



# Puma Biotechnology

March 2024

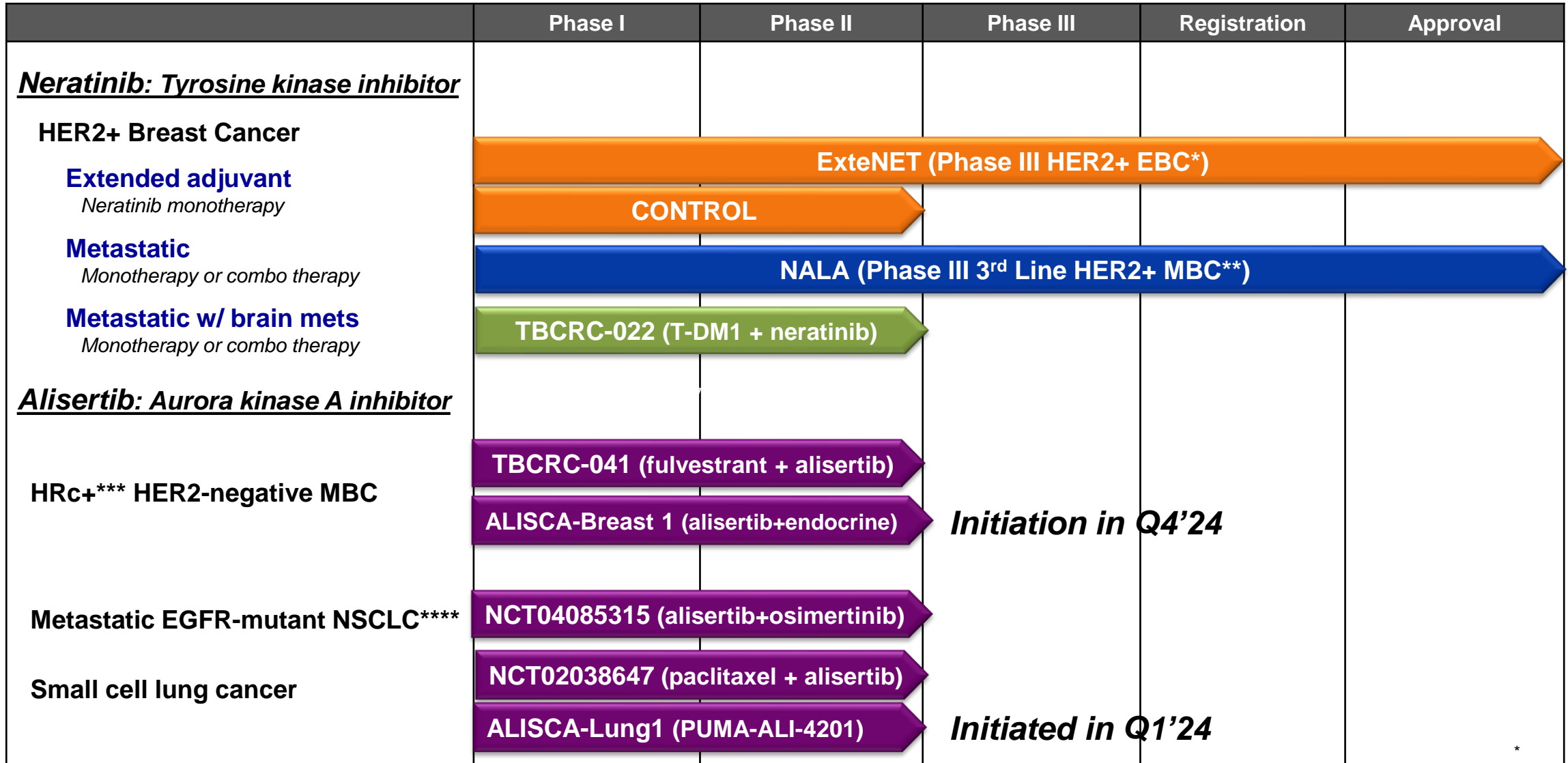


## Forward-Looking Safe-Harbor Statement

*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.*



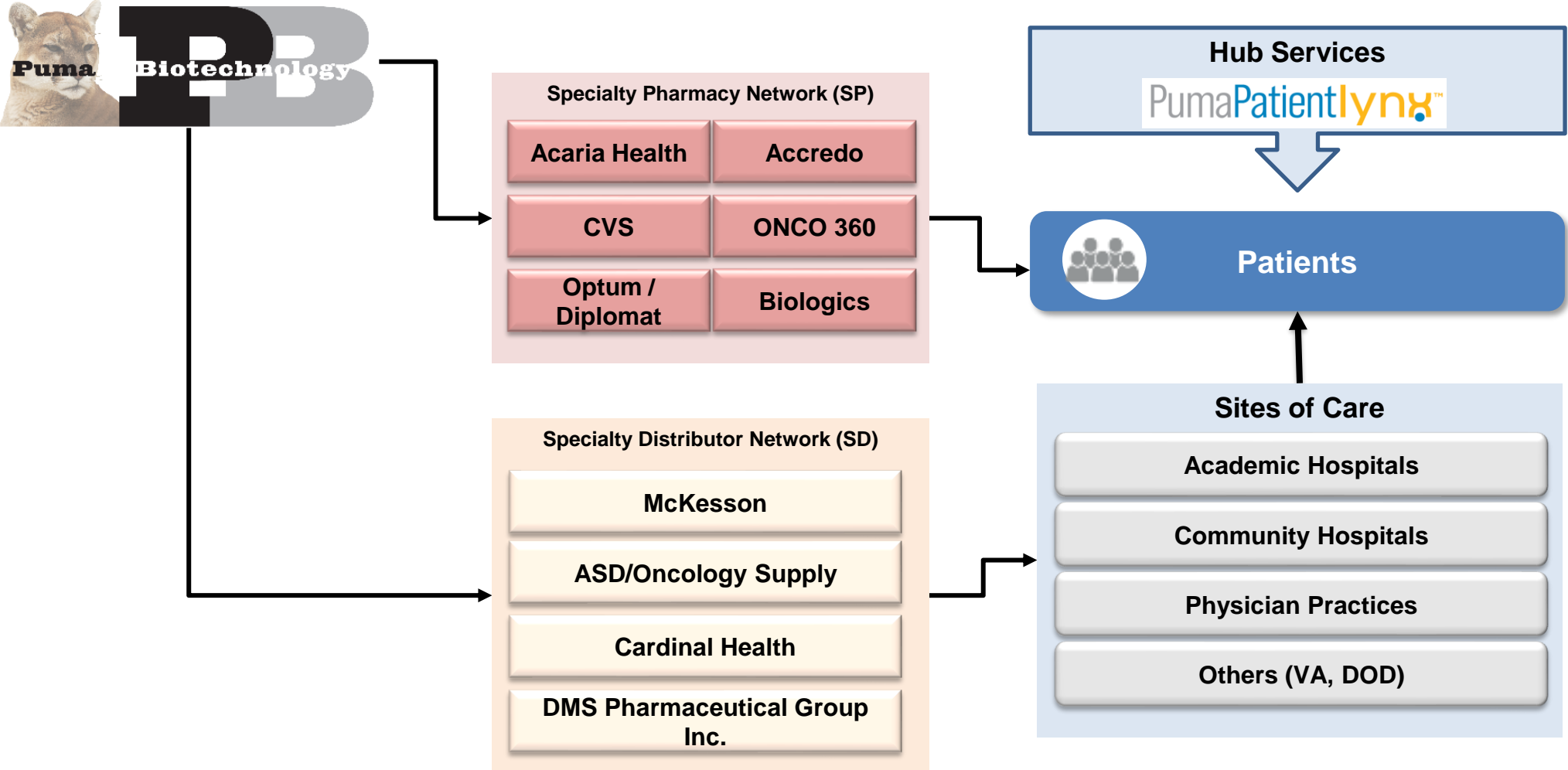
# Product Pipeline



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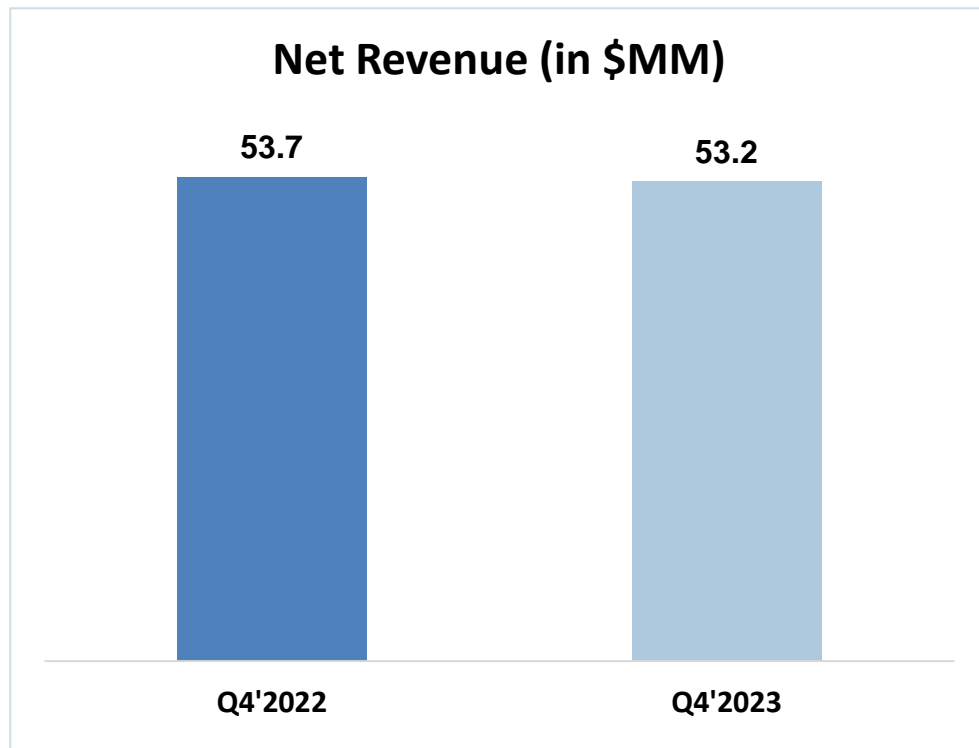


# Puma's Pharmacy and Distributor Network



# \$53.2 Million Net NERLYNX Revenue in Q4'23

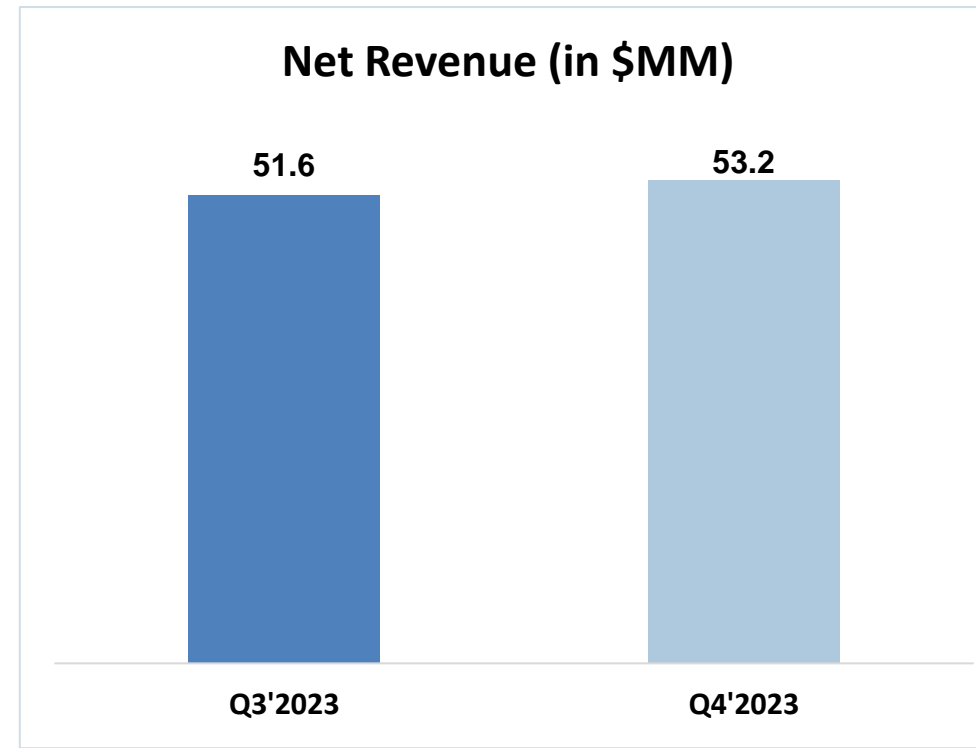
*~1% decline compared to Q4'22*



**Inventory Change (\$)**

Q4'22	Q4'23
+\$2.6 mil	+\$2.1 mil

*~3% increase Q4'23 compared to Q3'23*

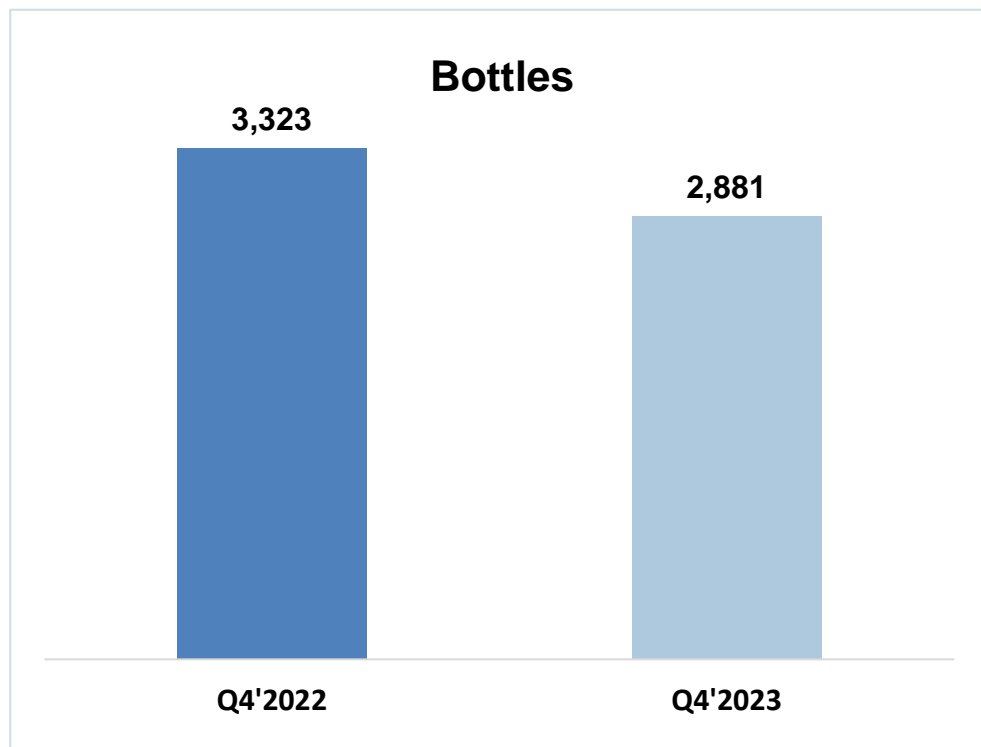


**Inventory Change (\$)**

Q3'23	Q4'23
+\$0.6 mil	+\$2.1 mil

# 2,881 Ex-Factory Bottles Were Sold in Q4'23

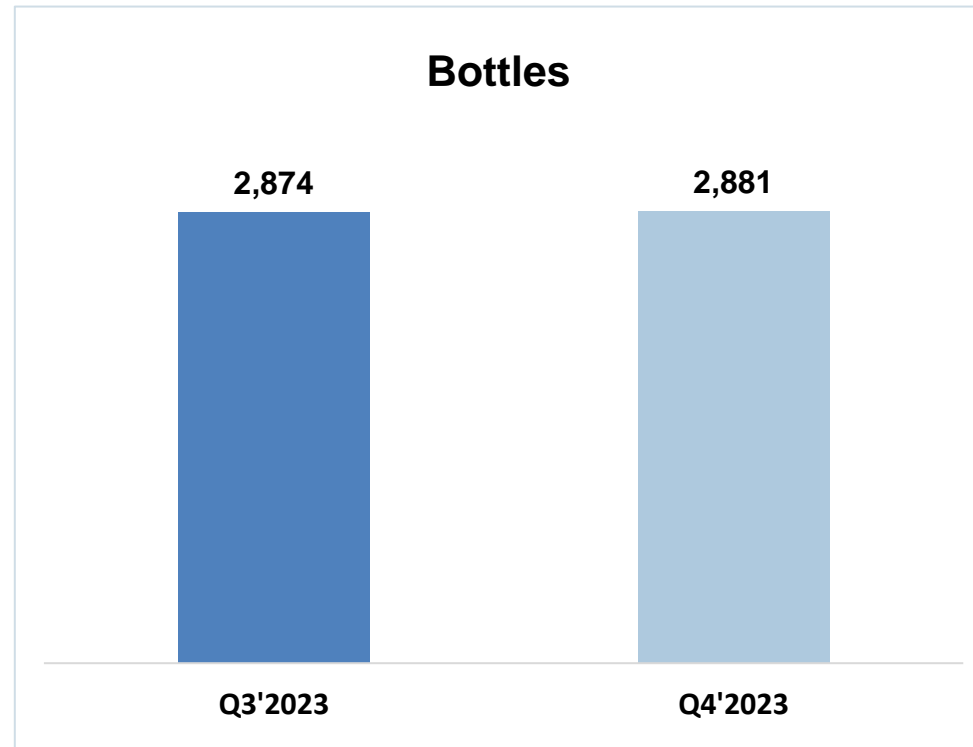
*~13% decline compared to Q4'22*



**Inventory Change Bottles**

Q4'22	Q4'23
+164	+127

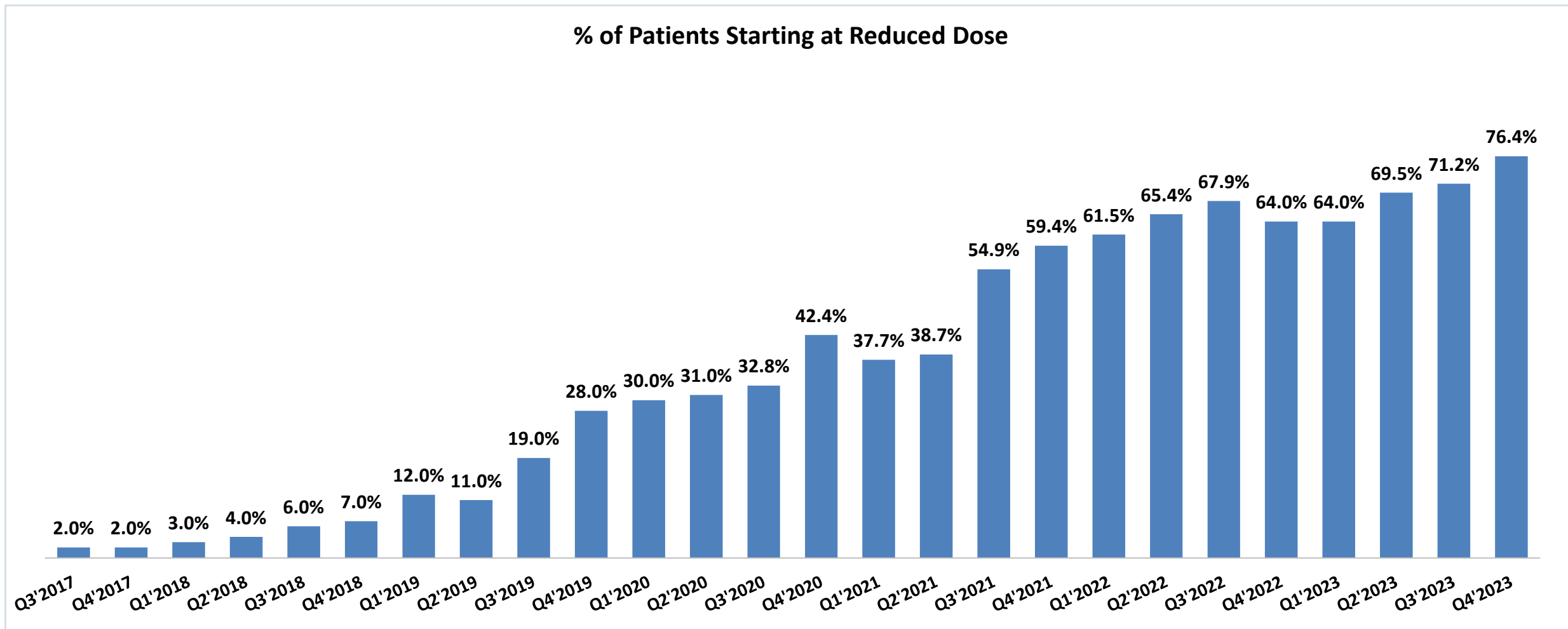
*~0.2% growth compared to Q3'23*



**Inventory Change Bottles**







Q3'23	Q4'23
+32	+127

# ~76% of Patients in Q4'23 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		<ul style="list-style-type: none"> <li>• 2019 – Ext. Adj. in Australia, Singapore</li> <li>• 2020 – Ext. Adj. in Brunei, Malaysia, New Zealand</li> <li>• Q2 2022 – Ext. Adj. in the Philippines</li> <li>• Q3 2022 – mBC in Singapore</li> <li>• Q3 2023 – mBC in Malaysia</li> </ul>	<ul style="list-style-type: none"> <li>• 2020 – Singapore</li> <li>• Q2 2021 – Malaysia</li> <li>• Q3 / Q4 2021 – Brunei, New Zealand</li> </ul>
Israel		<ul style="list-style-type: none"> <li>• 2020 – Approved in Ext. Adj. and mBC</li> </ul>	<ul style="list-style-type: none"> <li>• 2020 – Launched</li> </ul>
Canada		<ul style="list-style-type: none"> <li>• 2019 – Ext. Adj. approved</li> <li>• Q2 2021 – mBC approved</li> </ul>	<ul style="list-style-type: none"> <li>• 2020 – Launched</li> </ul>
Latin America		<ul style="list-style-type: none"> <li>• 2019 – Ext Adj in Argentina</li> <li>• 2020 – Ext. Adj in Chile, Ecuador; mBC in Argentina</li> <li>• 2021 – Ext Adj and mBC in Peru; mBC in Chile; Ext. Adj. in Brazil</li> <li>• Q1 2022 – Ext. Adj. in Mexico</li> <li>• Q3 2022 – mBC in Ecuador</li> <li>• Q1 2023 – mBC in Colombia</li> <li>• Q3 2023 – mBC in Mexico</li> </ul>	<ul style="list-style-type: none"> <li>• 2020 – Argentina</li> <li>• Q2 2021 – Chile</li> <li>• Q4 2021 – Peru</li> <li>• Q3 2022 – Brazil</li> <li>• Q1 2023 – Mexico</li> <li>• Q3 2023 – mBC in Colombia</li> </ul>
Europe Greater China Middle East North and West Africa South Africa Turkey		<ul style="list-style-type: none"> <li>• 2019 – EMA approval</li> <li>• 2019 – Ext. Adj. in Hong Kong</li> <li>• 2020 – Ext. Adj. in China, Taiwan</li> <li>• Q4 2021 – mBC in Taiwan</li> <li>• Q1 2023 – Ext Adj. in Morocco, South Africa</li> <li>• Q3 2023 – ext adj in UAE</li> <li>• Q1 2024 – ext adj Syria</li> </ul>	<ul style="list-style-type: none"> <li>• 2019 – Germany, UK, Austria</li> <li>• 2020 – Sweden, Finland, Scotland, Switzerland, Denmark</li> <li>• 2020 – Hong Kong</li> <li>• Q1 2021 – China (added to 2021 NRDL), Taiwan</li> <li>• Q1 2021 – Greece, Czech Republic</li> <li>• Q1 2022 – Ireland</li> <li>• Q3 2022 – Spain</li> <li>• Q2 2023 – Slovakia</li> <li>• Q1 2024 – Morocco</li> </ul>
South Korea		<ul style="list-style-type: none"> <li>• Q4 2021 – Ext. Adj. in S. Korea</li> </ul>	<ul style="list-style-type: none"> <li>• Q1 2022 – Launched</li> </ul>



# NERLYNX<sup>®</sup> Extended Adjuvant HER2+ Breast Cancer Market Size

- Approximately 28,300 patients (US) with early stage HER2+ breast cancer treated with adjuvant treatment<sup>1</sup>
  - 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<sup>1</sup>
  - Approximately 65–70% of patients have HR positive disease

<sup>1</sup>Roche epidemiology slides 09/18

# Puma Financial Guidance for Q1 and FY 2024

	<u>Q1 2024</u>	<u>Full Year 2024</u>
■ NERLYNX revenue guidance:	\$38 - \$40 million	\$183 to \$190 million
■ NERLYNX royalty guidance:	\$2.5 - \$3 million	\$30 - \$34 million
■ Net income guidance:	\$(10) - \$(12) million	\$12 - \$15 million

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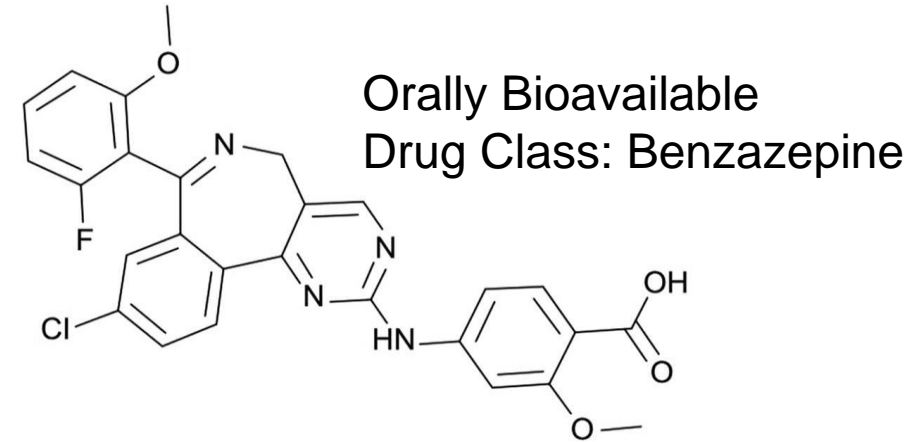
# ALISERTIB

**Breast Cancer and Small-Cell Lung Cancer**



# Alisertib (MLN 8237)

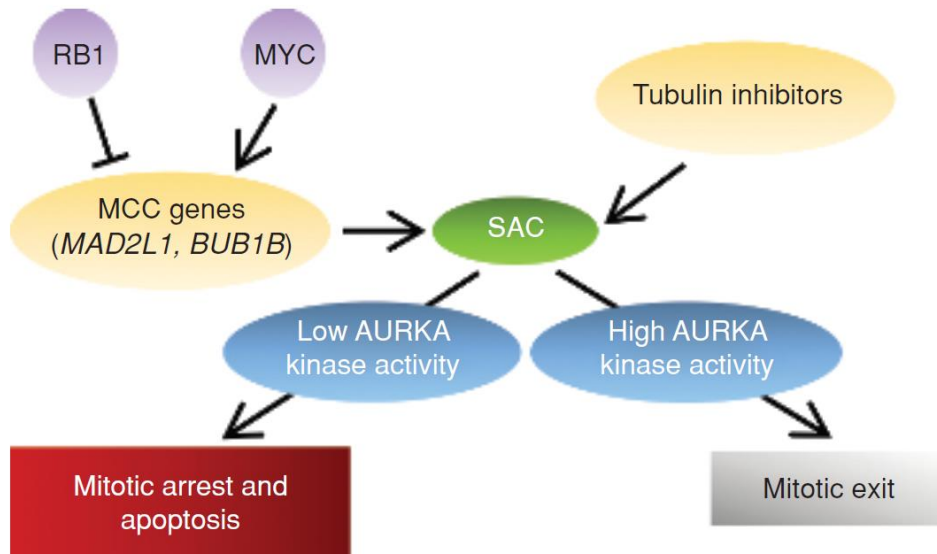
Aurora Kinase A  
(AURKA) inhibitor



- 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 lymphoma (NHL)
- Well-characterized safety profile: ~1,300 patients treated across 22 company-sponsored trials

# Synthetic Lethality of AURKA and Rb1

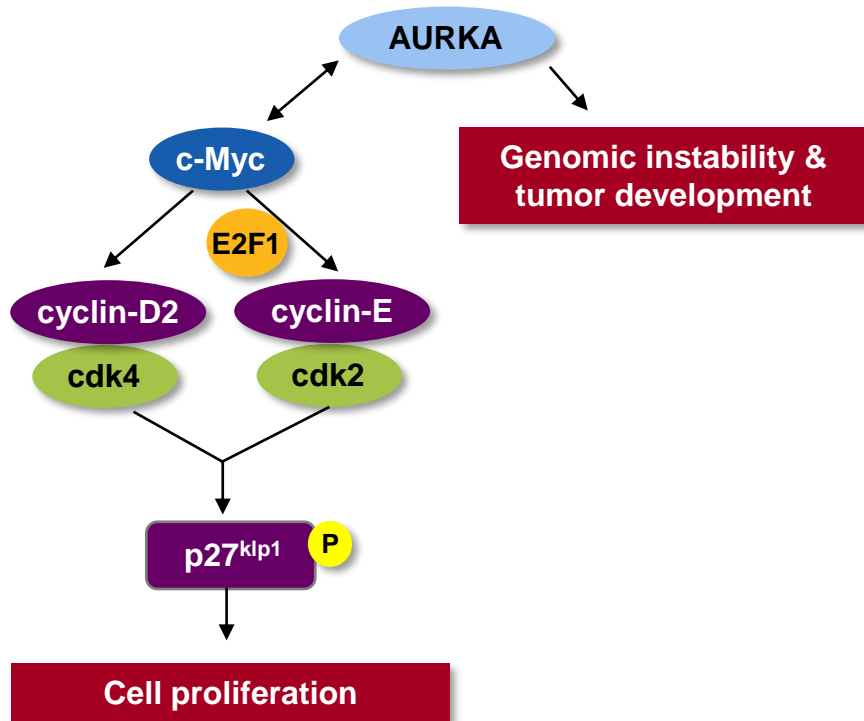
Cancers with a hypersensitive spindle assembly checkpoint (SAC) depend on AURKA for mitotic exit and survival<sup>1</sup>



- 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

# 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

# **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  $\leq 2$  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 $\geq 6$ 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)

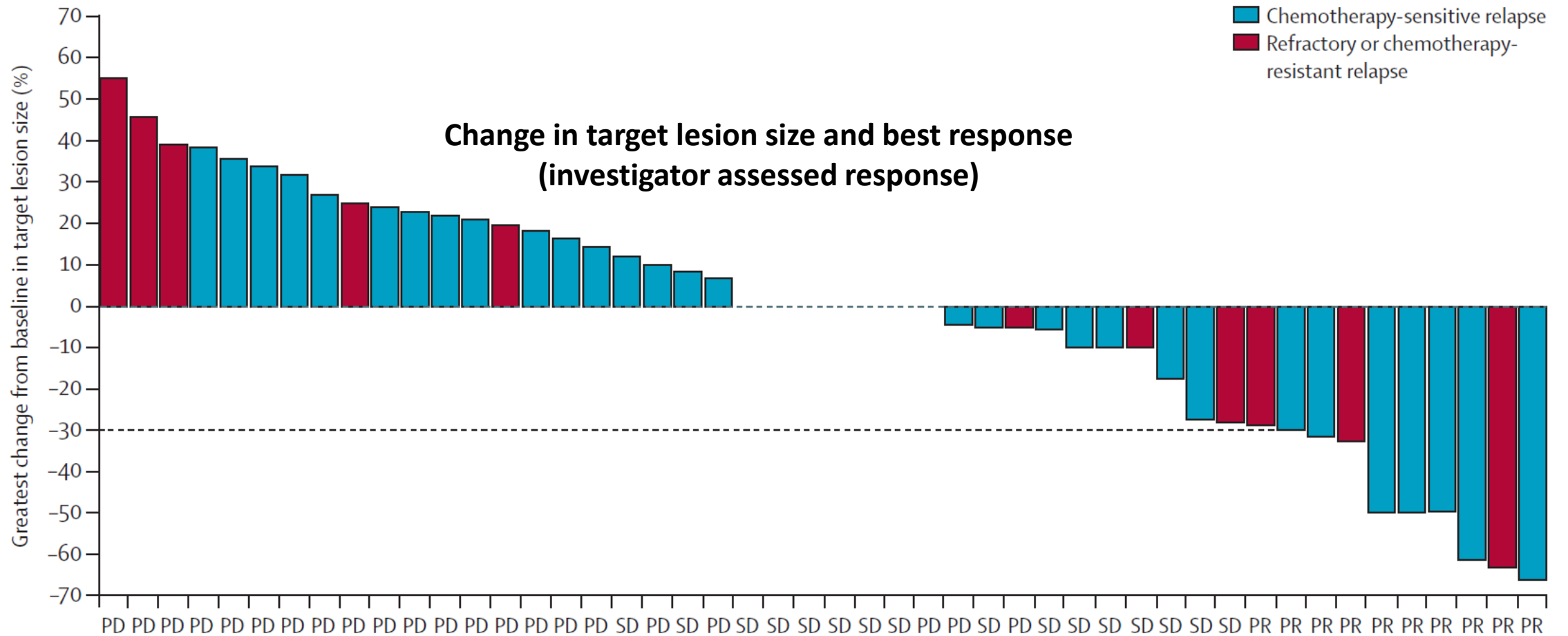
Table adapted from Melichar B Lancet Oncol 2015. Data are either number of patients (%) (95% CI), or median (95% CI), unless otherwise stated. NE=not estimable. \*Safety population. †All were partial responses. All responses were based on investigator tumor assessments (RECIST v1.1).



# 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).

# 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

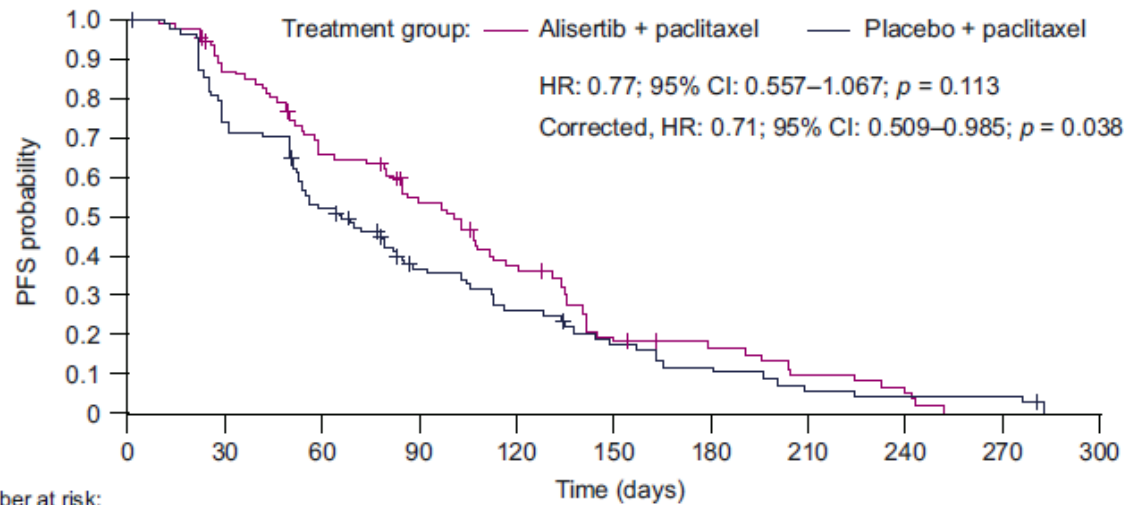
# Randomized Phase 2 Study of Paclitaxel plus Alisertib vs Paclitaxel plus Placebo as Second-Line SCLC: Primary Analysis

## Study design:

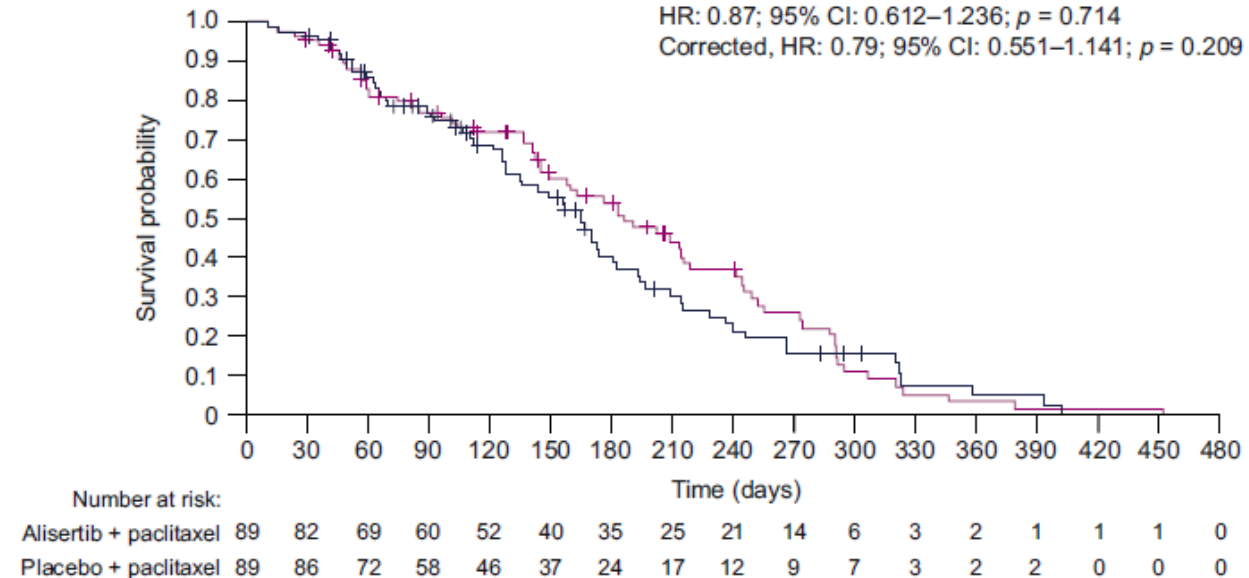
- Patients with relapsed or refractory SCLC stratified by relapse type (sensitive vs resistant or refractory)
- Randomized 1:1 to alisertib + paclitaxel or placebo + paclitaxel in 28-day cycles
- Alisertib (40 mg BID for 3 weeks on days 1–3, 8–10, and 15–17) plus paclitaxel (60 mg/m<sup>2</sup> intravenously on days 1, 8, and 15) or placebo plus paclitaxel (80 mg/m<sup>2</sup> 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



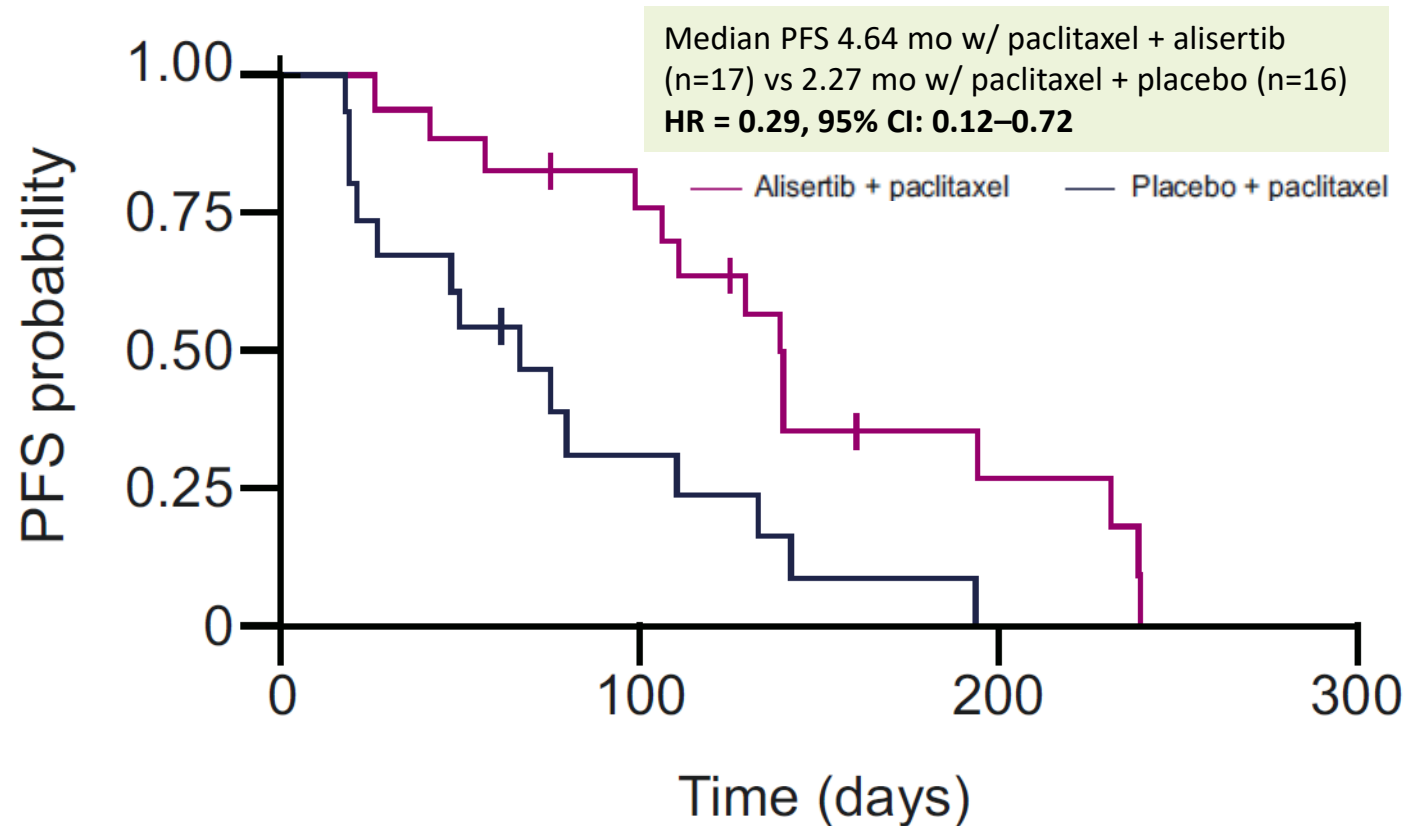
## OS in ITT



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

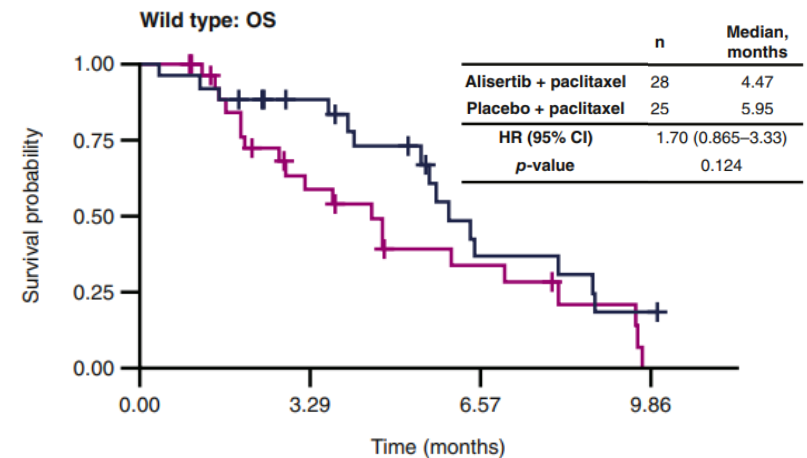
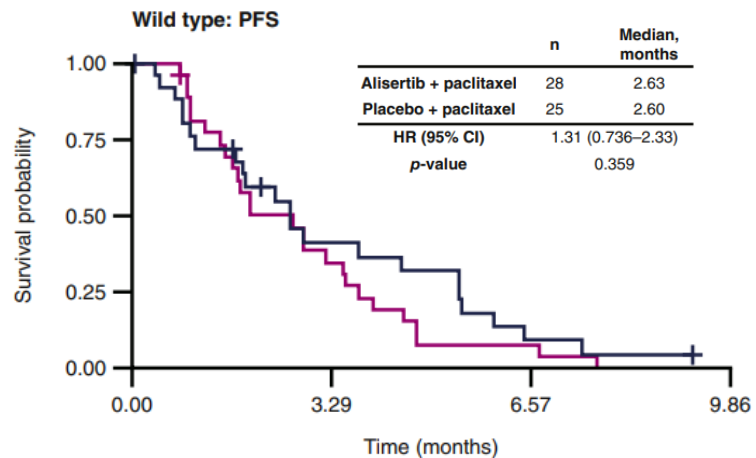
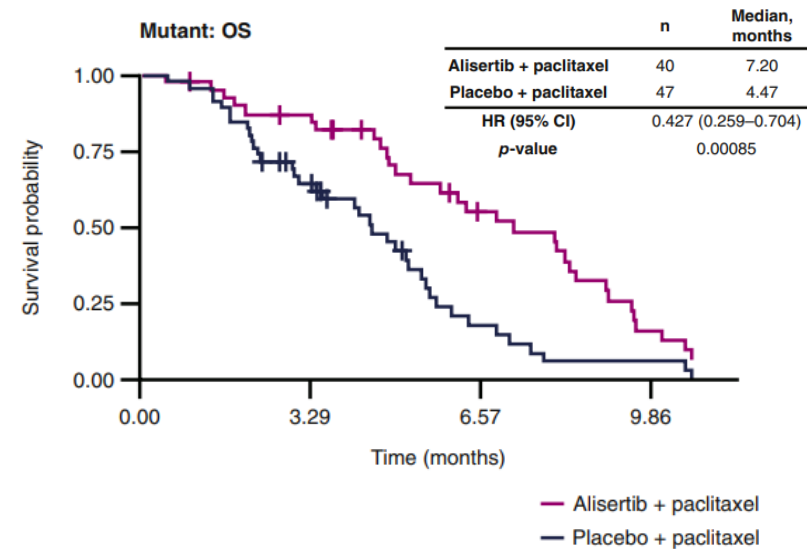
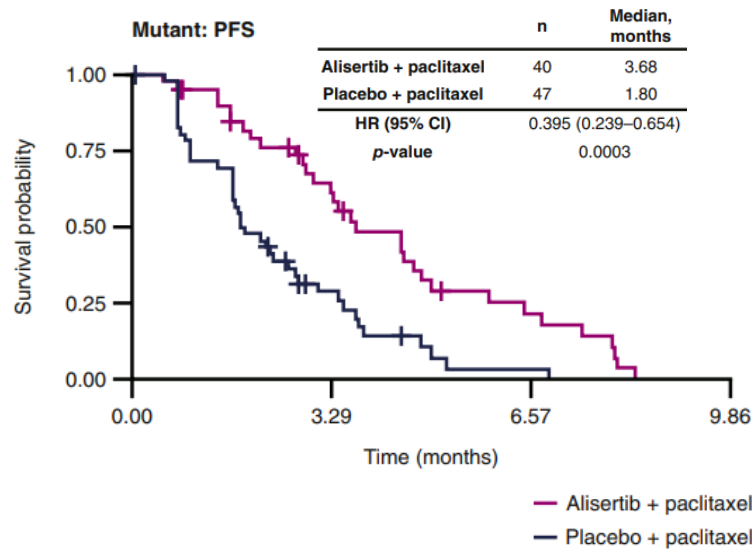
Improved PFS observed among patients positive versus negative for *c-Myc* expression

## 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**

AE	Alisertib/Paclitaxel (n = 87)		Placebo/Paclitaxel (n = 89)	
	Any Grade	Grade $\geq$ 3	Any Grade	Grade $\geq$ 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

N = up to 60

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

Anticipate initiation of PUMA-ALI-4201 Phase II trial in H1 2024

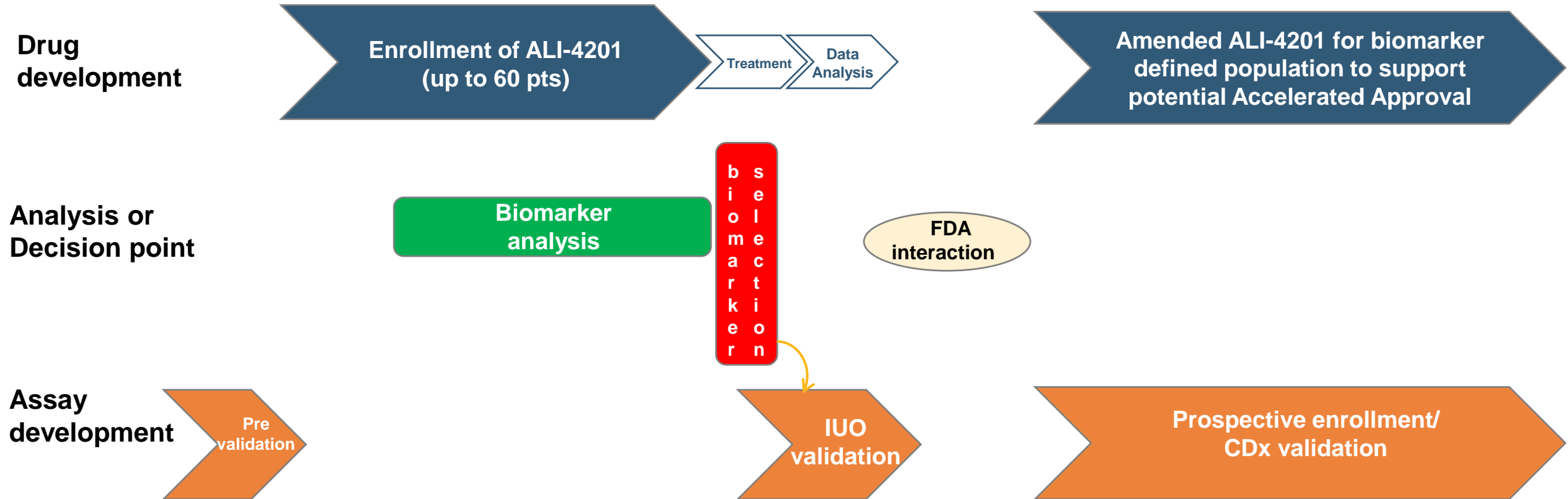
# Efficacy and safety objectives and endpoints

<b>Objective</b>
<b>Primary Endpoint</b>
<ul style="list-style-type: none"><li>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)</li></ul>
<b>Secondary Endpoints</b>
<ul style="list-style-type: none"><li>Duration of response (DOR)</li><li>Disease control rate (DCR)</li><li>Progression free survival (PFS)</li></ul>
<ul style="list-style-type: none"><li>Overall survival (OS)</li></ul>
<ul style="list-style-type: none"><li>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)</li></ul>
<ul style="list-style-type: none"><li>Plasma alisertib concentrations on Cycle 1 Day 1 and Day 8</li></ul>
<b>Exploratory Endpoints</b>
<ul style="list-style-type: none"><li>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])</li></ul>



# 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  $\leq 2$  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 $\geq 6$ 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).



# 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

# 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	n=10	n=14
6-month OS rate	90.6% (95% CI: 82.2-99.8%)	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
<b>Hematologic Adverse Events</b>				
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%
<b>Non-Hematologic Adverse Events</b>				
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

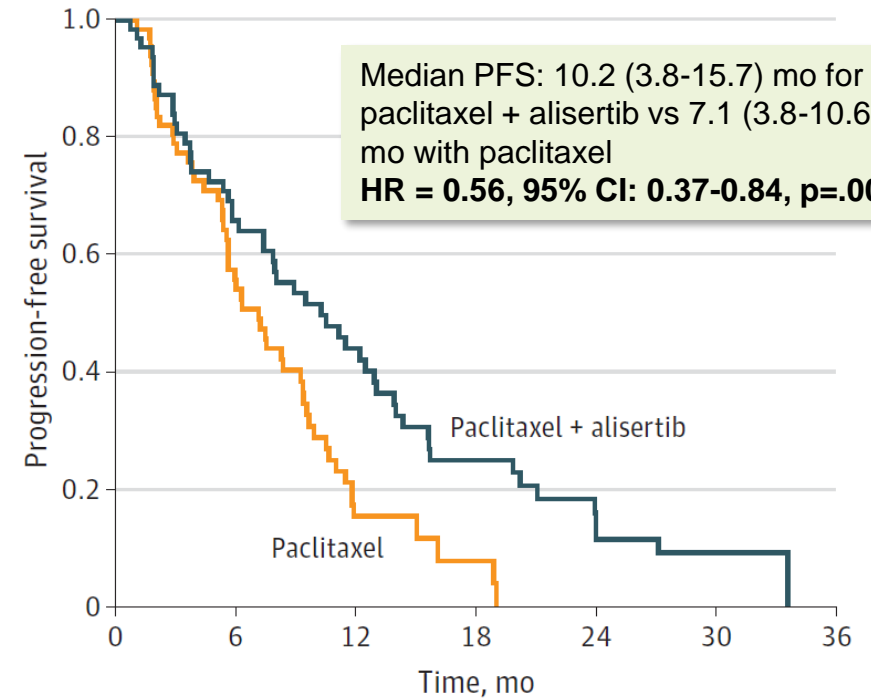
# Phase 2 Randomized Study of Paclitaxel + Alisertib vs Paclitaxel Alone

## - 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/m<sup>2</sup> 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/m<sup>2</sup> IV on days 1, 8, and 15 of a 28-day cycle
- 1° endpoint PFS

### PFS in ER+/HER2- ITT



No. at risk	0	6	12	18	24	30	36
Paclitaxel + alisertib	69	39	23	12	5	2	0
Paclitaxel	70	32	8	2	0		

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)



# Phase 2 Randomized Study of Paclitaxel + Alisertib vs Paclitaxel Alone

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

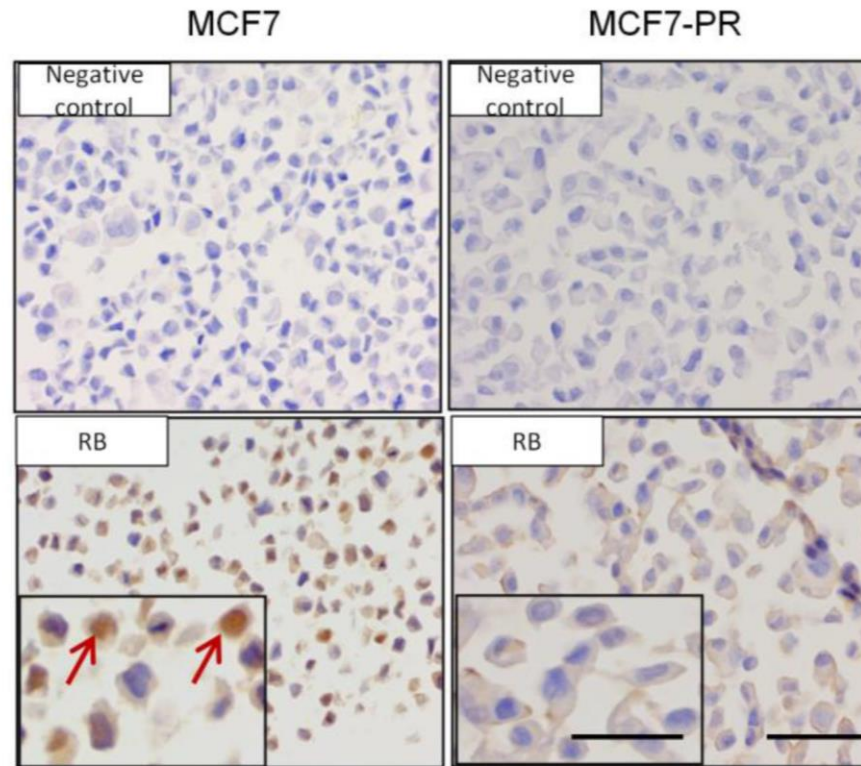
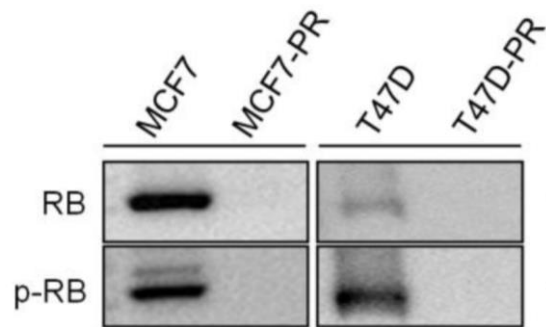
### Efficacy in patients pretreated with palbociclib (n=30)

- 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

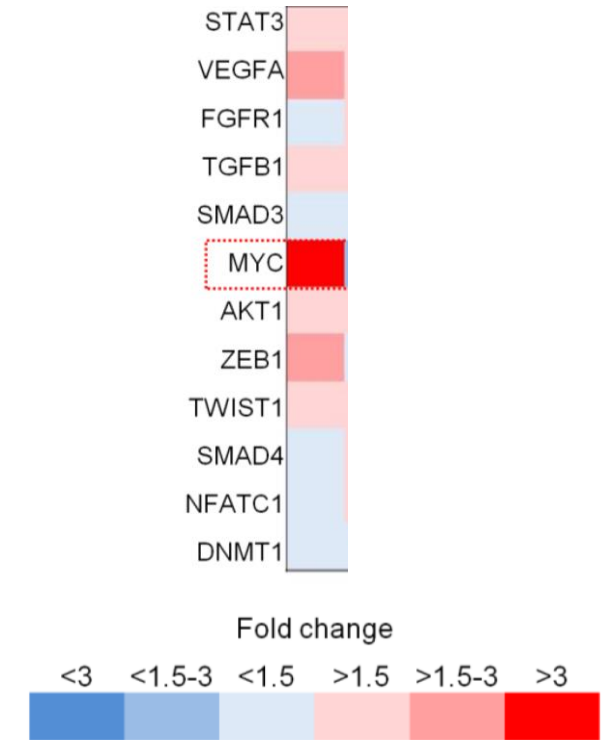
Both RB1 loss and MYC upregulation were observed in palbociclib-resistant HR+ breast cancer cell lines, supporting a role for alisertib in this setting

## RB1 Loss



## *C-Myc* Upregulation

MCF7-PR Vs MCF7



# 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 <sup>1</sup>	63% <sup>1</sup>	57% <sup>1</sup>	4% <sup>1</sup>
Alisertib monotherapy 50 mg BID <sup>2</sup>	Not reported <sup>2</sup>	42% <sup>2</sup>	Not reported <sup>2</sup>
Alisertib 50 mg BID + fulvestrant <sup>2</sup>	Not reported	42%	Not reported
Alisertib 40 mg BID + paclitaxel <sup>3</sup>	67.9%	59.5%	1.2%
Eribulin mesylate (HALAVEN) <sup>4</sup>	82%	57%	5%
Physician's Choice of Chemotherapy <sup>5</sup>	51.2%	40.7%	Not reported
Palbociclib (IBRANCE) <sup>6</sup> + fulvestrant (PALOMA-3) or letrozole (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) <sup>7</sup> for ER+	70%	51% (G ≥3 neutropenia)	5%
Sacituzumab govitecan (TRODELVY) <sup>8</sup> 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<sup>9</sup>**

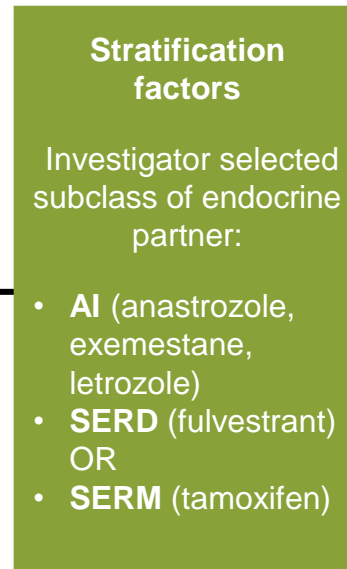
<sup>1</sup>Melichar B Lancet Oncol 2015, <sup>2</sup>Haddad SABCS 2020 PD2-05, <sup>3</sup>O'Shaughnessy J JAMA Netw Open 2021, <sup>4</sup>HALAVEN USPI, <sup>5</sup>Modi S N Engl J Med 2022, <sup>6</sup>IBRANCE USPI, <sup>7</sup>Rugo HS ASCO 2022, <sup>8</sup>TRODELVY USPI, <sup>9</sup>NCCN Guideline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

# PUMA-ALI-1201

## 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



1:1:1 RANDOMIZATION

N = up to 150

### Arm 1

Alisertib 50 mg BID on Days 1-3, 8-10, 15-17 of a 28-day cycle + Endocrine

### Arm 2

Alisertib 40 mg BID on Days 1-3, 8-10, 15-17 of a 28-day cycle + Endocrine

### Arm 3

Alisertib 30 mg BID on Days 1-3, 8-10, 15-17 of a 28-day cycle + Endocrine

### 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

Anticipate initiation of PUMA-ALI-1201 Phase II trial in H2 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
- Claims for the pharmaceutical composition for use in the treatment of cancer including lung cancer and non-small cell lung cancer

# 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 (H1 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 (H1 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 (H2 2024);
- Report interim data from ALISCA-Lung1, a Phase II clinical trial of alisertib monotherapy for the treatment of extensive-stage small cell lung cancer (H2 2024)



# 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*

## Alvin Wong, Pharm.D.

**Chief Scientific Officer**

– *Proteolix, Novacea, Genentech*

## Douglas Hunt

**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**

*CEO, Kura Oncology; CEO, Wellspring Biosciences; CEO Avidity Nanomedicines; Former CEO, President, Intellikine*

# Puma Biotechnology – Financial

- Currently trading on NASDAQ: PBYI
- Cash, cash equivalents and marketable securities at December 31, 2023: \$96 million
- Net income in Q4 2023: \$12.3 million  
Net income in FY 2023: \$21.6 million
- Cash earned in Q4 2023: \$10.4 million  
Cash earned in FY 2023: \$14.4 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: 48.2 million

# Company Highlights

- NERLYNX<sup>®</sup> – 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<sup>®</sup> – first HER2-directed tyrosine kinase inhibitor approved in both early stage and metastatic HER2+ breast cancer
- Retain full U.S. commercial rights to NERLYNX<sup>®</sup>
- 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

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# Puma Biotechnology

March 2024

