Puma Biotechnology

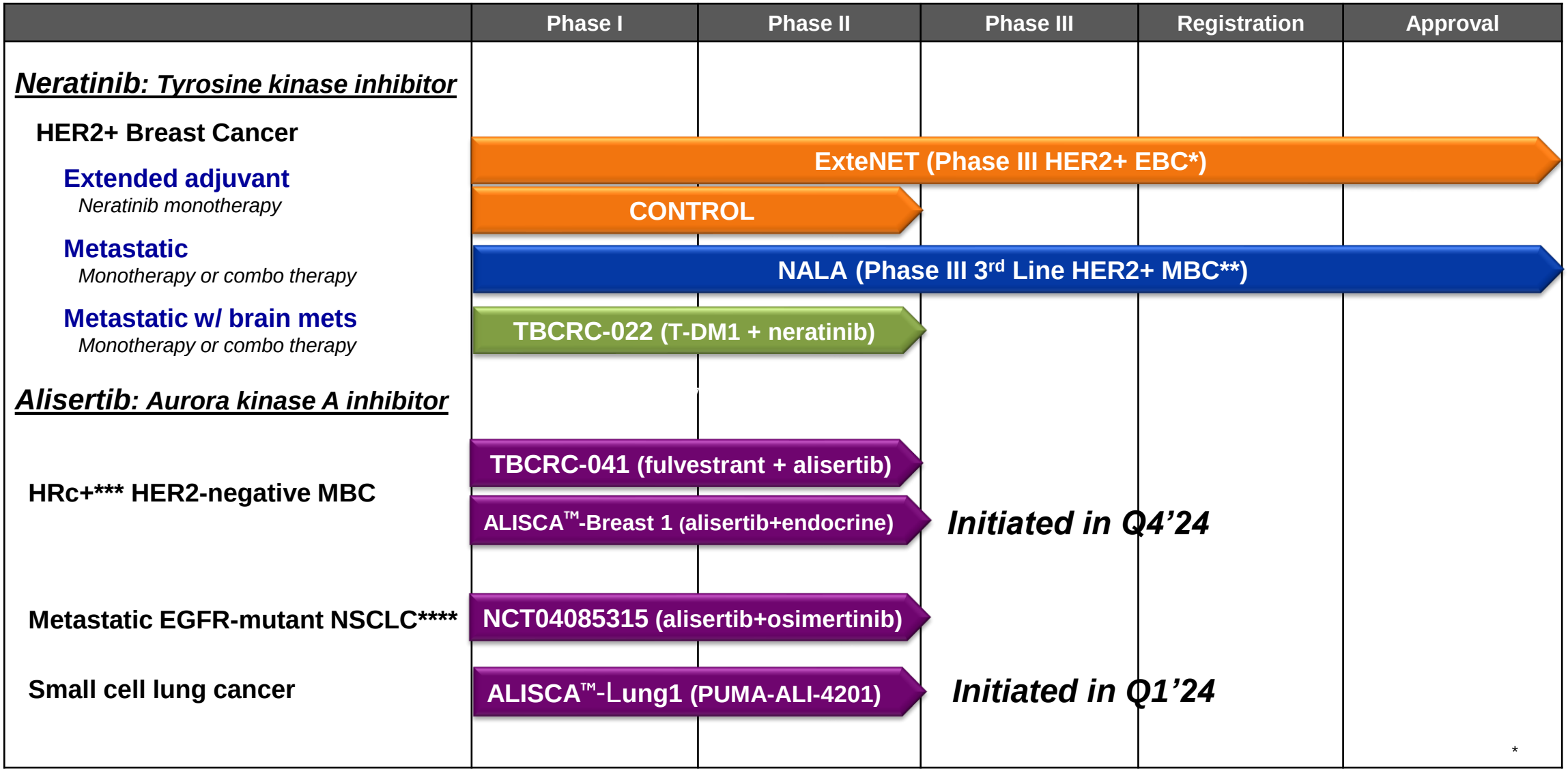
December 2024

Forward-Looking Safe-Harbor Statement

This presentation contains forward-looking statements, including statements regarding commercialization of NERLYNX® and the potential indications and development of our drug candidates. All forward-looking statements involve risks and uncertainties that could cause our actual results to differ materially from the anticipated results and expectations expressed in these forward-looking statements. These statements are based on our current expectations, forecasts and assumptions, and actual outcomes and results could differ materially from these statements due to a number of factors, which include, but are not limited to, any adverse impact on our business or the global economy and financial markets, generally, from the global COVID-19 pandemic, and the risk factors disclosed in our periodic and current reports filed with the Securities and Exchange Commission from time to time, including our Annual Report on Form 10-K for the year ended December 31, 2023, and subsequent filings. Readers are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. We assume no obligation to update these forward-looking statements except as required by law.

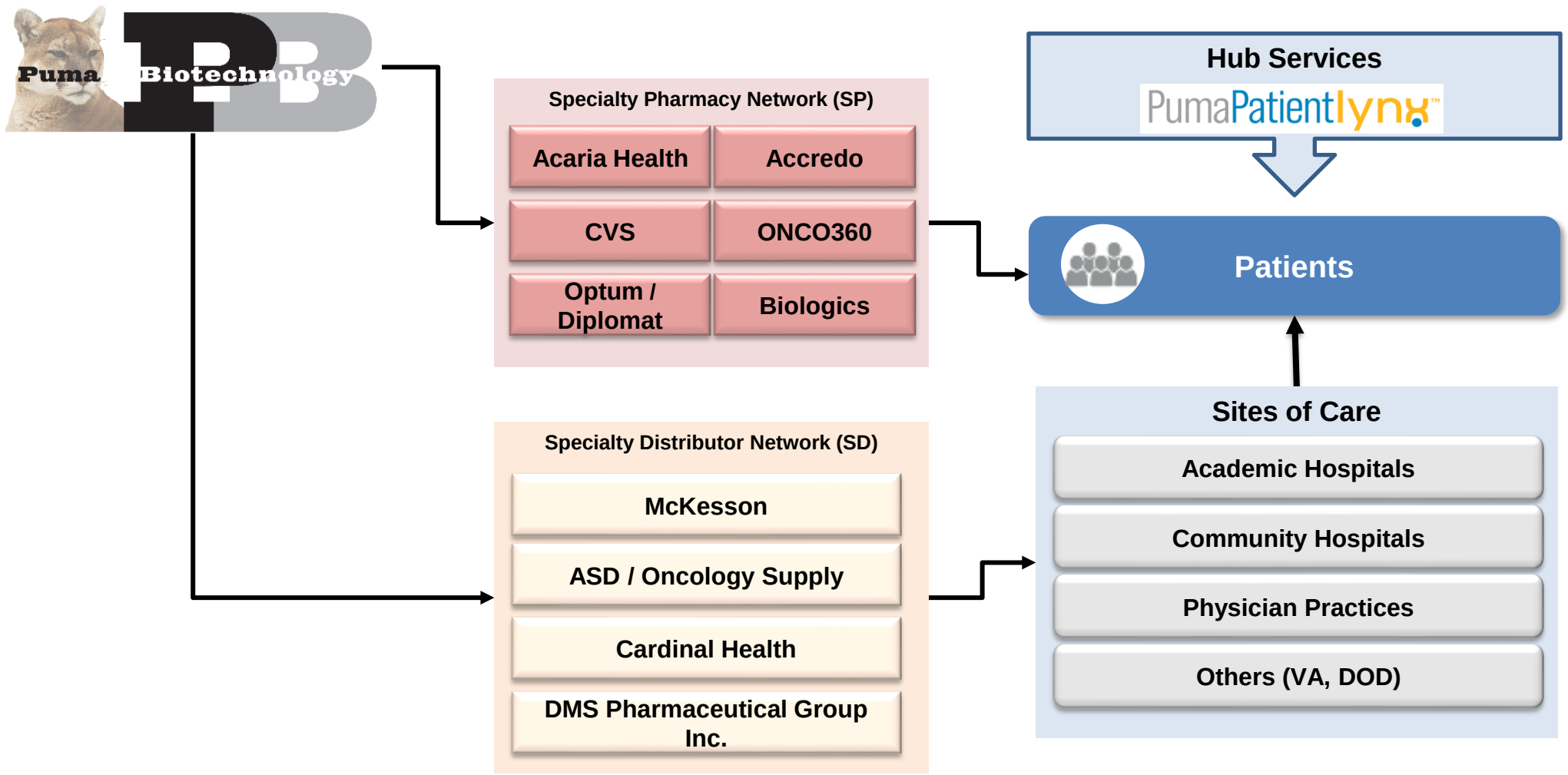
Puma Biotechnology

Product Pipeline



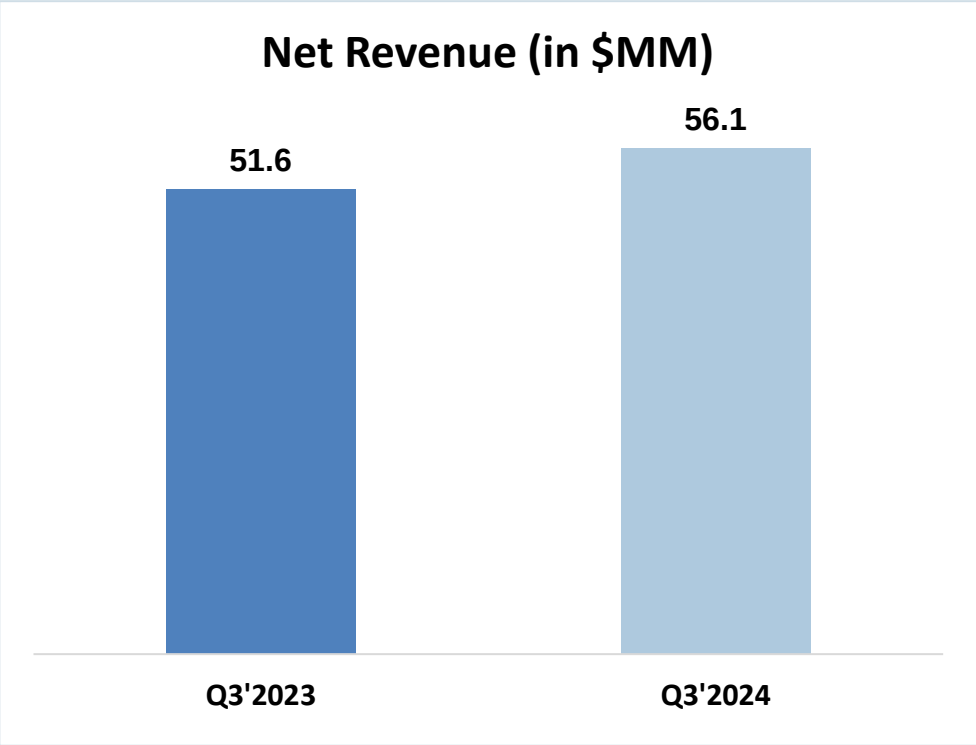
* ECB: Early breast cancer ** MBC: Metastatic breast cancer *** HRc+: Hormone receptor positive ****NSCLC: Non small cell lung cancer

Puma's Pharmacy and Distributor Network



$56.1 Million Net NERLYNX Revenue in Q3’24

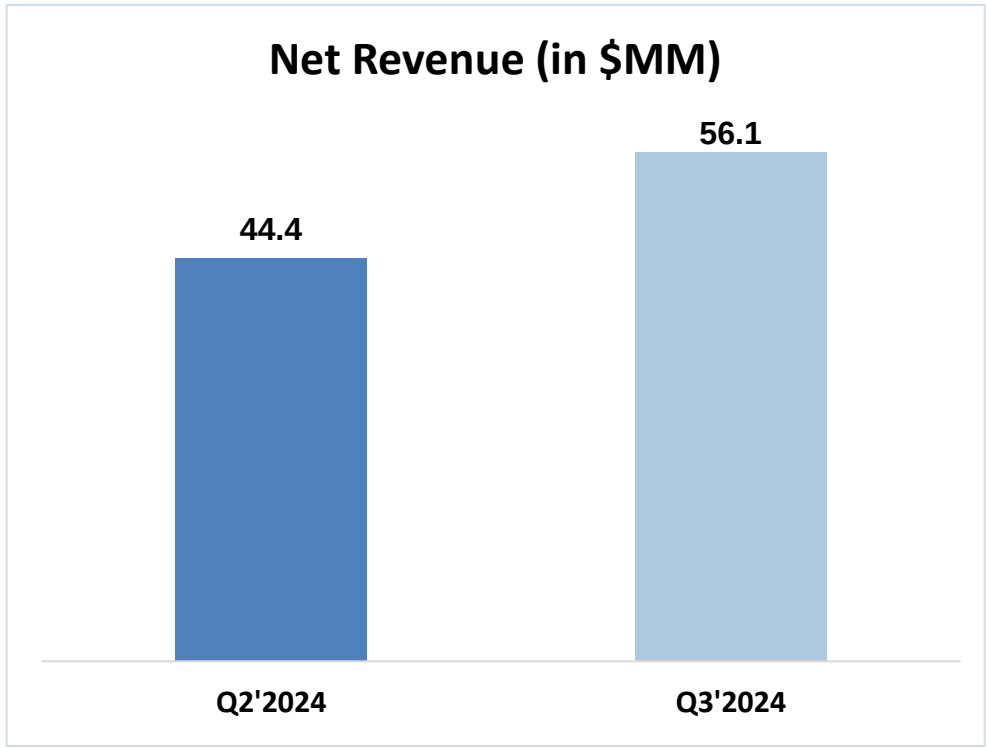
~9% increase in Q3’24 compared to Q3’23



Inventory Change ($)

Q3’23	Q3’24
$0.6 mil	$0.6 mil

~26% increase in Q3’24 compared to Q2’24

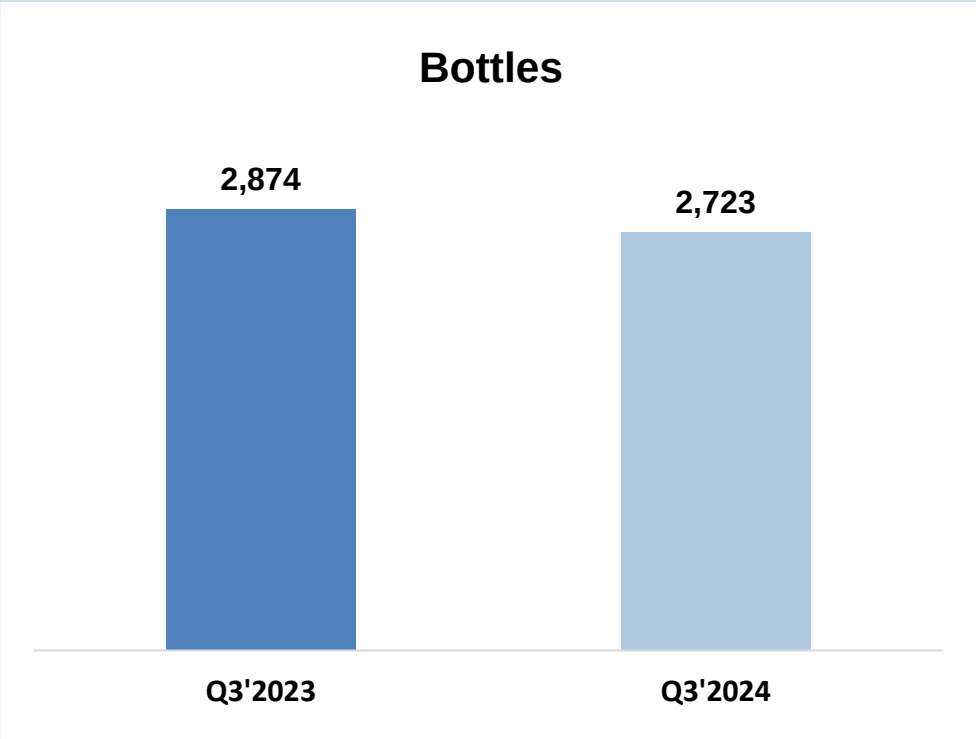


Inventory Change ($)

Q2’24	Q3’24
-$2.3 mil	$0.6 mil

2,723 Ex-Factory Bottles Were Sold in Q3’24

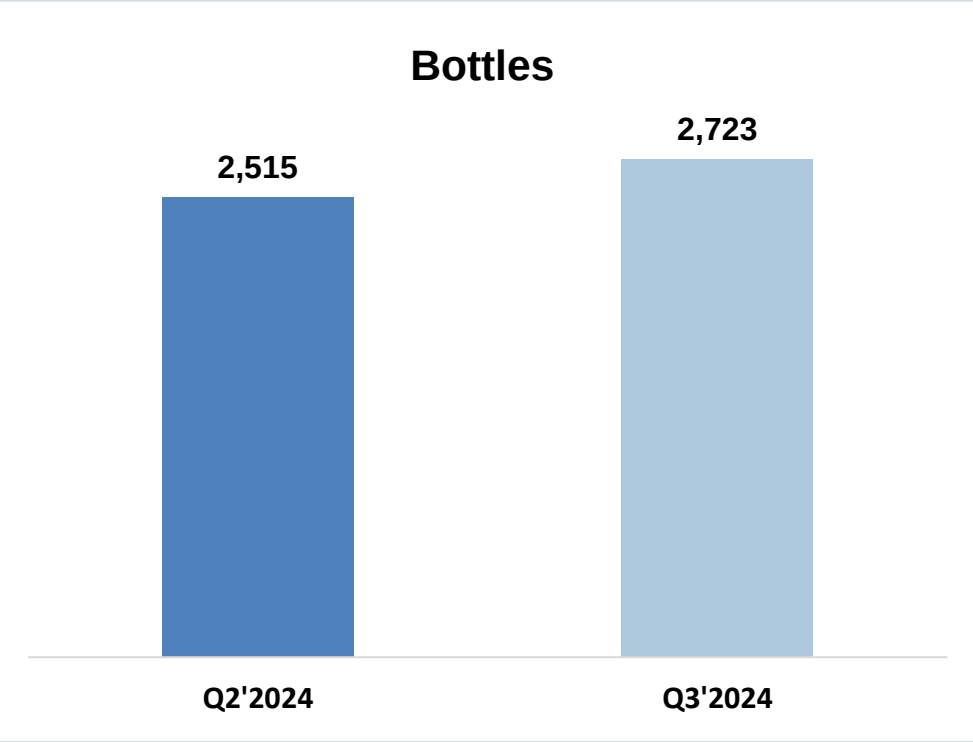
~5% decline in Q3’24 compared to Q3’23



Inventory Change Bottles

Q3’23	Q3’24
32	37

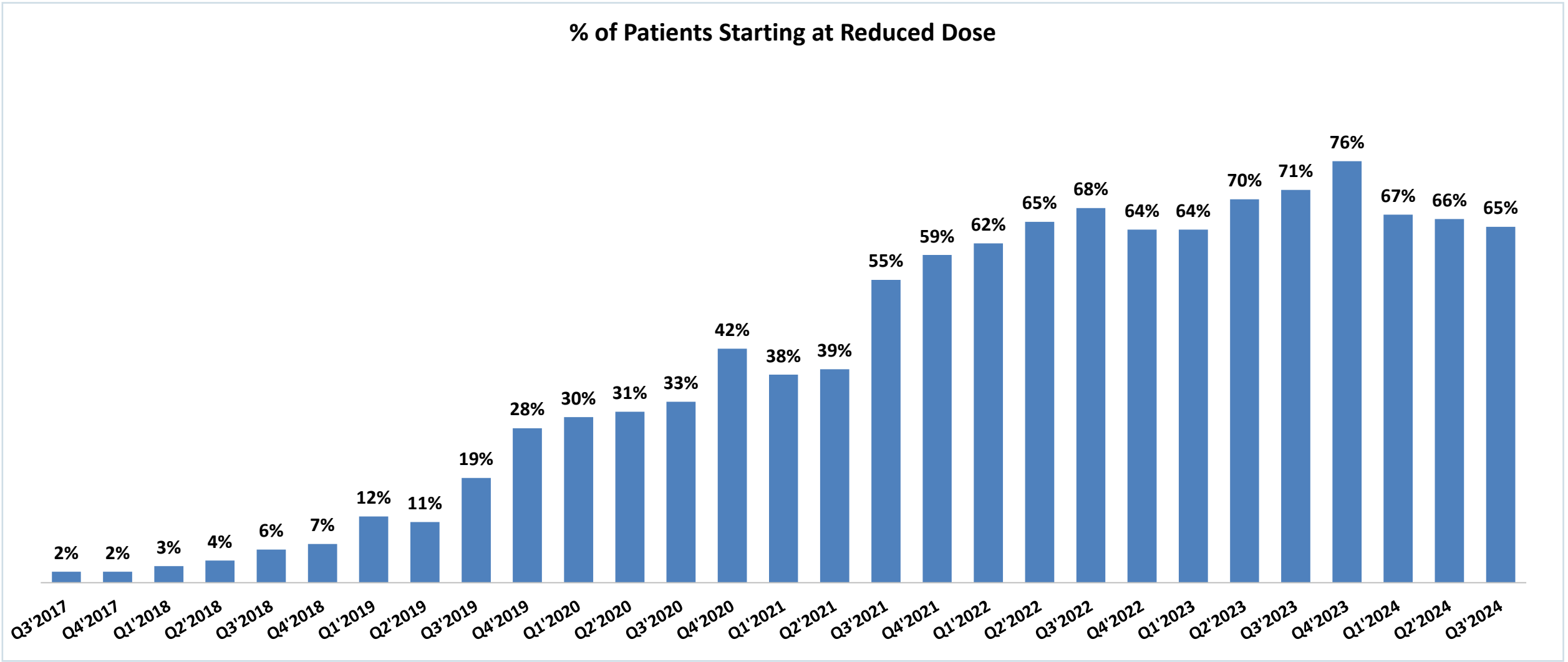
~8% increase in Q3’24 compared to Q2’24



Inventory Change Bottles

Q2’24	Q3’24
-132	37

~65% of Patients in Q3’24 Started at a Reduced Dose*



*Reduced dose defined as fewer than 6 pills per day

Rest of World Partnerships – Timelines

Region	Partner	Regulatory Approvals	Commercial Launches
Australia / SE Asia	Specialised Therapeutics	• 2019 – Ext. Adj. in Australia, Singapore • 2020 – Ext. Adj. in Brunei, Malaysia, New Zealand • 2022 – Ext. Adj. in the Philippines; mBC in Singapore • 2023 – mBC in Malaysia	• 2020 – Singapore • 2021 – Malaysia, Brunei, New Zealand
Israel	MEDISON	• 2020 – Approved in Ext. Adj. and mBC	• 2020 – Launched
Canada	Knight	• 2019 – Ext. Adj. approved • 2021 – mBC approved	• 2020 – Launched
Latin America	PINT PHARMA	• 2019 – Ext Adj in Argentina • 2020 – Ext. Adj in Chile, Ecuador; mBC in Argentina • 2021 – Ext Adj. and mBC in Peru; mBC in Chile; Ext. Adj. in Brazil • 2022 – Ext. Adj. in Mexico; mBC in Ecuador • 2023 – mBC in Colombia and Mexico • Q2 2024 – mBC in Brazil	• 2020 – Argentina • 2021 – Chile and Peru • 2022 – Brazil • Q1 2023 – Mexico and Colombia
Europe Greater China Middle East North and West Africa South Africa Turkey	Pierre Fabre	• 2019 – Ext. Adj. EMA and Hong Kong • 2020 – Ext. Adj. in China, Taiwan • 2021 – mBC in Taiwan • 2023 – Ext. Adj. in Morocco, South Africa, and UAE • Q1 2024 – Ext. Adj. in Syria • Q2 2024 – Ext. Adj. in Saudi Arabia • Q3 2024 – Ext. Adj. in Algeria	• 2019 – Germany, UK, Austria • 2020 – Sweden, Finland, Scotland, Switzerland, Denmark, and Hong Kong • 2021 – China (added to 2021 NRDL), Taiwan, Greece, Czech Republic, and Luxembourg • 2022 – Ireland and Spain • 2023 – Slovakia • Q1 2024 – Morocco • Q3 2024 – South Africa, United Arab Emirates
South Korea	BIXINK THERAPEUTICS	• 2021 – Ext. Adj. in S. Korea	• 2022 – Launched

NERLYNX® Extended Adjuvant HER2+ Breast Cancer Market Size

- Approximately 28,300 patients (US) with early stage HER2+ breast cancer treated with adjuvant treatment[1]
  - Approximately 6,000 patients (US) with HR positive early stage HER2+ breast cancer and no pathological complete response to neoadjuvant treatment (high risk disease)
- Approximately 37,000 patients (EU) with early stage HER2+ breast cancer treated with adjuvant treatment[1]
  - Approximately 65–70% of patients have HR positive disease

[1]Roche epidemiology slides 09/18

Puma Financial Guidance for Q4 and FY 2024

	Q4 2024	Full Year 2024 (previous)	Full Year 2024 (new)
NERLYNX revenue guidance:	$46–$48 mil	$183–$190 mil	$187–$190 mil
NERLYNX royalty guidance:	$3.5–$5 mil	$30–$34 mil	$34–$36 mil
NERLYNX license revenue:	$1–$2 mil	$1–$2 mil	$1–$2 mil
Net income (loss):	$4–$6 mil	$12–$15 mil	$15–$17 mil
Gross to net adjustment:	21%–22%	21%–22%	20.5%–21.5%

ALISERTIB

Breast Cancer and Small-Cell Lung Cancer

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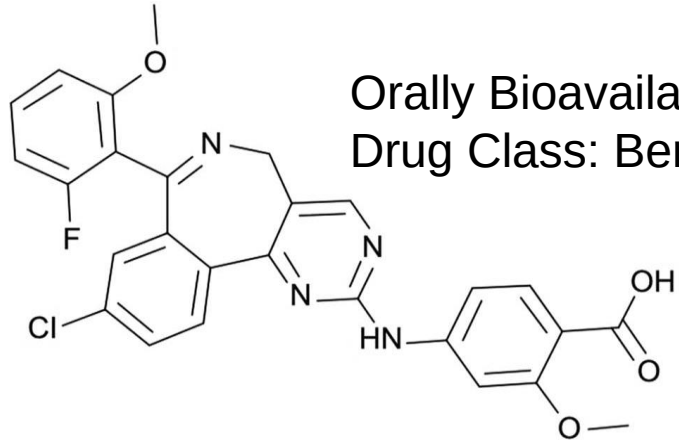
Alisertib (MLN 8237)

Aurora Kinase A (AURKA) inhibitor

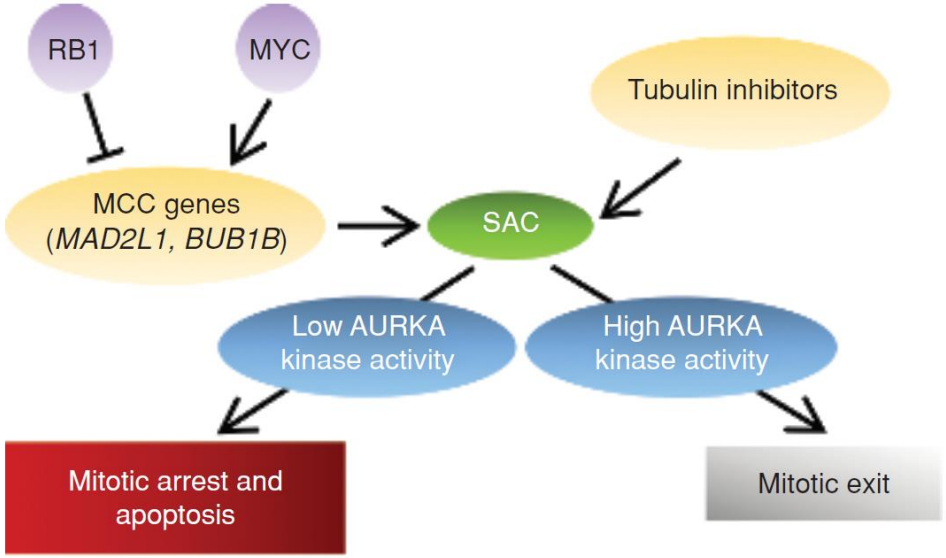


Orally Bioavailable
Drug Class: Benzazepine

- Single-agent and combinational clinical activity in solid tumors including hormone receptor-positive breast cancer (HR+ MBC), triple negative breast cancer (TNBC), small cell lung cancer (SCLC), and head and neck cancer
- Single-agent clinical activity in hematologic malignancies including peripheral T-cell lymphoma (PTCL) and aggressive non-Hodgkin's lympohoma (NHL)
- Well-characterized safety profile: ~1,300 patients treated across 22 company-sponsored trials

Synthetic Lethality of AURKA and Rb1

Cancers with a hypersensitive spindle assembly checkpoint (SAC) depend on AURKA for mitotic exit and survival[1]

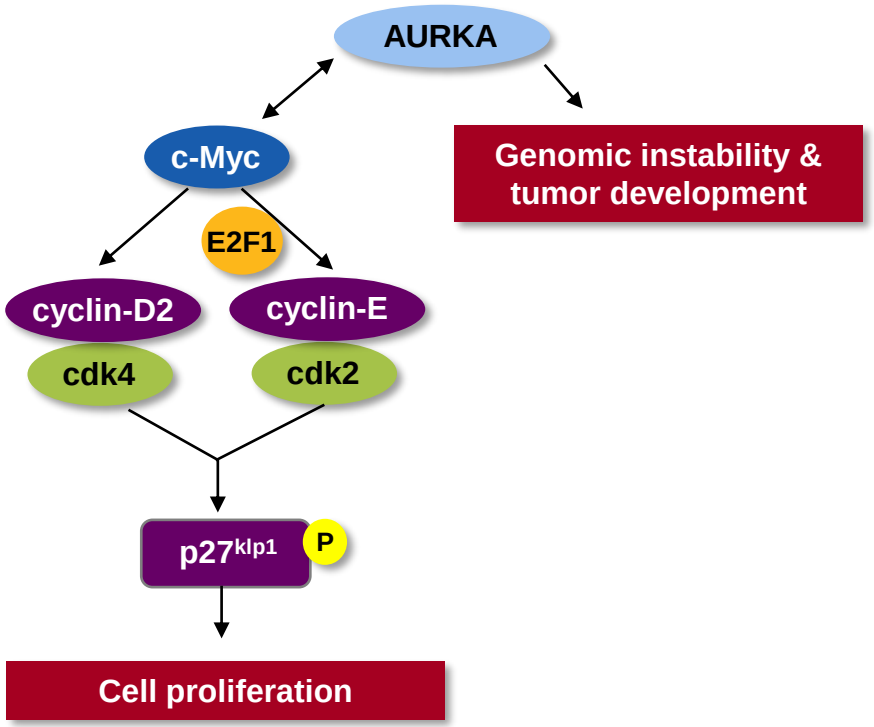


- Loss of function of Rb1 is a common event in cancer and can emerge as a mechanism of resistance to EGFR, CDK4, and ER-targeted therapies in breast and lung cancers
- Rb1 controls entry into S phase of mitosis, and loss of Rb1 function leads to a hyperactivated, primed, SAC
- Cancers with a hyperactivated SAC depend on AURKA in order to overcome SAC priming, which leads to stalled mitosis

[1]Dick F Cancer Discovery Feb 2019, Gong X Cancer Discov 2019

AURKA and c-Myc Co-regulate Each Other

Nuclear AURKA exerts kinase-independent functions by acting as a transcription factor



- AURKA and c-Myc transcriptionally upregulate each other, suggesting the existence of a positive feedback loop
- c-Myc upregulates Cyclin D2, CDK4, and cyclin-E, contributing to complex formation and subsequent phosphorylation of p27Kip1, which leads to cell proliferation

Naso FD Oncogene 2021, Tang A Oncotarget 2017

Clinical Development in Small-Cell Lung Cancer

Phase 2 Study of Alisertib Monotherapy in Solid Tumors

- SCLC Cohorts

Study design:

- Pts had to have undergone ≤ 2 previous cytotoxic regimens, not including adjuvant or neoadjuvant treatments
- Alisertib administration: orally in 21-day cycles at 50 mg twice daily for 7 days followed by a break of 14 days
- 1° Endpoint: Objective Response Rate (RECIST 1.1)

	All (n=48)	Chemotherapy-sensitive relapse (n=36)	Refractory or chemotherapy-resistant relapse (n=12)
Median (range) number of cycles	2·0* (1–17)	3·5 (1–17)	2·0 (2–6)
Best response			
Objective response†	10 (21%) (10–35)	7 (19%)	3 (25%)
Stable disease	16 (33%) (20–48)	13 (36%)	3 (25%)
Stable disease for ≥6 months	2 (4%)	2 (6%)	0
Progressive disease	22 (46%) (31–61)	16 (44%)	6 (50%)
Duration of response (months)	4·1 (3·1–NE)	3·1	4·3
Progression-free survival (months)	2·1 (1·4–3·4)	2·6 (1·4–3·7)	1·7 (1·2–3·9)
Time to progression (months)	2·6 (1·4–3·8)	2·8 (1·4–3·9)	1·4 (1·2–4·4)

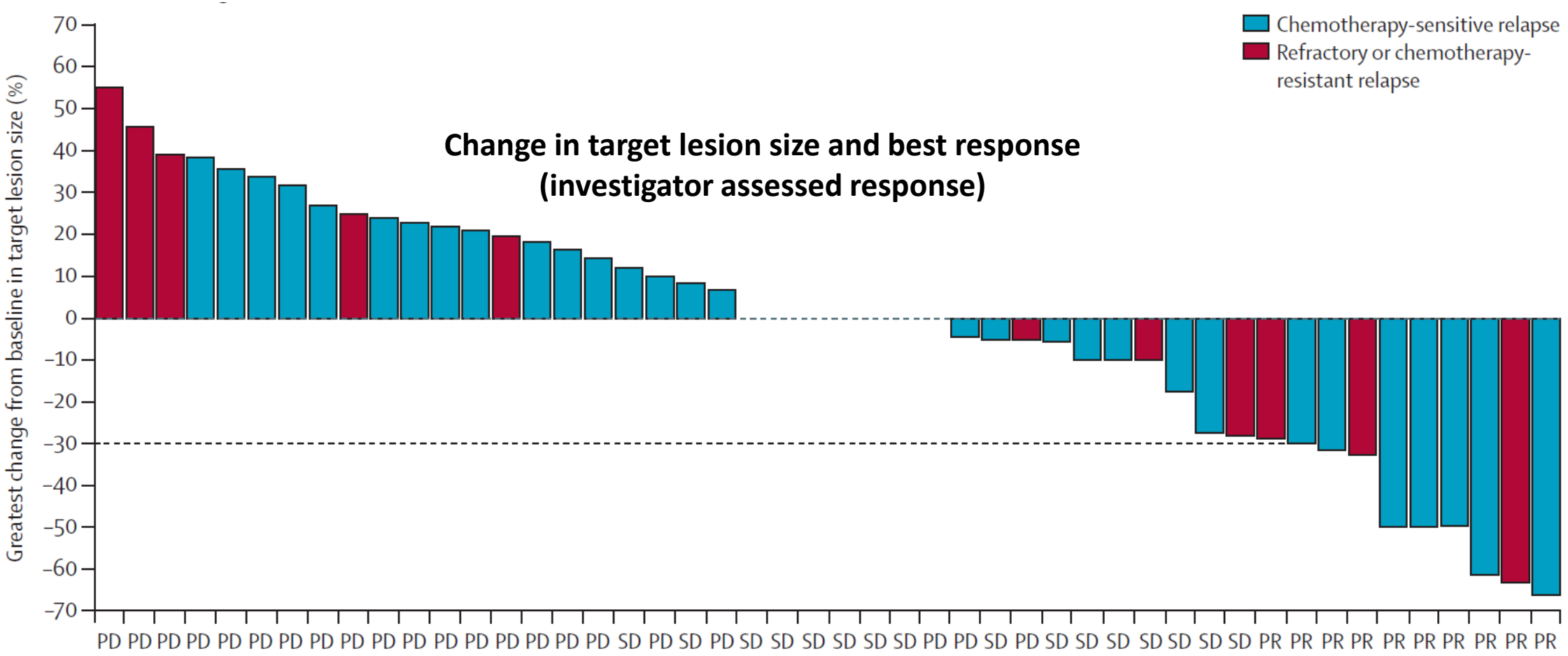
Table adapted from Melichar B Lancet Oncol 2015. Data are either number of patients (%) (95% CI), or median (95% CI), unless otherwise stated. NE=not estimable. *Safety population. †All were partial responses. All responses were based on investigator tumor assessments (RECIST v1.1).

Melichar B Lancet Oncol 2015

Phase 2 Study of Alisertib Monotherapy in Solid Tumors

- SCLC Cohorts

10 (21%; 95% CI 10–35) of 48 patients had an objective response; all responders achieved a partial response



PD=progressive disease. SD=stable disease. PR=partial response. Dotted line at –30% represents a partial response, according to RECIST 1.1 (investigator tumor assessments).

Melichar B Lancet Oncol 2015

Phase 2 Study of Alisertib Monotherapy in Solid Tumors

- SCLC Cohorts

All-cause adverse events in safety evaluable SCLC cohort (n=60)

	Grade 1–2	Grade 3–4
Any adverse event	14 (23%)	43 (72%)
Neutropenia	5 (8%)	22 (37%)
Fatigue	23 (38%)	5 (8%)
Anaemia	9 (15%)	10 (17%)
Alopecia	16 (27%)	NA
Diarrhoea	16 (27%)	2 (3%)
Nausea	18 (30%)	0
Leukopenia	4 (7%)	8 (13%)
Stomatitis	9 (15%)	4 (7%)
Decreased appetite	18 (30%)	0
Vomiting	10 (17%)	1 (2%)
Thrombocytopenia	5 (8%)	6 (10%)
Somnolence	8 (13%)	1 (2%)
Dyspnoea	10 (17%)	0
Constipation	5 (8%)	0
Pyrexia	4 (7%)	0
Peripheral oedema	4 (7%)	0
Headache	8 (13%)	1 (2%)
Insomnia	7 (12%)	0
Cough	5 (8%)	0
Asthenia	6 (10%)	1 (2%)
Dehydration	3 (5%)	3 (5%)

Table adapted from Melichar B Lancet Oncol 2015. Data are number of patients with AE (%) for AEs of any grade in at least 10% of patients overall. NA = not applicable

Melichar B Lancet Oncol 2015

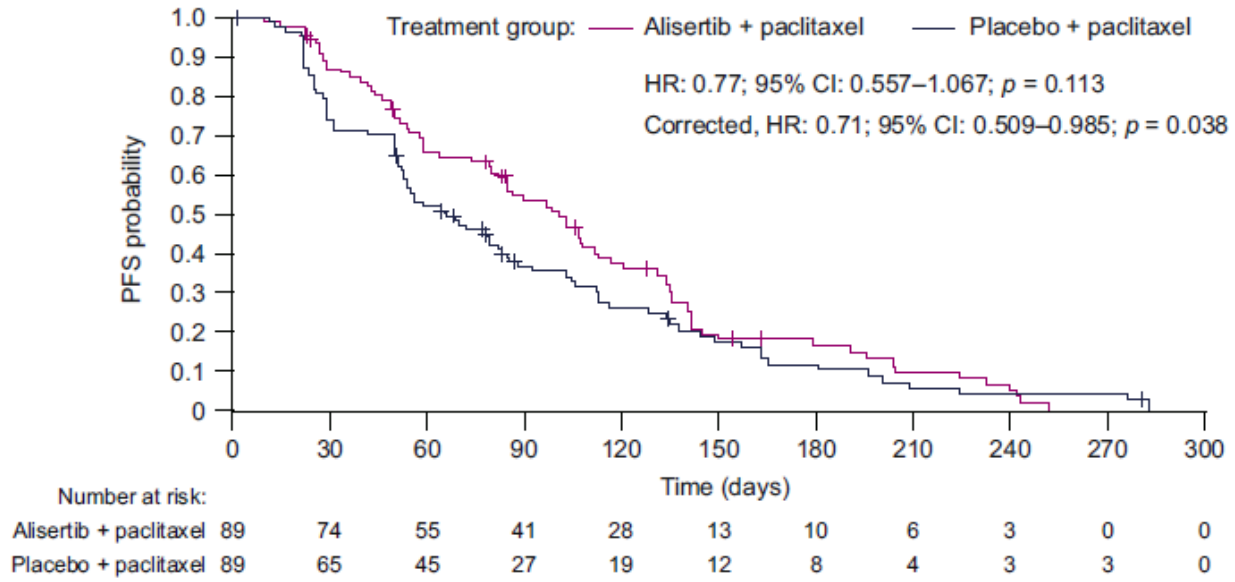
Randomized Phase 2 Study of Paclitaxel plus Alisertib vs Paclitaxel plus Placebo as Second-Line SCLC: Primary Analysis

Study design:

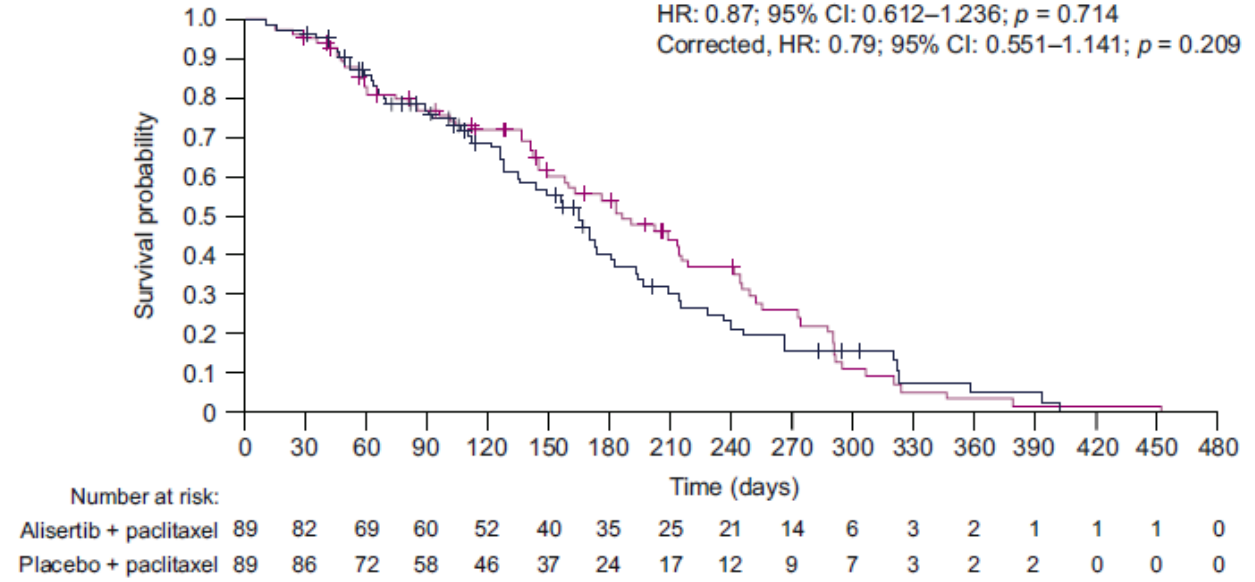
- Patients with relapsed or refractory SCLC stratified by relapse type (sensitive vs resistant or refractory)
- Randomized 1:1 to alisertib + paclitaxel or placebo + paclitaxel in 28-day cycles
- Alisertib (40 mg BID for 3 weeks on days 1–3, 8–10, and 15–17) plus paclitaxel (60 mg/m2 intravenously on days 1, 8, and 15) or placebo plus paclitaxel (80 mg/m2 intravenously on days 1, 8, and 15) in 28-day cycles
- 1° endpoint PFS

Biomarkers: associations between c-Myc expression in tumor tissue (prespecified) and genetic alterations in ctDNA (retrospective) with clinical outcome

PFS in ITT



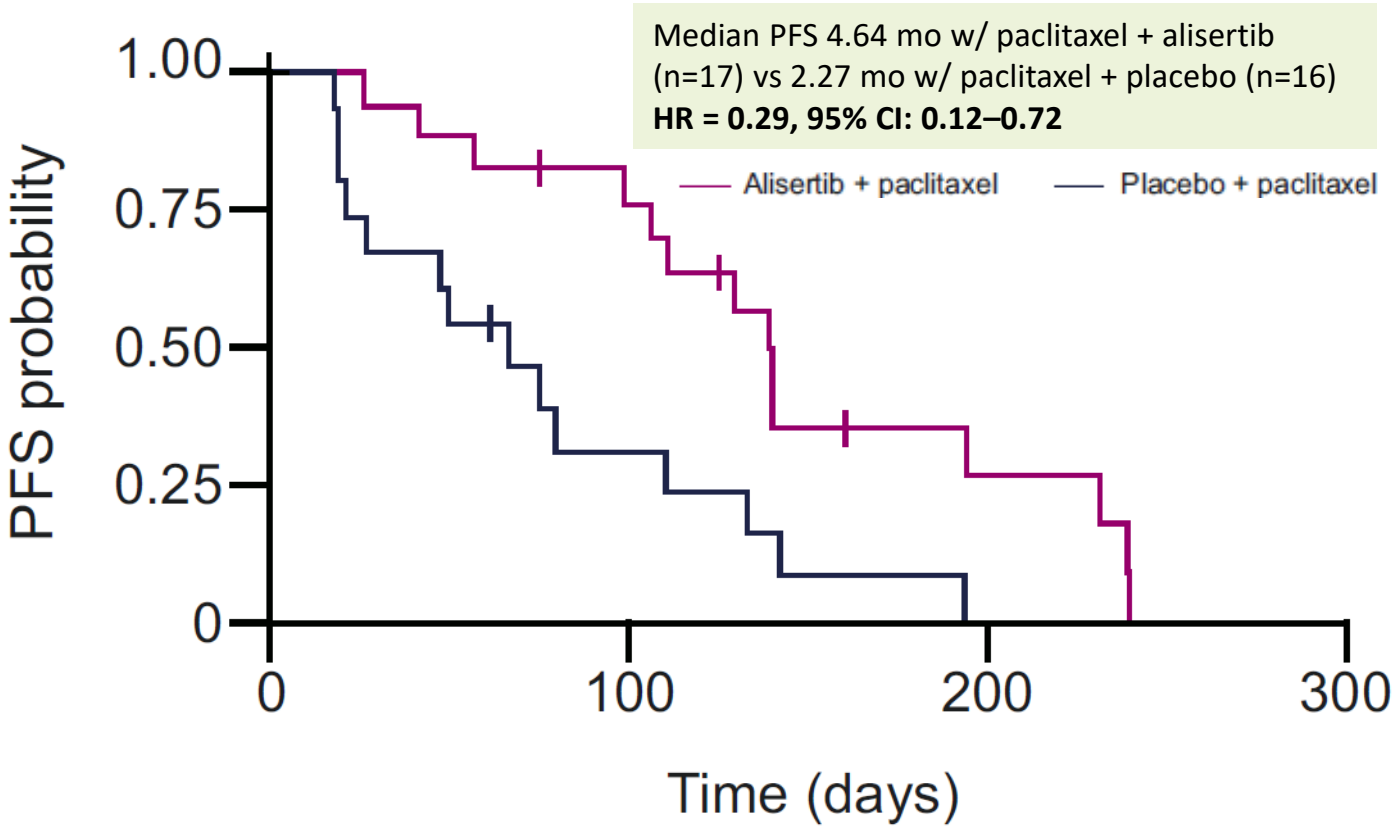
OS in ITT



Randomized Phase 2 Study of Paclitaxel plus Alisertib vs Paclitaxel plus Placebo as Second-Line SCLC: Correlative Biomarker Analysis

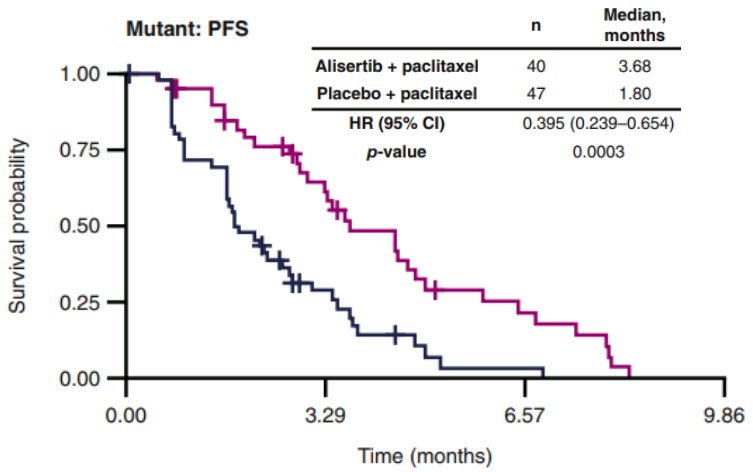
Improved PFS observed among patients positive versus negative for *c-Myc* expression

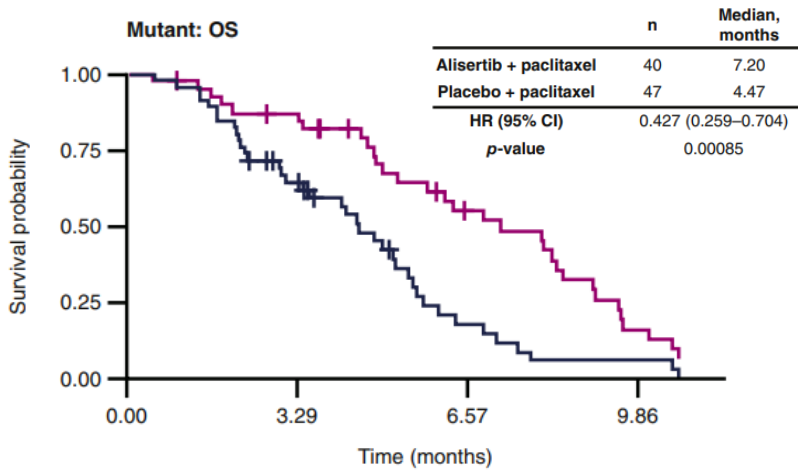
PFS in patients positive for *c-Myc* expression

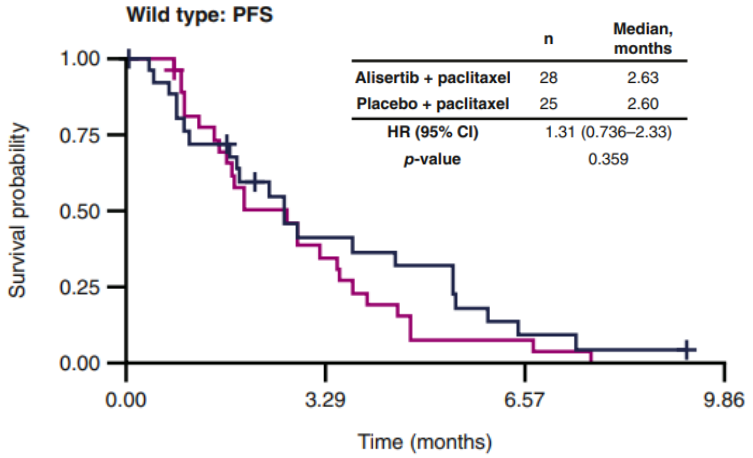


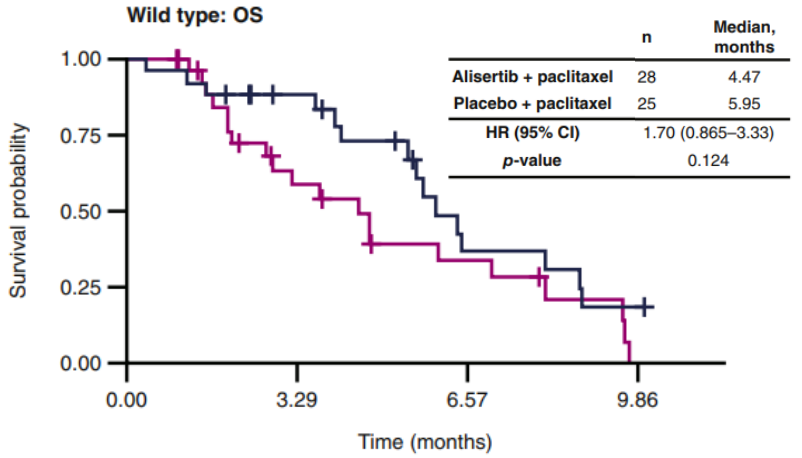
Randomized Phase 2 Study of Paclitaxel plus Alisertib vs Paclitaxel plus Placebo as Second-Line SCLC: Correlative Biomarker Analysis

Improved outcomes among pts with genetic alternations in cell cycle genes *CDK6*, *RBL1*, *RBL2*, and *RB1* (collectively referred to as "mutant")









Randomized Phase 2 Study of Paclitaxel plus Alisertib vs Paclitaxel plus Placebo as Second-Line SCLC: Safety

Table 3. Most Frequently Reported All-Cause and Drug-Related Treatment-Emergent AEs, Occurring in at Least 15% (All-Cause) or at Least 10% (Drug-Related) of Patients Overall (Any Grade) in Either Arm, Respectively, with the Corresponding Grade 3 or higher AEs (Safety Population), and All Drug-Related Fatal AEs

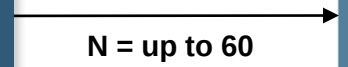
	Alisertib/Paclitaxel (n = 87)		Placebo/Paclitaxel (n = 89)	
AE	Any Grade	Grade ≥3	Any Grade	Grade ≥3
All-cause AE, n (%)	86 (99)	66 (76)	85 (96)	45 (51)
Diarrhea	51 (59)	14 (16)	18 (20)	1 (1)
Fatigue	38 (44)	9 (10)	29 (33)	5 (6)
Nausea	29 (33)	2 (2)	30 (34)	4 (4)
Anemia	38 (44)	12 (14)	18 (20)	3 (3)
Neutropenia	43 (49)	35 (40)	7 (8)	5 (6)
Vomiting	28 (32)	2 (2)	21 (24)	3 (3)
Decreased appetite	29 (33)	3 (3)	19 (21)	3 (3)
Dyspnea	21 (24)	4 (5)	19 (21)	2 (2)
Stomatitis	29 (33)	12 (14)	6 (7)	2 (2)
Cough	17 (20)	0	17 (19)	0
Constipation	8 (9)	1 (1)	21 (24)	0
Asthenia	14 (16)	3 (3)	11 (12)	0
Dizziness	14 (16)	0	8 (9)	0
Alopecia	14 (16)	0	5 (6)	0
Leukopenia	13 (15)	7 (8)	5 (6)	2 (2)
Decreased neutrophil count	14 (16)	11 (13)	4 (4)	1 (1)
Weight decreased	13 (15)	0	5 (6)	0
Drug-related fatal AE, n (%)				
Neutropenic sepsis	–	1 (1)	–	0
Sepsis	–	1 (1)	–	0
Febrile neutropenia	–	1 (1)	–	0
Septic shock	–	1 (1)	–	0

AE, adverse event

PUMA-ALI-4201 Phase II study design

Key inclusion criteria

- Pathologically confirmed ES-SCLC
- Progression on or after first-line platinum-based chemo; must have prior immunotherapy
- Measurable disease per RECIST v1.1
- Must provide tissue biopsy, archival tissue acceptable; if unavailable, fresh tissue biopsy required
- Treated, stable brain mets allowed
- ECOG PS 0-1



Alisertib
50 mg po BID on days 1-7 of every 21-day cycle

PUMA-ALI-4201 Phase II trial was initiated in Q1 2024

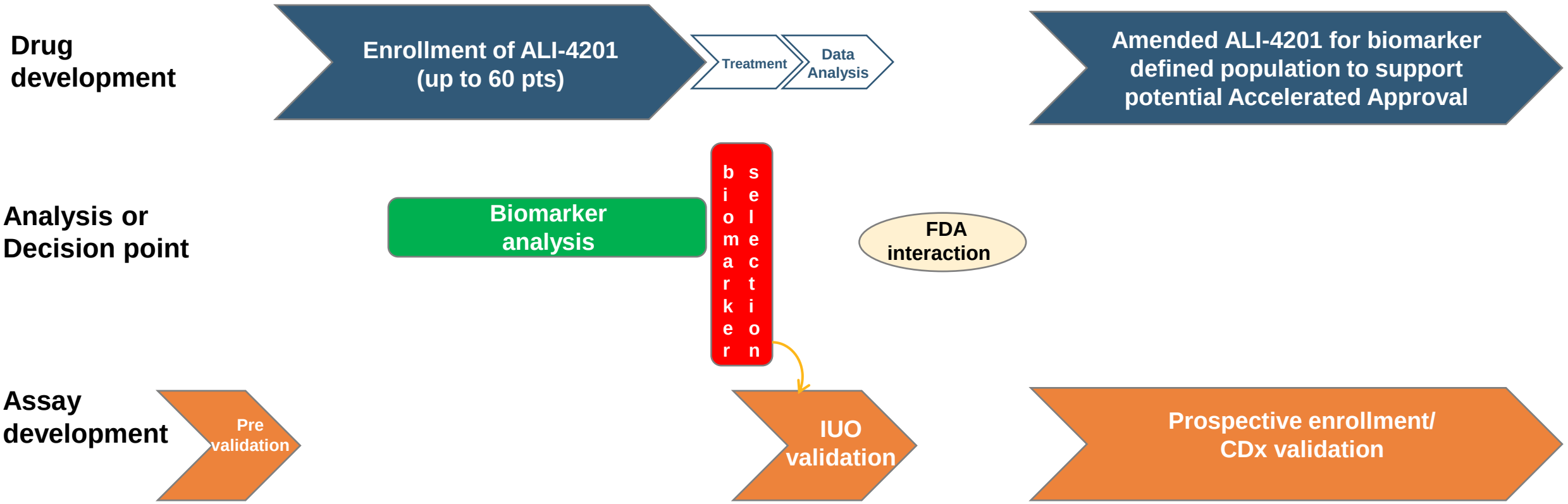
Additional interim data in 2025

Efficacy and safety objectives and endpoints

Objective
Primary Endpoint
• Proportion of patients with confirmed complete responses (CR) or partial responses (PR) as defined by Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1)
Secondary Endpoints
• Duration of response (DOR) • Disease control rate (DCR) • Progression free survival (PFS)
• Overall survival (OS)
• Adverse events (AEs) and serious adverse events (SAEs) per National Cancer Institute Common Terminology Criteria for Adverse Events Version 5.0 (NCI CTCAE v.5.0)
• Plasma alisertib concentrations on Cycle 1 Day 1 and Day 8
Exploratory Endpoints
• ORR, DOR, DCR, PFS, and OS within selected biomarker subgroups from formalin-fixed paraffin-embedded (FFPE) tissue and/or from plasma (circulating tumor DNA [ctDNA])

Parallel Clinical and Biomarker Development

- Comprehensive biomarker strategy supports clinical development and commercialization



Clinical Development of Alisertib in Breast Cancer

Phase 2 Study of Alisertib Monotherapy in Solid Tumors

- Breast Cancer Cohorts

Study design:

- Pts had to have undergone ≤ 2 previous cytotoxic regimens, not including adjuvant or neoadjuvant treatments
- Alisertib administered orally in 21-day cycles at 50 mg twice daily for 7 days followed by a break of 14 days
- 1° Endpoint: Objective Response Rate (RECIST 1.1)

	All (n=49)	Hormone receptor-positive and HER2-negative (n=26)	HER2-positive (n=9)	Triple negative (n=14)
Median (range) number of cycles	4·0* (1–23)	8·0 (1–23)	6·0 (1–19)	2·0 (1–14)
Best response				
Objective response†	9 (18%) (9–32)	6 (23%)	2‡ (22%)	1 (7%)
Stable disease	25 (51%) (36–66)	17 (65%)	3 (33%)	5 (36%)
Stable disease for ≥6 months	10 (20%)	8 (31%)	1 (11%)	1 (7%)
Progressive disease	15 (31%) (18–45)	3 (12%)	4 (44%)	8 (57%)
Duration of response (months)	5·6 (2·8–12·0)	4·2	11·2	4·2
Progression-free survival (months)	5·4 (2·6–7·9)	7·9 (4·2–12·2)	4·1 (0·95–15·0)	1·5 (1·2–3·2)
Time to progression (months)	5·4 (2·6–7·9)	7·9 (4·2–12·2)	4·1 (0·95–15·0)	1·5 (1·2–3·2)

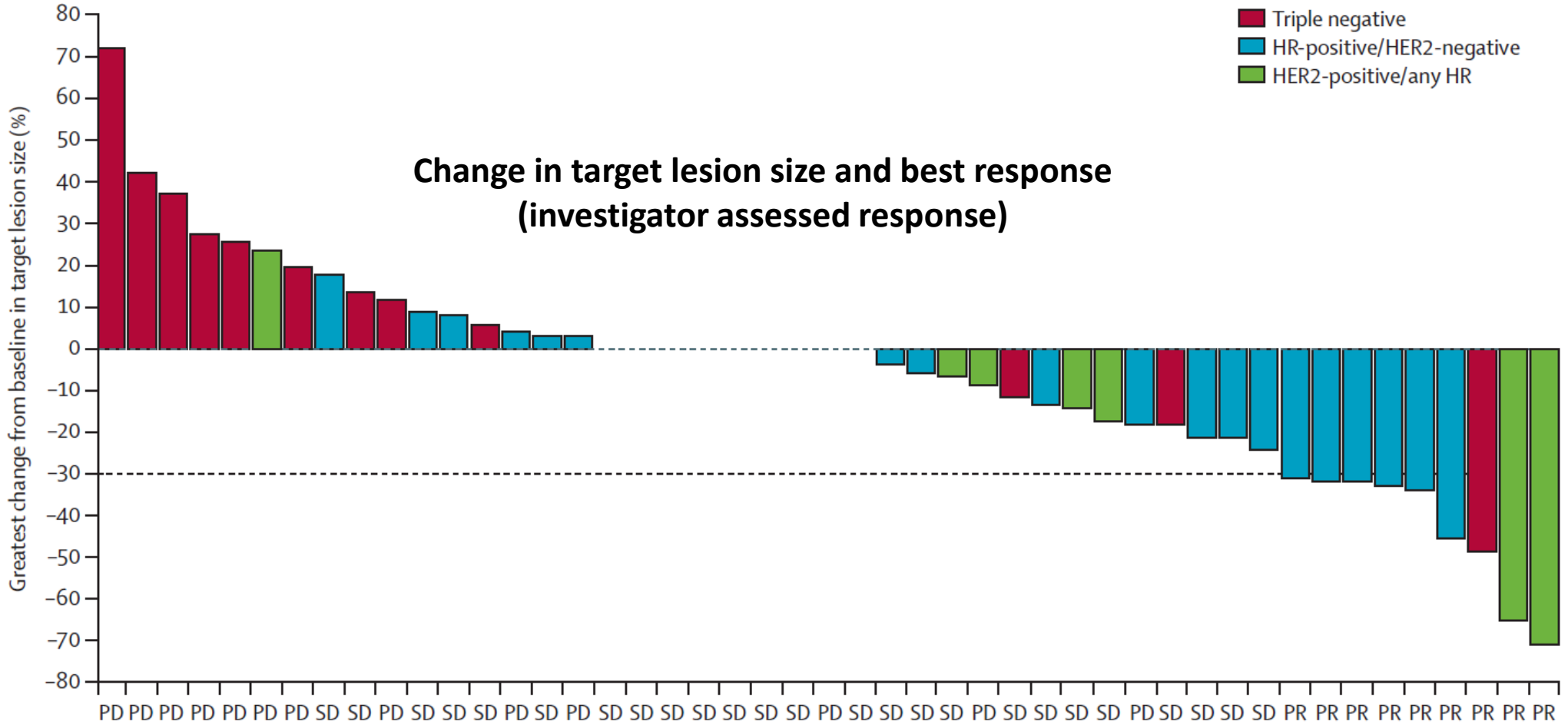
Data are either number of patients (%) (95% CI), or median (95% CI), unless otherwise stated. For the breast cancer subgroup, numbers of patients were too small to calculate 95% CIs. *Safety population. †All were partial responses. . ‡ These two patients had the only hormone receptor-negative tumors in the cohort. All responses were based on investigator tumor assessments (RECIST v1.1).

Melichar B Lancet Oncol 2015

Phase 2 Study of Alisertib Monotherapy in Solid Tumors

- Breast Cancer Cohorts

9 / 49 patients (18%; 95% CI 9–32) had an objective response; all responders achieved a partial response



PD=progressive disease. SD=stable disease. PR=partial response. Dotted line at –30% represents a partial response, according to RECIST 1.1 (investigator tumor assessments).

Melichar B Lancet Oncol 2015

Phase 2 Study of Alisertib Monotherapy in Solid Tumors

- Breast Cancer Cohorts

All-cause adverse events in safety evaluable breast cancer cohort (n=53)

	Grade 1-2	Grade 3-4
Any adverse event	8 (15%)	44 (83%)
Neutropenia	3 (6%)	30 (57%)
Fatigue	23 (43%)	6 (11%)
Anaemia	17 (32%)	4 (8%)
Alopecia	26 (49%)	NA
Diarrhoea	25 (47%)	2 (4%)
Nausea	15 (28%)	2 (4%)
Leukopenia	5 (9%)	19 (36%)
Stomatitis	16 (30%)	8 (15%)
Decreased appetite	13 (25%)	0
Vomiting	11 (21%)	1 (2%)
Thrombocytopenia	8 (15%)	4 (8%)
Somnolence	14 (26%)	1 (2%)
Dyspnoea	9 (17%)	3 (6%)
Constipation	9 (17%)	0
Pyrexia	4 (8%)	1 (2%)
Peripheral oedema	9 (17%)	0
Headache	11 (21%)	0
Insomnia	6 (11%)	0
Cough	8 (15%)	1 (2%)
Asthenia	2 (4%)	3 (6%)
Dehydration	5 (9%)	3 (6%)

Table adapted from Melichar B Lancet Oncol 2015. Data are number of patients with AE (%) for AEs of any grade in at least 10% of patients overall. NA = not applicable

Melichar B Lancet Oncol 2015

Phase 2 Randomized Trial of Alisertib + Fulvestrant vs Alisertib in Advanced HR+ Breast Cancer

Patients (n=96)

Inclusion Criteria

- Post-menopausal women
- Histologically-proven ER+ (>10% expression) and HER2 negative
- No more than two prior chemotherapy regimens
- Prior treatment with fulvestrant in the metastatic setting required
- Disease that is measurable as defined by the RECIST criteria

Regimen & Schedule

- **Alisertib + Fulvestrant**: Alisertib 50 mg PO BID on days 1-3, 8-10, 15-17 q 28-day cycle with fulvestrant 500 mg IM on days 1 and 15 of cycle 1 then day 1 of all subsequent cycles
- **Alisertib Alone**: Alisertib 50 mg PO BID on days 1-3, 8-10, 15-17 q 28-day cycle

Patient Characteristics

	Alisertib (n=45)	Alisertib + Fulvestrant (n=45)
Prior Chemotherapy		
(Neo)Adjuvant Setting	27 (60.0%)	27 (60.0%)
Metastatic Setting	21 (46.7%)	31 (69.9%)
Prior Adjuvant Endocrine Therapy		
Aromatase Inhibitor	24 (53.3%)	20 (44.4%)
Tamoxifen	14 (31.1%)	22 (48.8%)
Fulvestrant	7 (15.5%)	2 (4.4%)
Prior Endocrine Therapy for MBC		
Anastrozole/Letrozole	26 (57.8%)	35 (77.8%)
Exemestane	15 (33.3%)	26 (57.8%)
Fulvestrant	44 (97.8%)	45 (100.0%)
Prior Targeted Therapy for MBC		
CDK 4/6 inhibitor	45 (100%)	45 (100%)
Everolimus	16 (35.6%)	26 (57.8%)

Clinical Outcomes

	Alisertib (n=45)	Alisertib + Fulvestrant (n=45)
Confirmed Responses	8 PR	1 CR; 8 PR
Objective Response Rate	17.8% (90% CI: 9.2-29.8%)	20.0% (90% CI: 10.9-32.3%)
Clinical Benefit Rate (24-week)	42.2% (90% CI: 29.7-55.6%)	28.9% (90% CI: 18.0-42.0%)
Median PFS (months)	5.6 (95%CI: 3.9 – 9.3)	5.1 (95%CI: 3.8 – 7.6)
Deaths 6-month OS rate	n=10 90. 6% (95% CI: 82.2-99.8%)	n=14 75.6% (95% CI: 63.9-90.2%)

Phase 2 Randomized Trial of Alisertib + Fulvestrant vs Alisertib in Advanced HR+ Breast Cancer

Safety

	Alisertib (n=45)		Alisertib + Fulvestrant (n=45)	
	G3	G4	G3	G4
Hematologic Adverse Events				
Anemia	13%	2%	9%	0%
Lymphocyte Count Decreased	2%	0%	13%	0%
Neutropenia Count Decreased	24%	18%	20%	22%
White Blood Cell Count Decreased	13%	4%	22%	9%
Non-Hematologic Adverse Events				
Fatigue	0%	0%	11%	0%

Reason for Treatment Discontinuation	Alisertib* (n=45)	Alisertib + Fulvestrant (n=45)
Disease progression	28	28
Intolerability	2	6
Patient Refusal	0	4
Physician Decision	1	0
Second Primary	0	1
Death	2	1

*Discontinuation of monotherapy

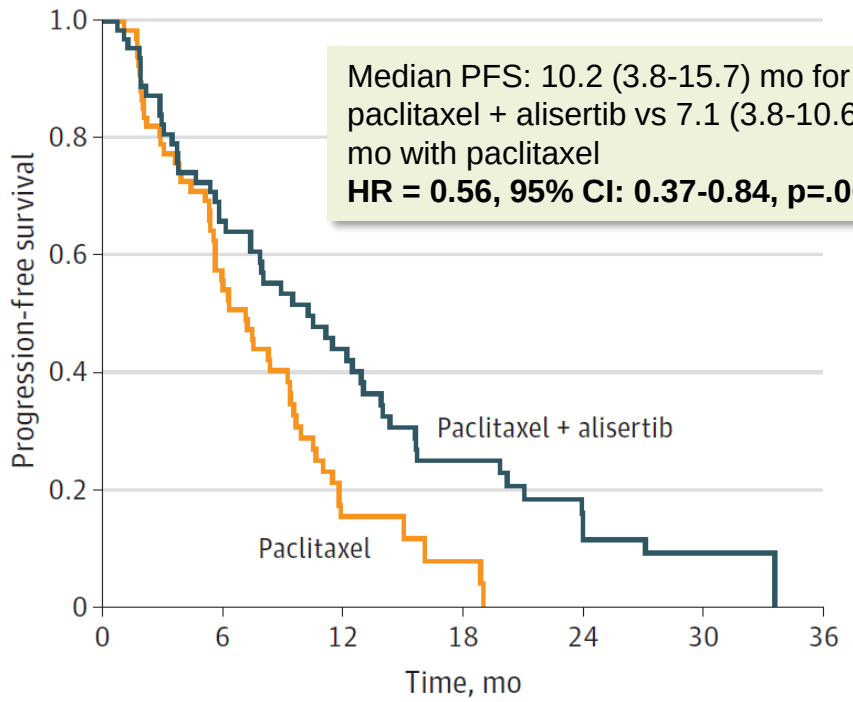
Phase 2 Randomized Study of Paclitaxel + Alisertib vs Paclitaxel Alone

- Efficacy in ER+/HER2- MBC Cohort

Study design:

- Patients with ER+/HER2- or triple negative metastatic breast cancer stratified by prior neo or adjuvant taxane and by line of metastatic therapy
- Randomized 1:1 to paclitaxel + alisertib or paclitaxel alone in 28-day cycles
- Paclitaxel 60mg/m2 intravenously (IV) on days 1, 8, and 15 plus alisertib 40 mg twice daily on days 1 to 3, 8 to 10, and 15 to 17 of a 28-day cycle or to single agent paclitaxel 90mg/m2 IV on days 1, 8, and 15 of a 28-day cycle
- 1° endpoint PFS

PFS in ER+/HER2- ITT



Median OS: 26.3 (12.4-37.2) mo for paclitaxel + alisertib vs 25.1 (11.0-31.4) mo for paclitaxel (HR, 0.89; 95%CI, 0.58-1.38; *P* = .61)

O'Shaughnessy J JAMA Netw Open 2021

Phase 2 Randomized Study of Paclitaxel + Alisertib vs Paclitaxel Alone

- Efficacy in ER+/HER2- MBC Cohort Pretreated with Palbociclib

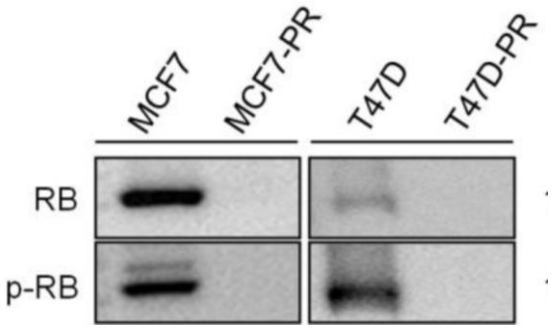
Efficacy in patients pretreated with palbociclib (n=30)

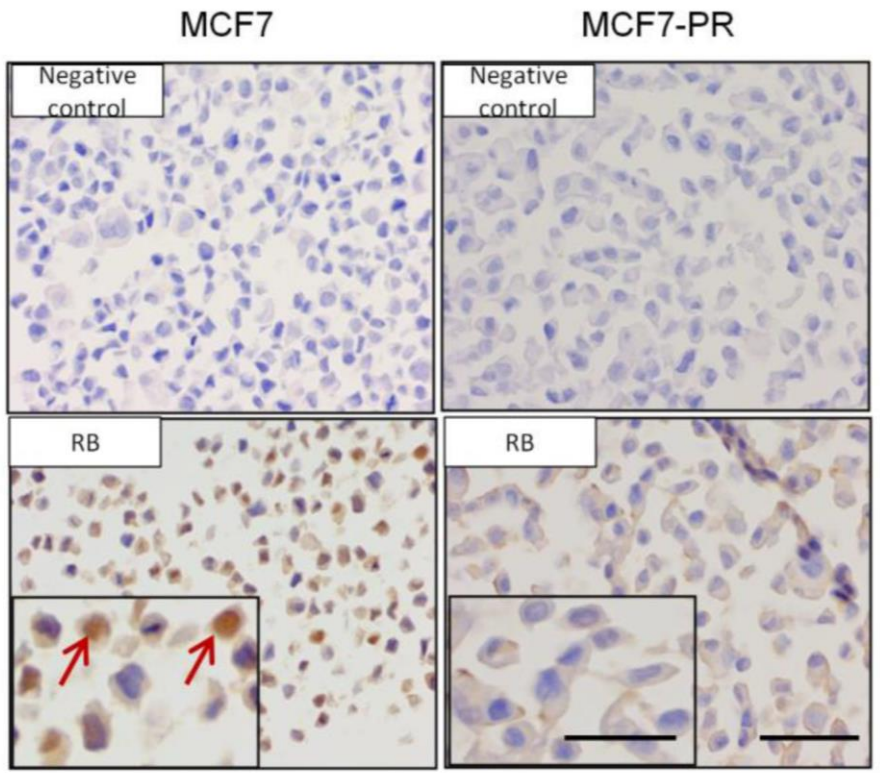
- Median PFS: 13.9 (5.6-15.6) mo (14 pts) w/ paclitaxel + alisertib vs 5.6 (3.0-10.6) mo (16 pts) w/ paclitaxel alone (HR, 0.58; 95%CI, 0.26-1.32; *P* = .19)
- CBR: 61.5% w/ paclitaxel + alisertib (95%CI,31.6%-86.1%) vs 37.5% (95%CI, 15.2%-64.6%) w/ paclitaxel alone

Rb1 Loss and *c-Myc* Upregulation Correlate with Palbociclib Resistance

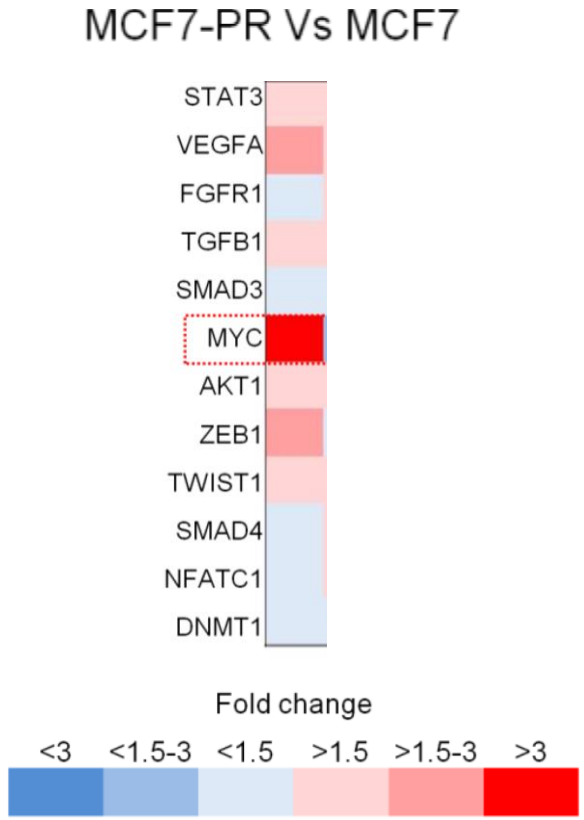
Both RB1 loss and MYC upregulation were observed in palbociclib-resistant HR+ breast cancer cell lines, supporting a role for alisertib in this setting

RB1 Loss





C-Myc Upregulation



Study-related Neutropenia in Metastatic Breast Cancer - Alisertib compared to other agents

Regimen	All-grade Neutropenia (%)	Grade 3/4 Neutropenia (%)	Febrile Neutropenia (%)
Alisertib monotherapy 50 mg BID[1]	63%[1]	57%[1]	4%[1]
Alisertib monotherapy 50 mg BID[2]	Not reported[2]	42%[2]	Not reported[2]
Alisertib 50 mg BID + fulvestrant[2]	Not reported	42%	Not reported
Alisertib 40 mg BID + paclitaxel[3]	67.9%	59.5%	1.2%
Eribulin mesylate (HALAVEN)[4]	82%	57%	5%
Physician's Choice of Chemotherapy[5]	51.2%	40.7%	Not reported
Palbociclib (IBRANCE)[6] + fulvestrant (PALOMA-3) or letrazole (PALOMA-2)	P+F: 83% P+L: 80%	P+F: 66% P+L: 66%	P+F: 0.9% P+L: 2.5%
Sacituzumab govitecan (TRODELVY)[7] for ER+	70%	51% (G ≥3 neutropenia)	5%
Sacituzumab govitecan (TRODELVY)[8] for TNBC	64%	52%	6%

1. alisertib: 21-day cycle, 7 days followed by 14-day break, 2. alisertib: 28-day cycle, on days 1-3, 8-10, 15-17, 3. paclitaxel: 28-day cycle on days 1, 8, and 15

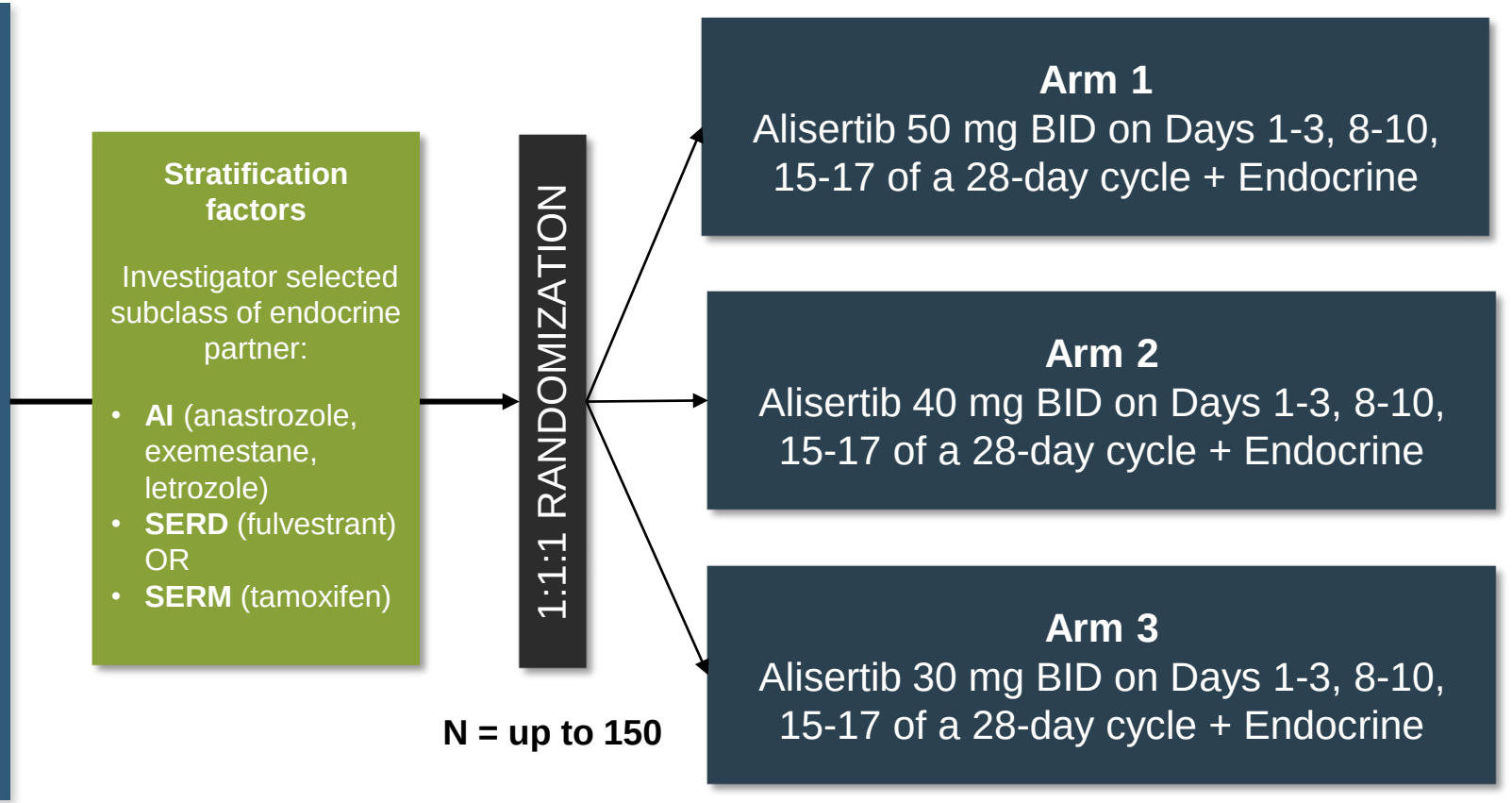
Alisertib-associated neutropenia is thought to be cumulative and possibly can be managed/reduced with G-CSFs for prophylaxis of neutropenia per NCCN Guidelines[9]

[1]Melichar B Lancet Oncol 2015, [2]Haddad SABCS 2020 PD2-05, [3]O'Shaughnessy J JAMA Netw Open 2021, [4]HALAVEN USPI, [5]Modi S N Engl J Med 2022, [6]IBRANCE USPI, [7]Rugo HS ASCO 2022, [8]TRODELVY USPI, [9]NCCN Guideline Hematopoietic Growth Factors Version 1.2022

ALISCA™-Breast1
Phase 2 dose optimization, biomarker evaluation in HR+/HER- MBC

Key inclusion criteria:

- HR+/HER2- mBC patients who have received at least 2 prior lines of endocrine therapy in the recurrent or metastatic setting
  - Must have received CDK4/6 inhibitors with endocrine therapy
  - Disease recurrence while receiving endocrine therapy in the adjuvant setting will count toward prior line of endocrine therapy
- RECIST v1.1 evaluable disease
- No prior chemotherapy



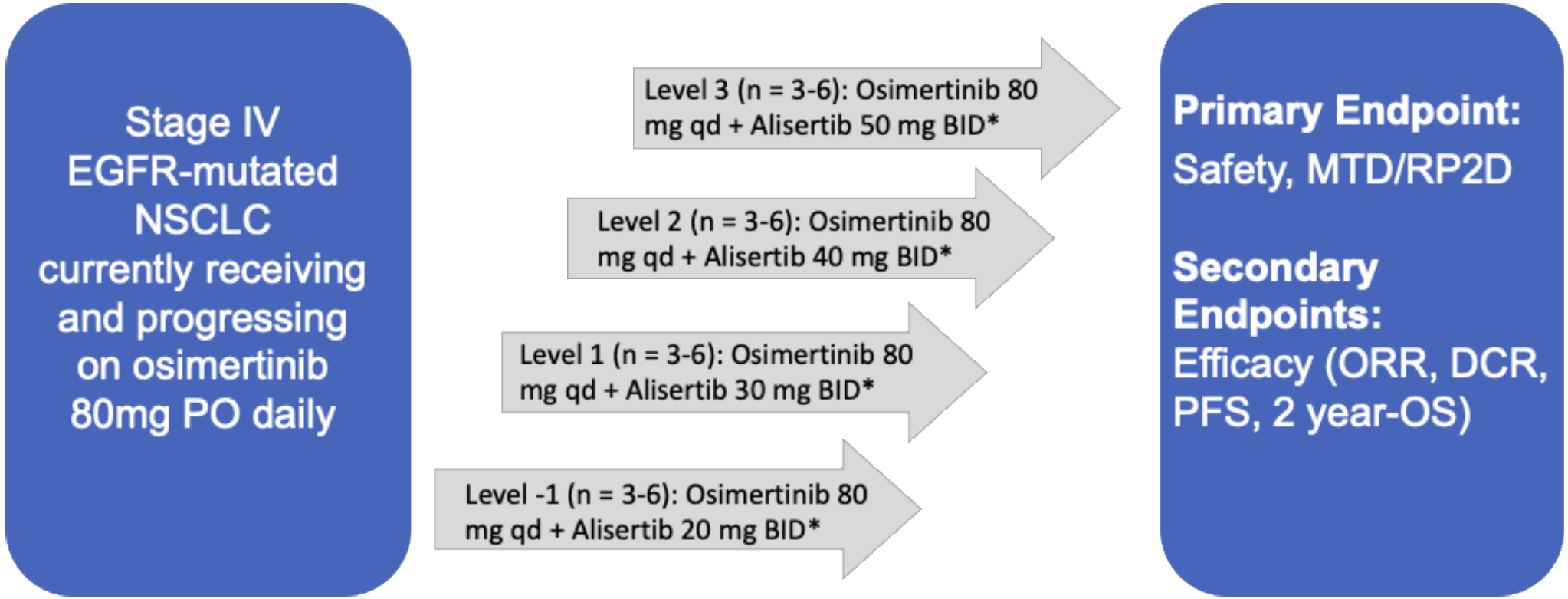
Primary objective: Dose optimization in combination based on safety and efficacy (ORR, DOR, DCR, PFS)

Secondary objective: PK/Dose response, biomarker selection based on efficacy

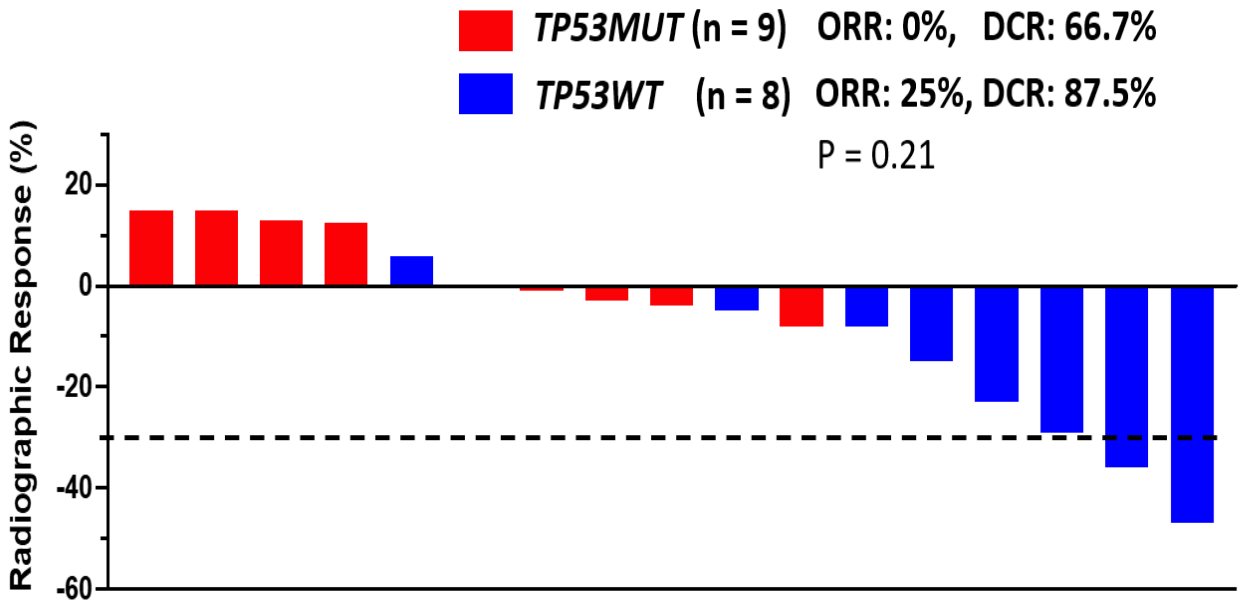
Phase II trial was initiated in Q4 2024

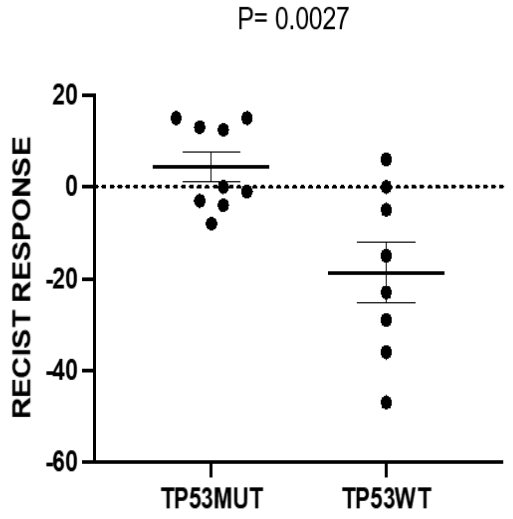
Clinical Development in Non-Small Cell Lung Cancer

A Phase I Investigator-Initiated Trial of Osimertinib + Alisertib in EGFR-Mutated NSCLC



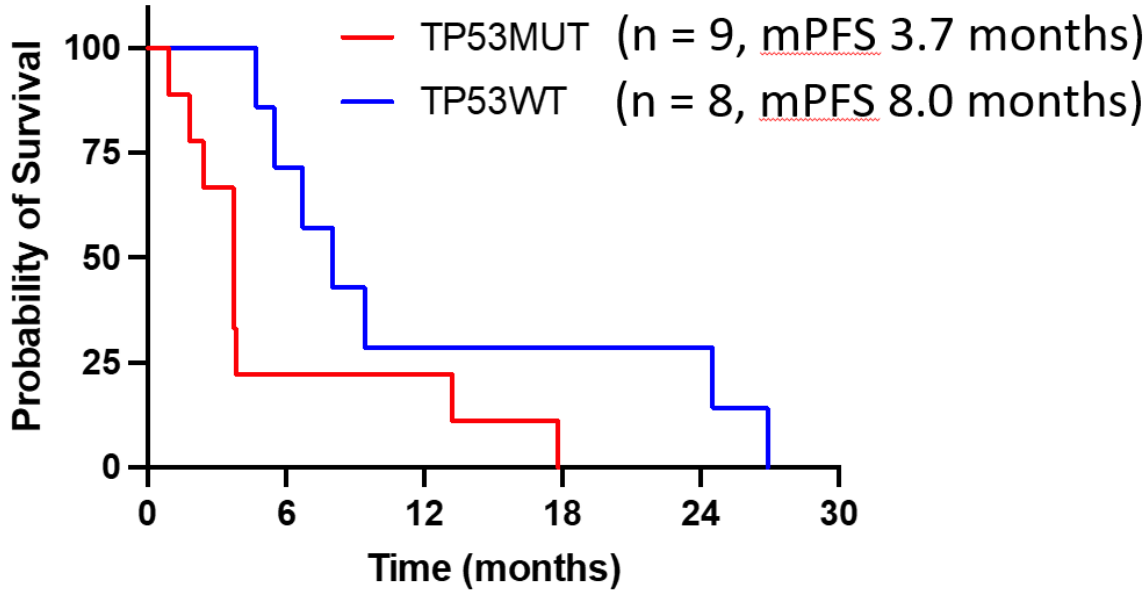
A Phase I Investigator-Initiated Trial of Osimertinib + Alisertib in EGFR-Mutated NSCLC





A Phase I Investigator-Initiated Trial of Osimertinib + Alisertib in EGFR-Mutated NSCLC

Progression free survival based on *TP53* status



HR: 0.42 (0.15 – 1.2) P = 0.05

ASCO Annual Meeting 2024

Intellectual Property for NERLYNX (neratinib)

- Composition of matter patent issued (expires 2030)
  - Extended by USPTO in November 2021 per Hatch/Waxman
- Use in the treatment of cancer issued (expires 2025)
- Two polymorph patents issued (both expire 2028)
- Combination with capecitabine (expires 2031)
- Use in extended adjuvant breast cancer (expires 2030)
- Composition of specific salt of neratinib (recently issued)

Intellectual Property for alisertib

- Composition of matter patent issued (expires 2029)
- Use in the treatment of proliferative disorders (expires 2032)
- Use in the treatment of small cell lung cancer (expires 2033)
- Use in the treatment of breast cancer (expires 2034)
- Additional patents being filed and prosecuted

Potential for up to 5-year Hatch/Waxman extension on expiration date of above listed patents

Intellectual Property on *EGFR* T790M Mutations

- Issued claims in Europe, Asia, Australia (expires 2026)
  - Possibility to extend up to 5 years
- Issued claims in United States (expires 2026)
- Patent claims upheld after European Opposition Hearing (February 2014)
  - Patent claims upheld after Appeal to European Opposition (December 2020)
- Claims for the pharmaceutical composition comprising an irreversible EGFR inhibitor for use in treating cancer having a T790M mutation and for use in the treatment of cancer including lung cancer and non-small cell lung cancer
- A jury trial found the patents to be valid and infringed by AstraZeneca and awarded Plaintiffs $107.5 million in damages for past acts of infringement (May 2024)
- Judge ruled patent invalid for lacking enablement and adequate written description as to a particular claim limitation (August 2024)
- Appeal was filed in September 2024

Puma – Expected Milestones

- ✓ Present biomarker studies from the randomized trial of alisertib plus fulvestrant versus alisertib alone in hormone receptor-positive, HER2-negative breast cancer (Q2 2024)
- ✓ Update data from the clinical trial of alisertib in combination with osimertinib in patients with metastatic EGFR-mutant non-small cell lung cancer who have developed osimertinib resistance (Q2 2024)
- ✓ Initiate ALISCA™-Breast1, a Phase II trial of alisertib in combination with endocrine treatment in patients with chemotherapy-naïve HER2-negative, hormone receptor-positive metastatic breast cancer (Q4 2024)
- Additional interim data from ALISCA™-Lung1, a Phase II clinical trial of alisertib monotherapy for the treatment of extensive-stage small cell lung cancer (2025)
- Report interim data from ALISCA™-Breast1, a Phase II trial of alisertib in combination with endocrine treatment in patients with chemotherapy-naïve HER2-negative, hormone receptor-positive metastatic breast cancer (2025)

Experienced Management Team

Alan H. Auerbach

Chairman, Chief Executive Officer, President, Founder

- *Chief Executive Officer, President, Founder, Cougar Biotechnology*

Jeff Ludwig

Chief Commercial Officer

- *Eli Lilly, Astellas, Amgen*

Maximo F. Nougues

Chief Financial Officer

- *Getinge AB, Boston Scientific, The Clorox Company*

Douglas Hunt

Chief Scientific Officer (interim)

Senior Vice President, Regulatory Affairs

- *ArmaGen, Baxter Healthcare, Amgen*

Board of Directors

Alan H. Auerbach
Chairman, Chief Executive Officer, President, Founder, Puma Biotechnology, Inc.

Alessandra Cesano, MD, PhD
Chief Medical Officer, ESSA Pharmaceuticals; NanoString; Cleave Biosciences; Nodality; Amgen; Biogen; SmithKline

Allison Dorval
CFO, Verve Therapeutics; Former CFO Voyager Therapeutics, Inc.; VP and Controller, Juniper Pharmaceuticals, Inc.

Michael Miller
Former EVP U.S. Commercial, Jazz Pharmaceuticals; VP, Sales & Marketing, Genentech

Jay Moyes
CFO, Sera Prognostics, Inc.; Former CFO, Myriad Genetics

Adrian Senderowicz, MD
Senior Advisor and former SVP and Chief Medical Officer, Constellation Pharmaceuticals; Ignyta; Sanofi; Astrazeneca; FDA (Division of Oncology Drug Products)

Brian Stuglich, R.Ph.
CEO, Verastem; Founder, Proventus Health Solutions; Former VP and Chief Marketing Officer, Eli Lilly Oncology

Troy Wilson, PhD, JD
President and CEO, Kura Oncology; CEO, Wellspring Biosciences; Chairman, Avidity Biosciences; Former CEO, President, Intellikine

Puma Biotechnology – Financial

- Currently trading on NASDAQ: PBYI
- Cash, cash equivalents and marketable securities at September 30, 2024: $97 million
- Net income in Q3 2024: $20.3 million
- Cash burn in Q2 2024: $0.1 million
- Private placements:
  - March 2022: 3,584,228 shares issued to Alan Auerbach and Athyrium Capital Management
  - December 2022: 568,181 shares issued to Alan Auerbach
- Shares issued and outstanding: 49.1 million

Company Highlights

- NERLYNX® – first HER2-directed drug approved by FDA for extended adjuvant treatment of early-stage HER2+ breast cancer in patients who have received prior trastuzumab
- NERLYNX® – first HER2-directed tyrosine kinase inhibitor approved in both early stage and metastatic HER2+ breast cancer
- Retain full U.S. commercial rights to NERLYNX®
- Clinical activity demonstrated for alisertib in Phase II clinical trials in HR-positive, HER2-negative breast cancer, Triple Negative Breast Cancer (TNBC), Small Cell Lung Cancer (SCLC)
- Potential for novel biomarker directed commercial opportunities with alisertib compared to other marketed drugs and drugs in development

Puma Biotechnology

December 2024