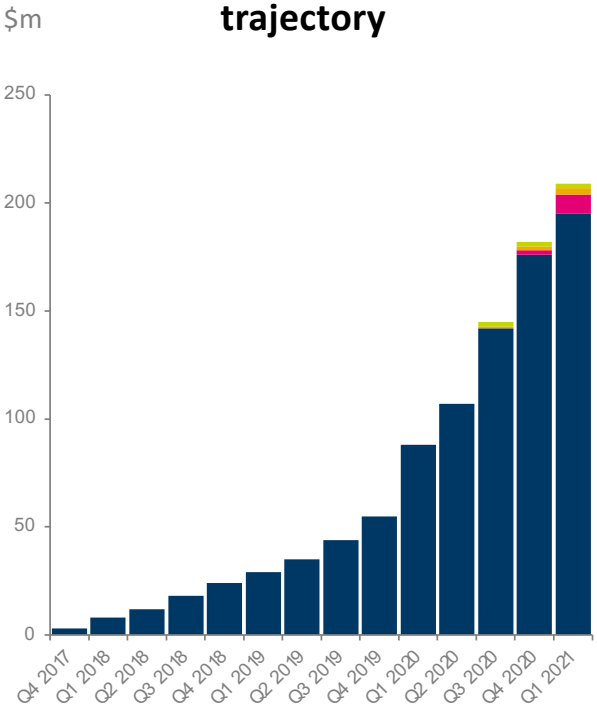
Source: abstract LB2606, The European Hematology Association 2019.

Source: abstract 31, The American Society of Hematology, 2019.

Calquence: launch trajectory confirms clinical value

Inflection point from chronic lymphocytic leukaemia uptake

Solid launch trajectory



US Europe Established RoW Emerging markets

Product sales at actual exchange rates.

US: high up-take in CLL[2]

- 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%

1. Bruton's tyrosine kinase inhibitor.
2. Chronic lymphocytic leukaemia.

Source: IQVIA market research.

Ex-US: Europe launch and reimbursement underway

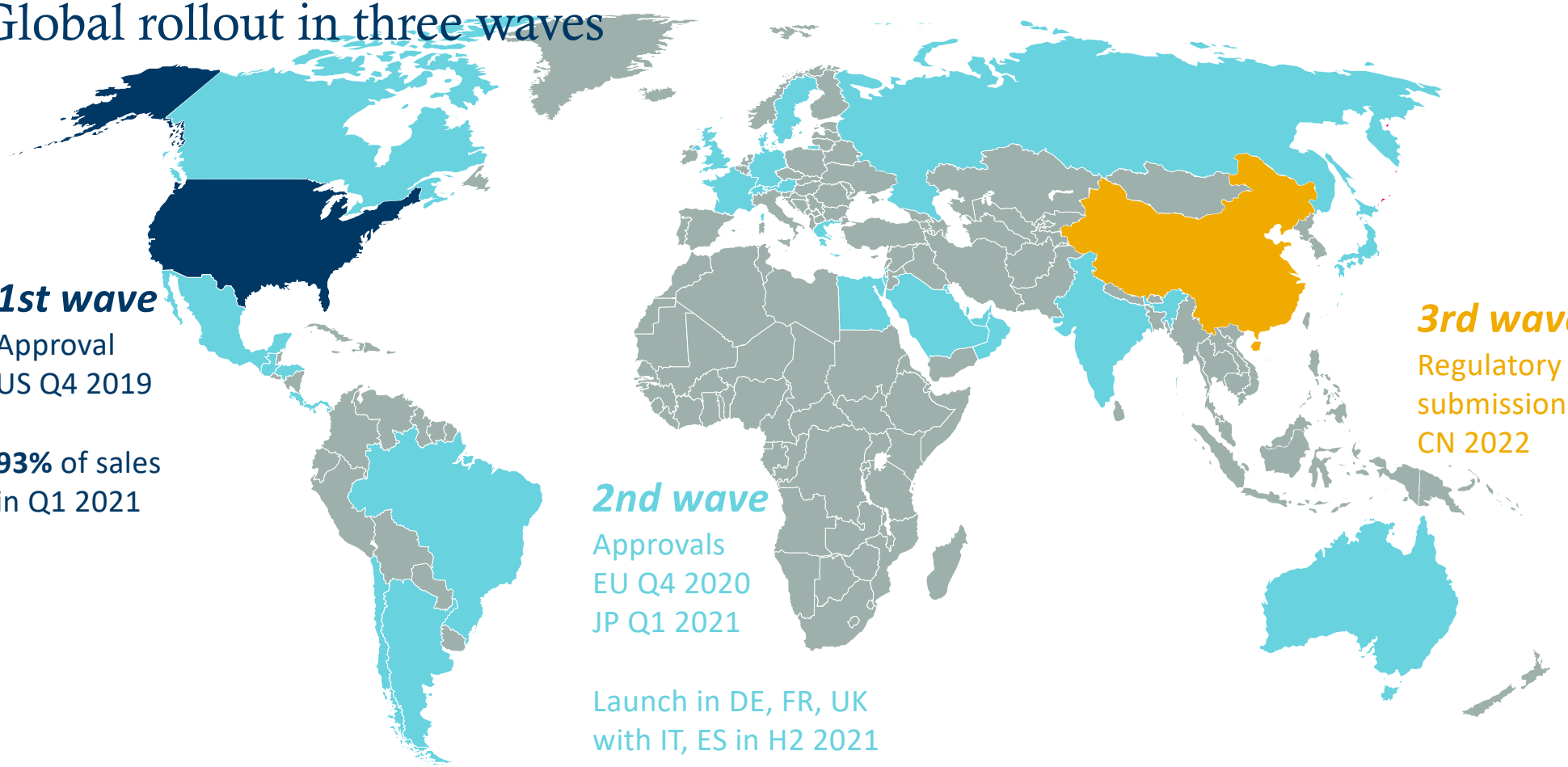
- **Approval**
  60 countries (CLL) and 27 (MCL[3])
- **Reimbursement**
  10 countries (CLL) and 9 (MCL)
- **Sales in >25 countries**
  Largest contribution from DE, UK, FR

Accelerating uptake after reimbursement

3. Mantle cell lymphoma.

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**

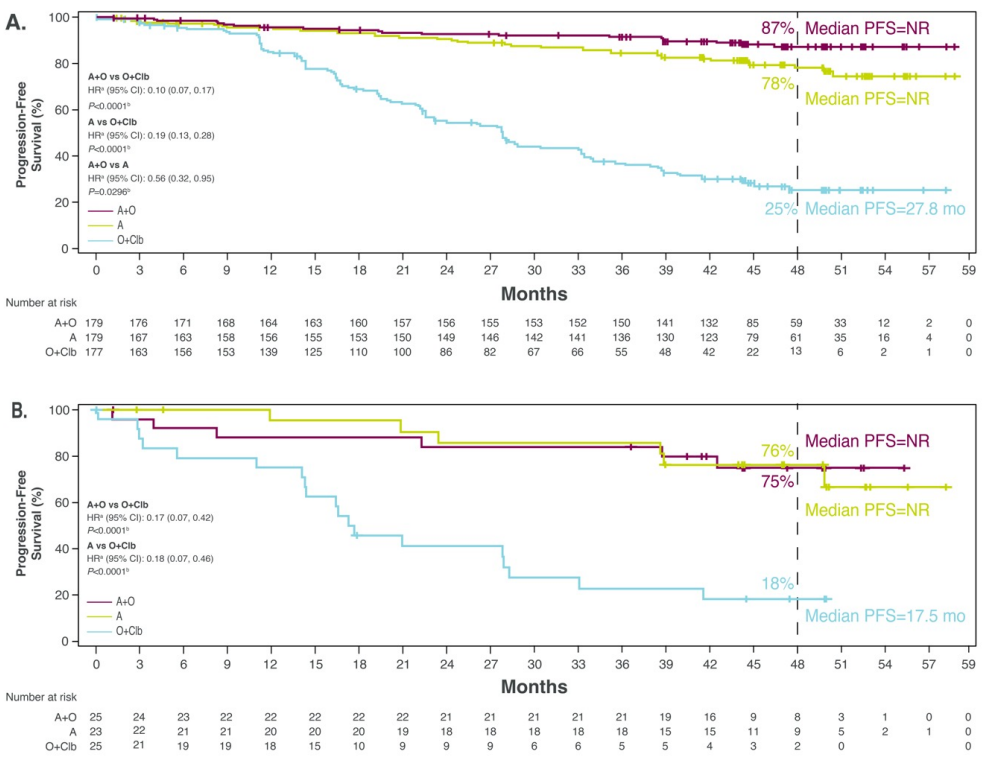
3rd wave
Regulatory
submission
CN 2022

Calquence at ASCO: ELEVATE-TN Phase III trial

Sustained patient benefit at four years in a front-line setting

Overall population

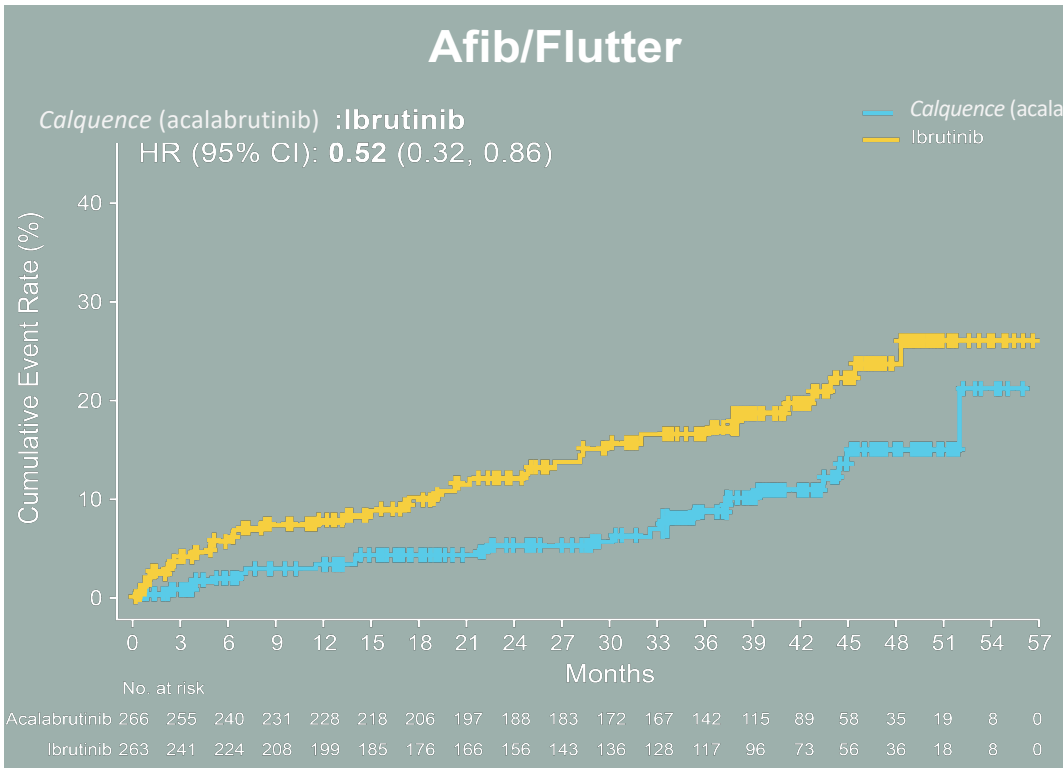
Patients with del(17p) and/or mutated TP53



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



Events, n (%)	Any grade		Grade ≥3	
	Acalabrutinib (n=266)	Ibrutinib (n=263)	Acalabrutinib (n=266)	Ibrutinib (n=263)
Cardiac events	64 (24.1)	79 (30.0)	23 (8.6)	25 (9.5)
Atrial fibrillation[a]*	25 (9.4)	**42 (16.0)**	13 (4.9)	10 (3.8)
Ventricular arrhythmias[b]	0	3 (1.1)	0	1 (0.4)
Bleeding events*	101 (38.0)	**135 (51.3)**	10 (3.8)	12 (4.6)
Major bleeding events[c]	12 (4.5)	14 (5.3)	10 (3.8)	12 (4.6)
Hypertension[d]*	25 (9.4)	**61 (23.2)**	11 (4.1)	**24 (9.1)**
Infections[e]	208 (78.2)	214 (81.4)	82 (30.8)	79 (30.0)
ILD/pneumonitis*	7 (2.6)	**17 (6.5)**	1 (0.4)	2 (0.8)
SPMs excluding NMSC	24 (9.0)	20 (7.6)	16 (6.0)	14 (5.3)

Higher incidence indicated in **bold yellow** for terms with statistical differences.
*Two-sided P-value for event comparisons <0.05 without multiplicity adjustment.
[a]Includes events with preferred terms atrial fibrillation and atrial flutter.
[b]Includes events with preferred terms torsade de pointes, ventricular arrhythmia, ventricular extrasystoles, ventricular fibrillation, ventricular flutter, ventricular tachyarrhythmia, and ventricular tachycardia.
[c]Defined as any hemorrhagic event that was serious, grade ≥3 in severity, or a central nervous system hemorrhage (any severity grade).
[d]Included events with the preferred terms of hypertension, blood pressure increased, and blood pressure systolic increased.
[e]Most common grade ≥3 infections were pneumonia (acalabrutinib, 10.5%; ibrutinib, 8.7%), sepsis (1.5% vs 2.7%, respectively), and UTI (1.1% vs 2.3%).
ILD, interstitial lung disease; NMSC, nonmelanoma skin cancer; SPMs, second primary malignancies; UTI, urinary tract infection.

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

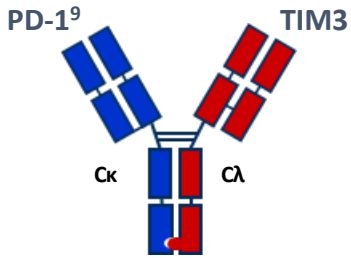
Broad portfolio in cell death

Target/ medicine	Bcl-2[1]	Bcl-xL	BFL1	MCL1[2]
venetoclax				
AZD0466 (Bcl-2/xL)	✓	✓		
AZD5991 (MCL1)				✓
AZD4573 (CDK9[3])			✓	✓

Potential in:
AML[4], MDS[5], NHL[6], HL[7], PTCL[8]

1. B-cell lymphoma 2 2. Induced myeloid leukaemia cell differentiation protein 3. Cyclin-dependent kinase 9 4. Acute myelogenous leukaemia 5. Myelodysplastic syndromes 6. Non-Hodgkin lymphoma 7. Hodgkin lymphoma 8. Peripheral T-cell lymphoma.

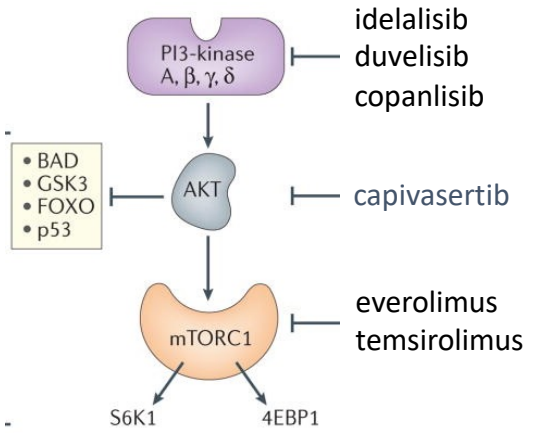
First immunotherapy bispecific antibody



Potential in:
Hodgkin lymphoma

9. Programmed cell death protein 1.
Source: AstraZeneca.

Tumour drivers of resistance

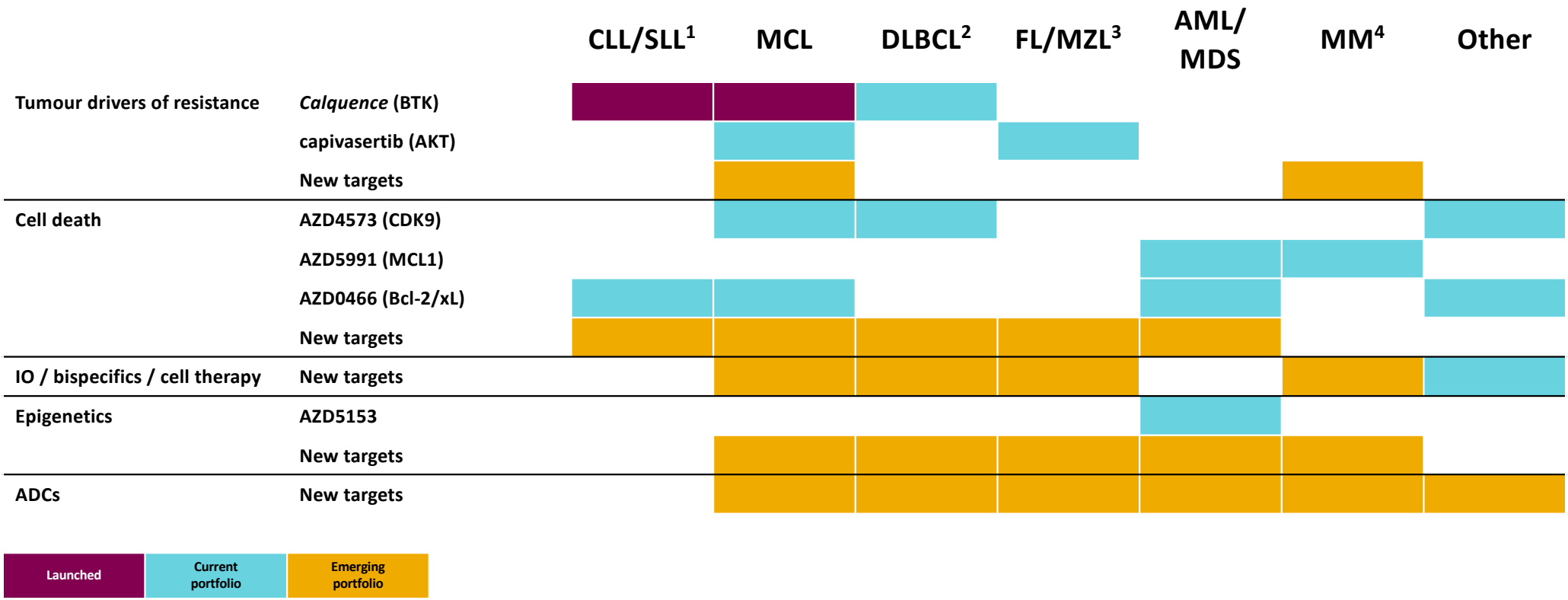


Potential in:
follicular lymphoma, MCL

Source: modified from *Nature* (https://www.nature.com/articles/nrclinonc.2016.205).

Haematology: 'What's next'

Growing pipeline across medicines and indications



1. Small lymphocytic lymphoma 2. Diffuse large B-cell lymphoma 3. Marginal zone lymphoma 4. Multiple myeloma.

AstraZeneca
What science can do

‘What’s next’

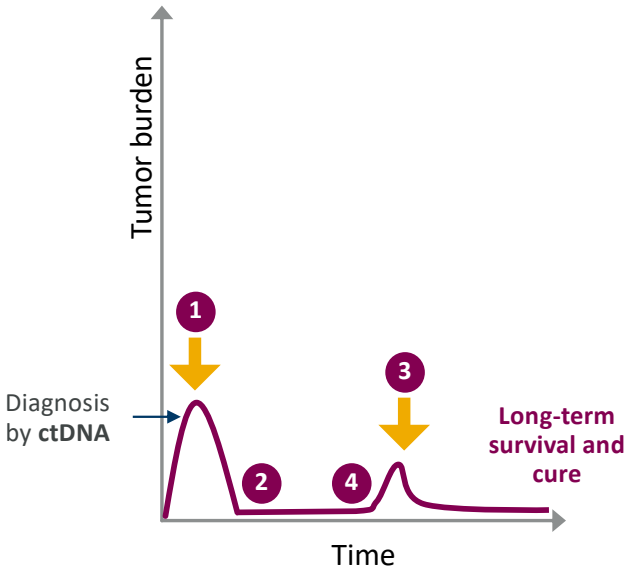
Susan Galbraith, Senior Vice President, Oncology R&D, early stage

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

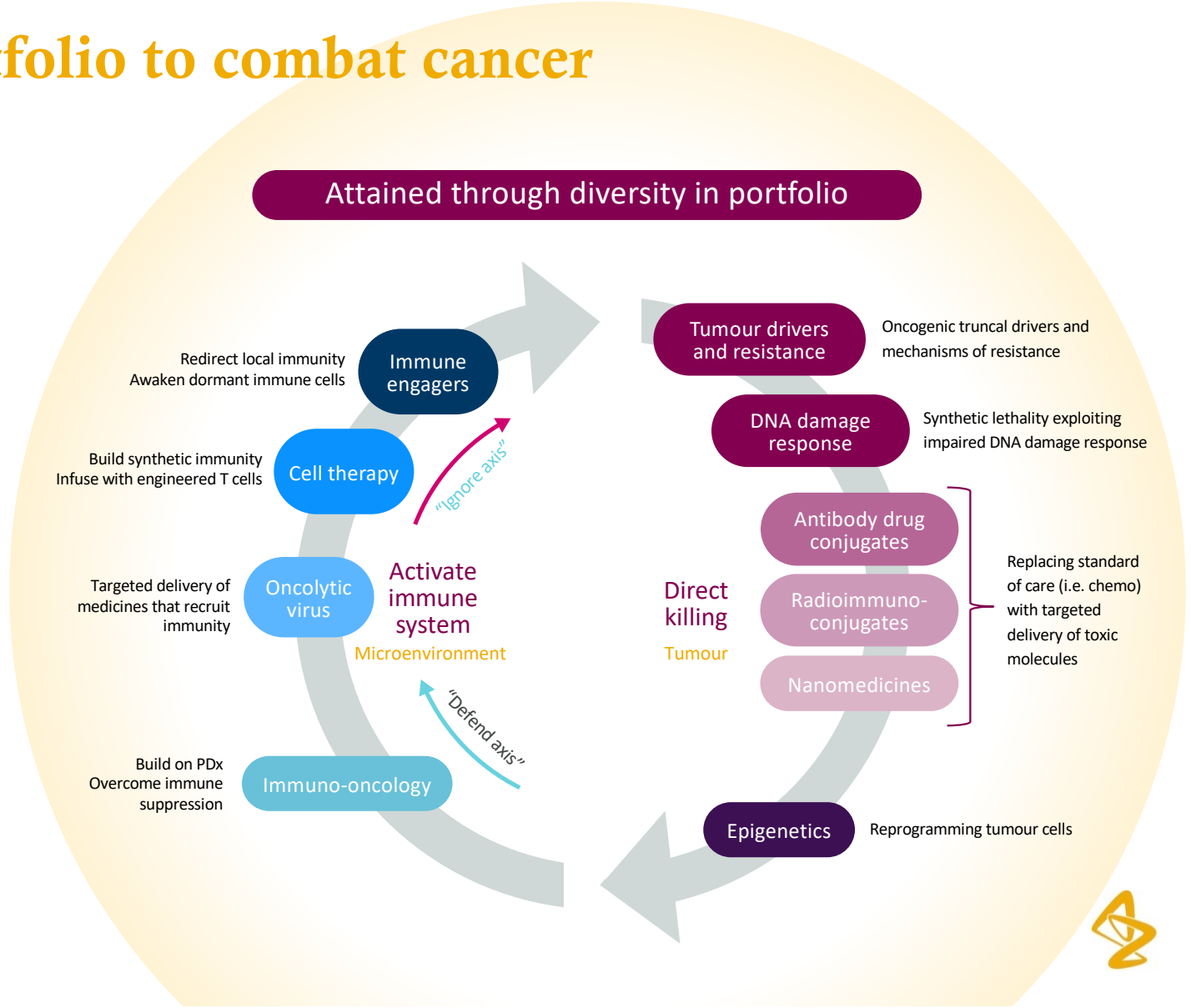
For additional questions and IR support, please email henry.wheeler@astrazeneca.com.

Comprehensive portfolio to combat cancer

Oncology ambition



Attained through diversity in portfolio

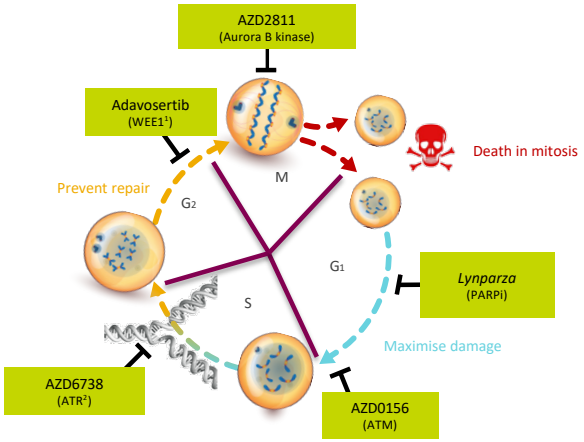


Source: AstraZeneca.

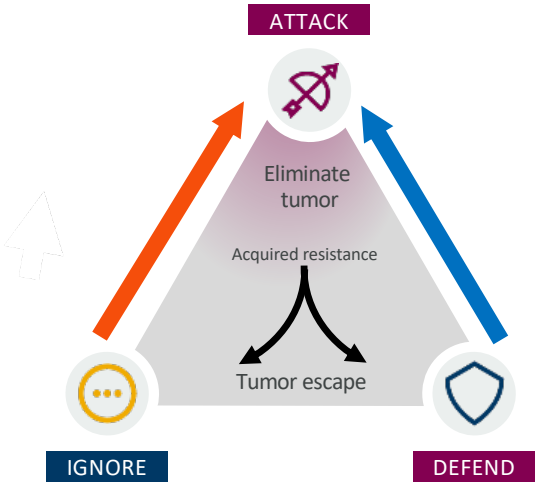
What's next?

Selectively expanding technologies and platforms

DDR



Next-wave IO



Next-wave modalities

ADCs & RIC[4]s

PROTAC[5]s

Functional genomic capabilities

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

Source: AstraZeneca.

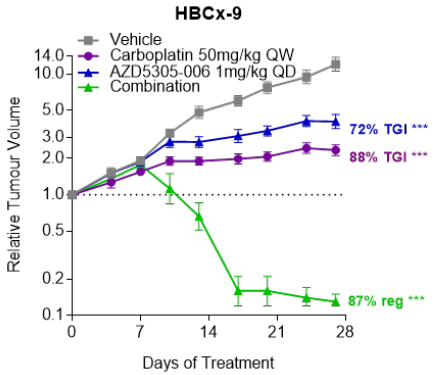
4. Radioimmunoconjugate 5. Proteolysis targeting chimeras.

Advancing the DDR portfolio

Key data at ASCO and AACR

AZD5305
PARP-1 selective inhibitor

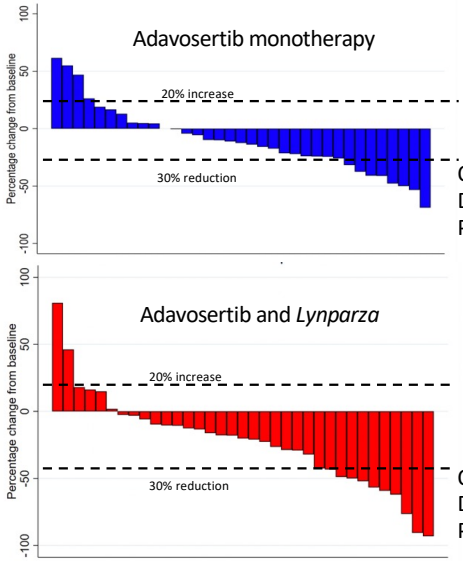
- Five abstracts at AACR[1]
- Selective PARP1-DNA trapper
- More potent and efficacious than first-generation PARP inhibitors



Strong combination activity with carboplatin (non-BRCA setting)

AZD5305 now in Phase I trials

EFFORT
Adavosertib Phase II trial

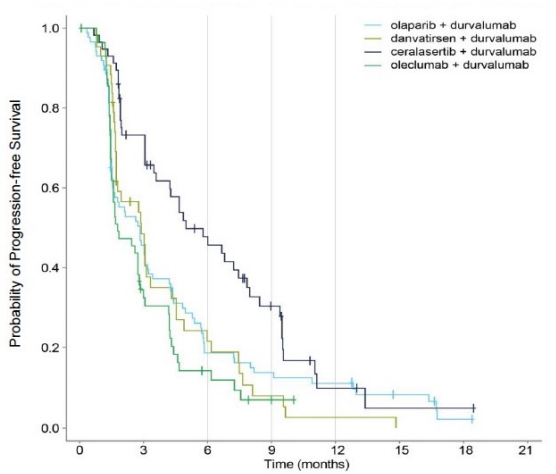


ORR[2]: 23%
DOR[3] 5.5 months
PFS 5.5 months

ORR: 29%
DOR 5.5 months
PFS 6.4 months

WEE1 activity in PARP-resistant patients

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[1]) or monalizumab (NKG2A[2])**

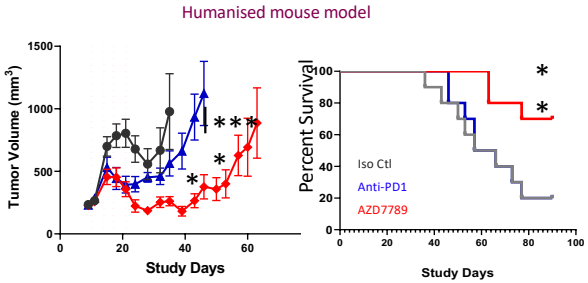
- COAST (Stage III unresectable NSCLC)
- NeoCOAST (early-stage NSCLC)

***Imfinzi* + ceralasertib (ATR)**

- HUDSON (NSCLC)
- MONETTE (melanoma)

COAST/NeoCOAST data presentation H2 2021

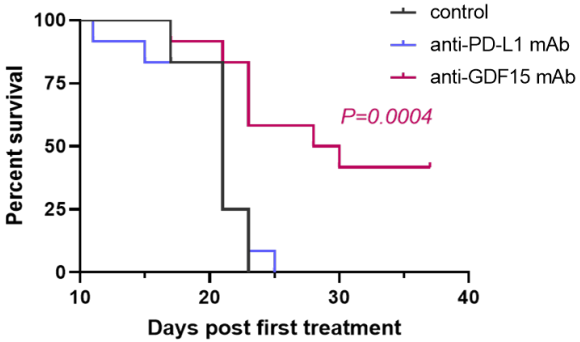
AZD7789 PD1/TIM3 bispecific



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

Targeting PD-1/TIM-3 increases survival in IO-naïve & PD-1 resistant models

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.

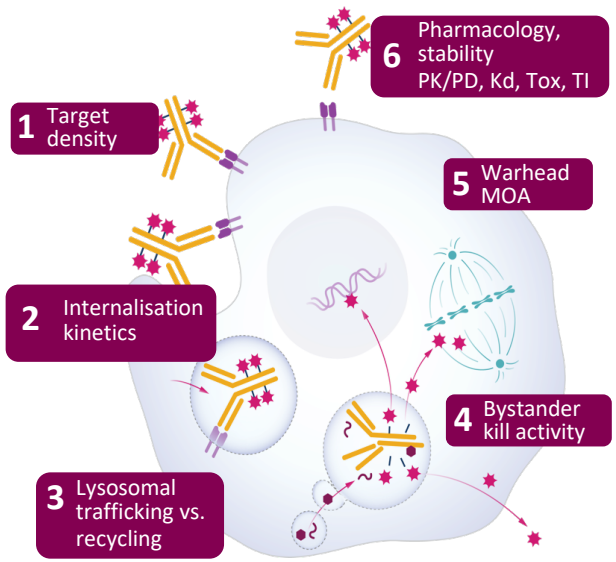
Source: AstraZeneca.

Source: AstraZeneca.

Next-wave modalities

Innovative use of new modalities to deliver transformational change

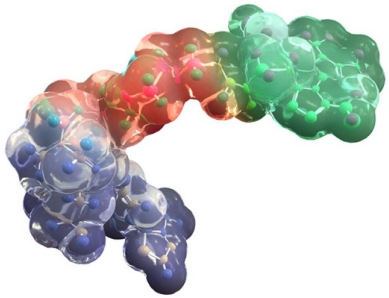
ADCs & RICs



Targeted killing by targeting proteins immune to conventional approaches

Source: AstraZeneca.

PROTACS

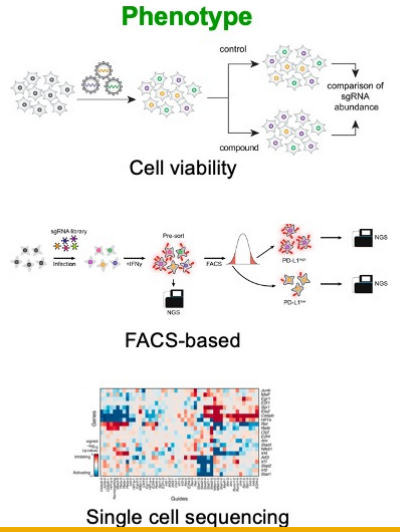


Harnessing the cell's natural waste disposal system

Source: AstraZeneca.

Genomics capabilities

CRISPR screens and DepMap-enhancing target identification



Selective targeting of the key resistance and survival pathways

Source: AstraZeneca.

Early-stage oncology pipeline

Phase I		Phase II
MEDI1191 modIL-12	AZD0466 Bcl2-xL	oleclumab CD73
IPH5201 CD39	AZD5991 MCL1	imaradenant A2AR[1]
AZD5069 CXCR2-ESR	AZD1390 ATM	MEDI5752 PD-1/CTLA4[2]
AZD0171 LIF1	AZD7648 DNAPK	MEDI0457 HPV Vax
AZD8701 FOXP3 ASO	AZD5305 PARP1Sel	camizestrant SERD
MEDI5395 rNDV GMCSF		AZD4573 CDK9
MEDI9253 rNDV IL-12		ceralasertib ATR
AZD5153 BRD4-ESR		AZD2811 AURN

- Immuno-oncology
- Oncolytic virus
- Epigenetics
- Haematology
- Tumour drivers and resistance
- DNA damage response

1. Adenosine A2A receptor 2. Cytotoxic T-lymphocyte-associated protein 4.

‘What’s next’

Phase I/II new medicines, selected

adavosertib (WEE1 inhibitor) uterine, ovarian cancer	**ceralasertib** (ATR inhibitor) solid tumours, blood cancers
oleclumab (CD73 mAb) solid tumours	**imaradenant** (A2AR inhibitor) solid tumours
AZD5305 (PARP1 inhibitor) solid tumours	**MEDI5752** (PD-1/CTLA4 mAb) solid tumours
AZD4573 (CDK9 inhibitor) blood cancers	**AZD2811** (Aurora B inhibitor) solid tumours, blood cancers
AZD5991 (MCL1 inhibitor) blood cancers	**AZD0466** (Bcl-2/xL) solid tumours, blood cancers

1. Potentially pivotal Phase II.

What’s now

Phase III new medicines

datopotamab deruxtecan lung cancer	**camizestrant** breast cancer
monalizumab head & neck cancer	**capivasertib** breast, prostate cancer
savolitinib NSCLC[1]	**tremelimumab** multiple cancers

Phase III lifecycle management, major

	Lynparza multiple cancers
Tagrisso NSCLC	***Enhertu*** multiple cancers
Imfinzi multiple cancers	***Calquence*** multiple cancers

AstraZeneca
What science can do

Questions & Answers

<u>To ask a question</u>
Webinar
Click 'Raise Hand' (preferred):

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

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

Use of AstraZeneca conference call, webcast and presentation slides