

# Puma Biotechnology

H.C. Wainwright 24<sup>th</sup> Annual Global Investment Conference

September 2022



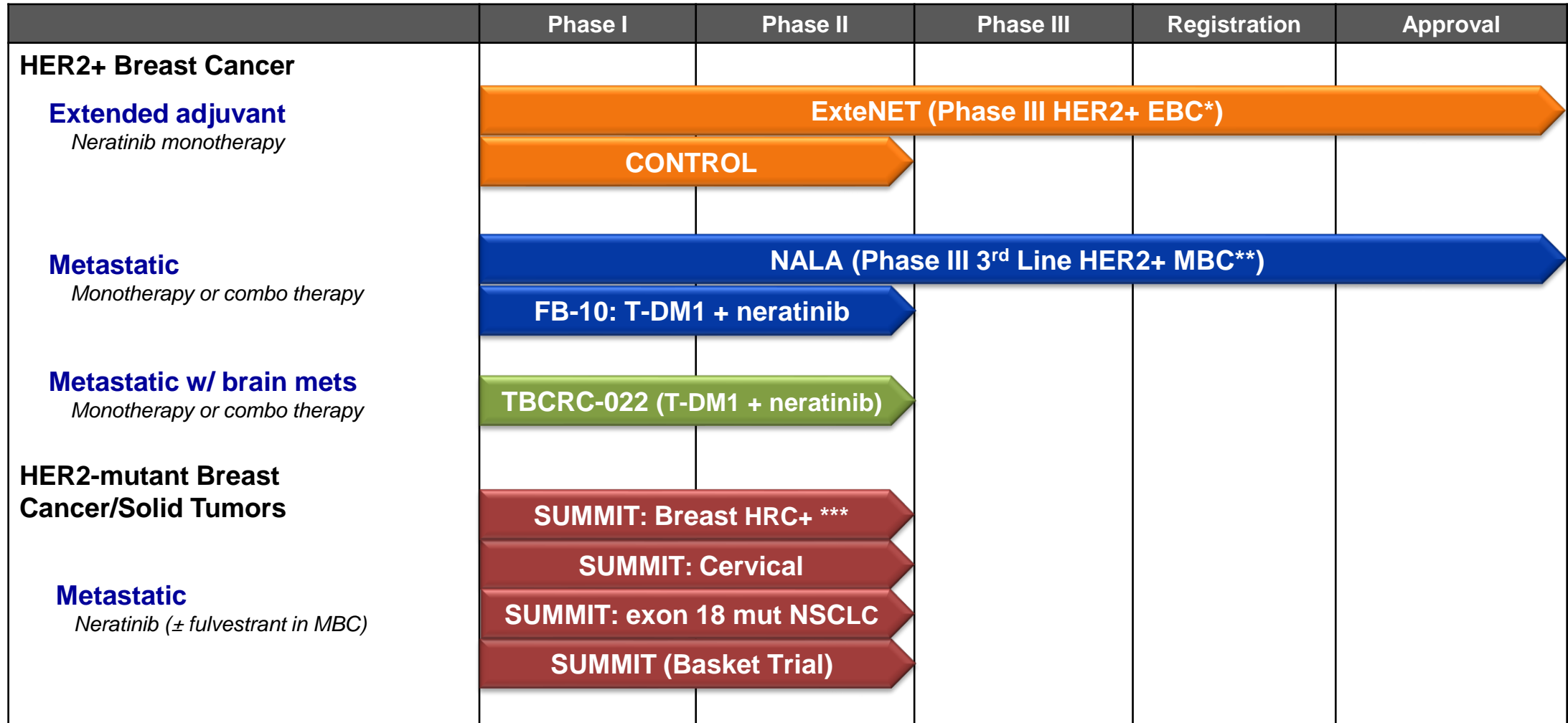
## Forward-Looking Safe-Harbor Statement

*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, 2021, and our Quarterly Report on Form 10-Q for the quarter ended June 30, 2022. 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.*



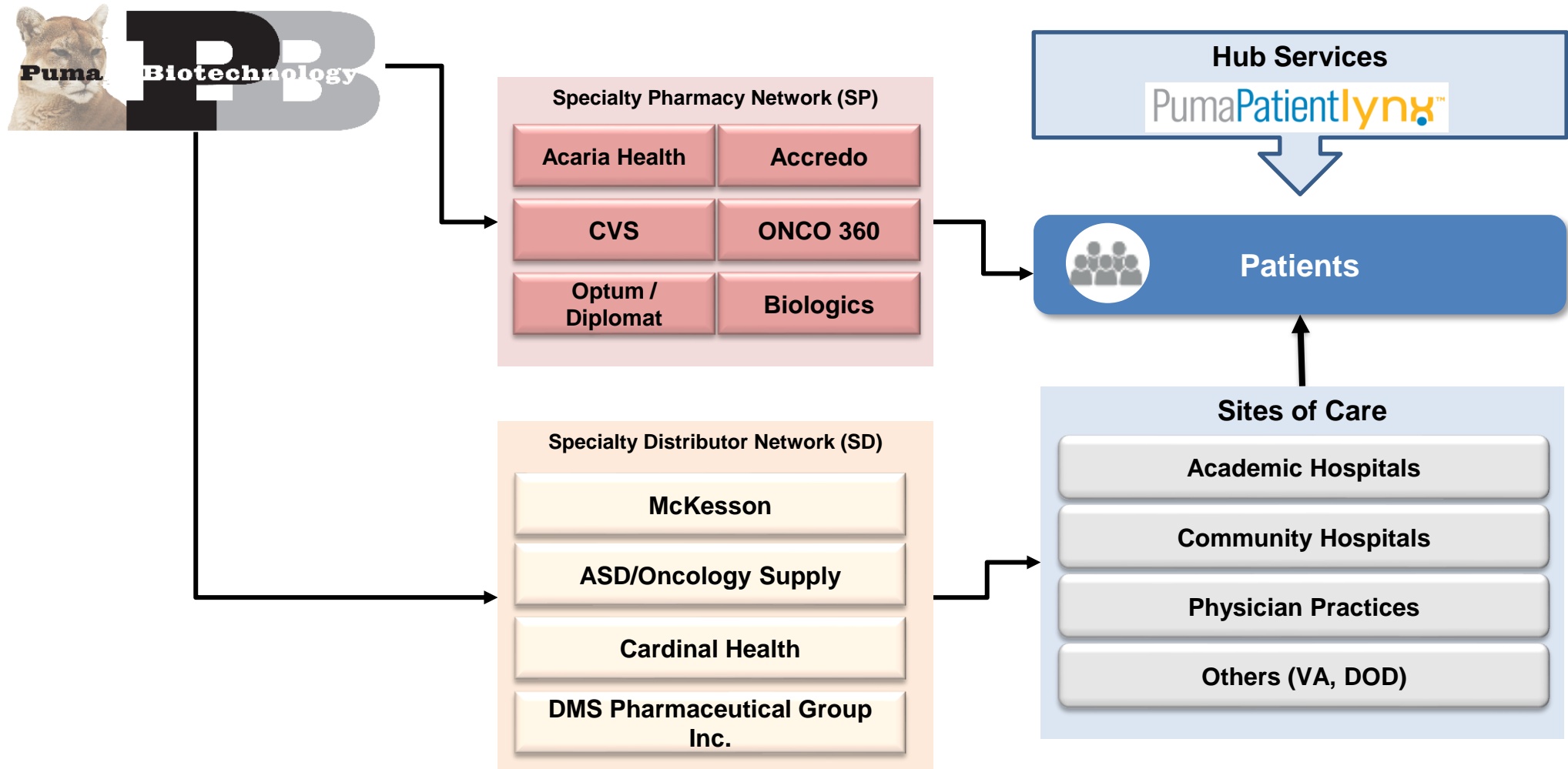
# Product Pipeline

## *Neratinib across the breast cancer therapy spectrum*

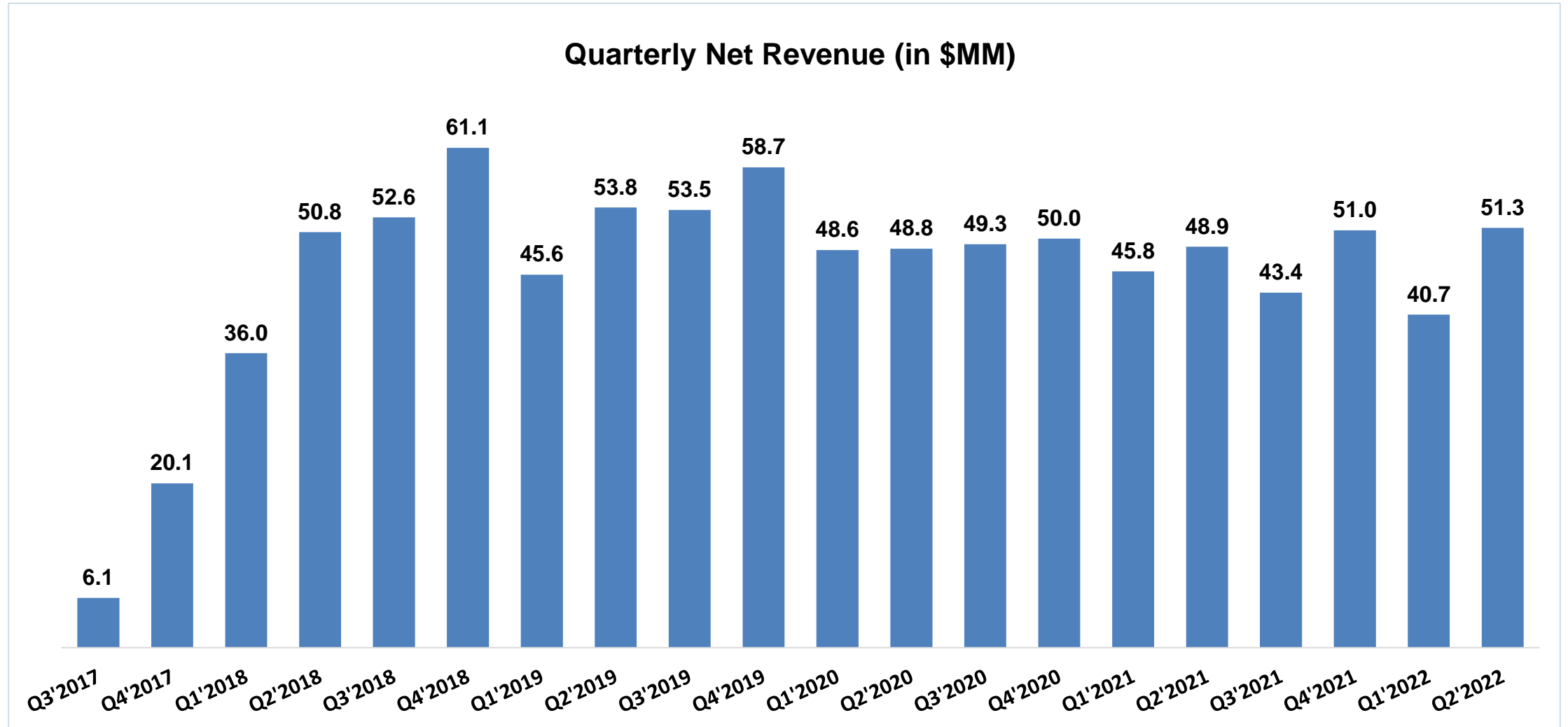


\* EBC: Early breast cancer    \*\* MBC: Metastatic breast cancer    \*\*\* HRC+: Hormone receptor positive

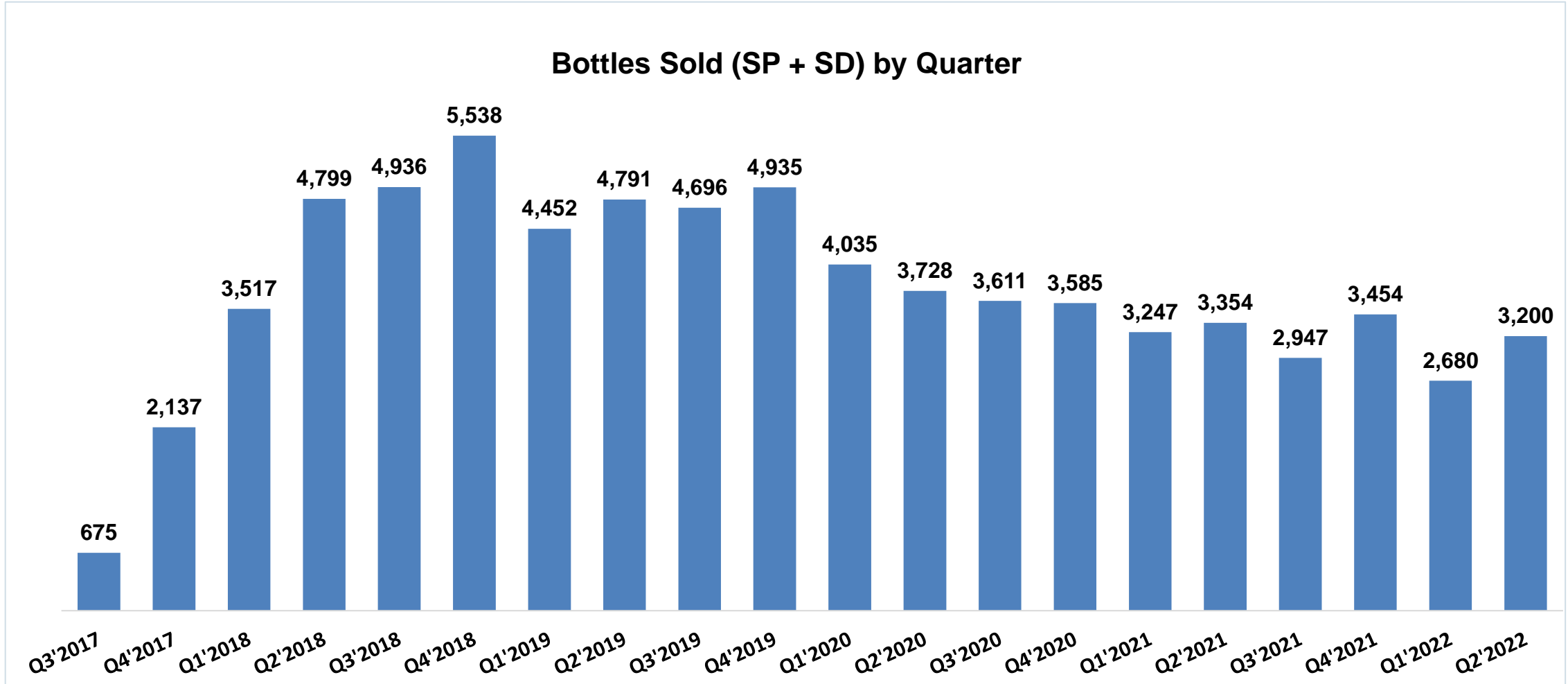
# PUMA's Pharmacy and Distributor Network



# ~\$51 Million net NERLYNX revenue in Q2'22

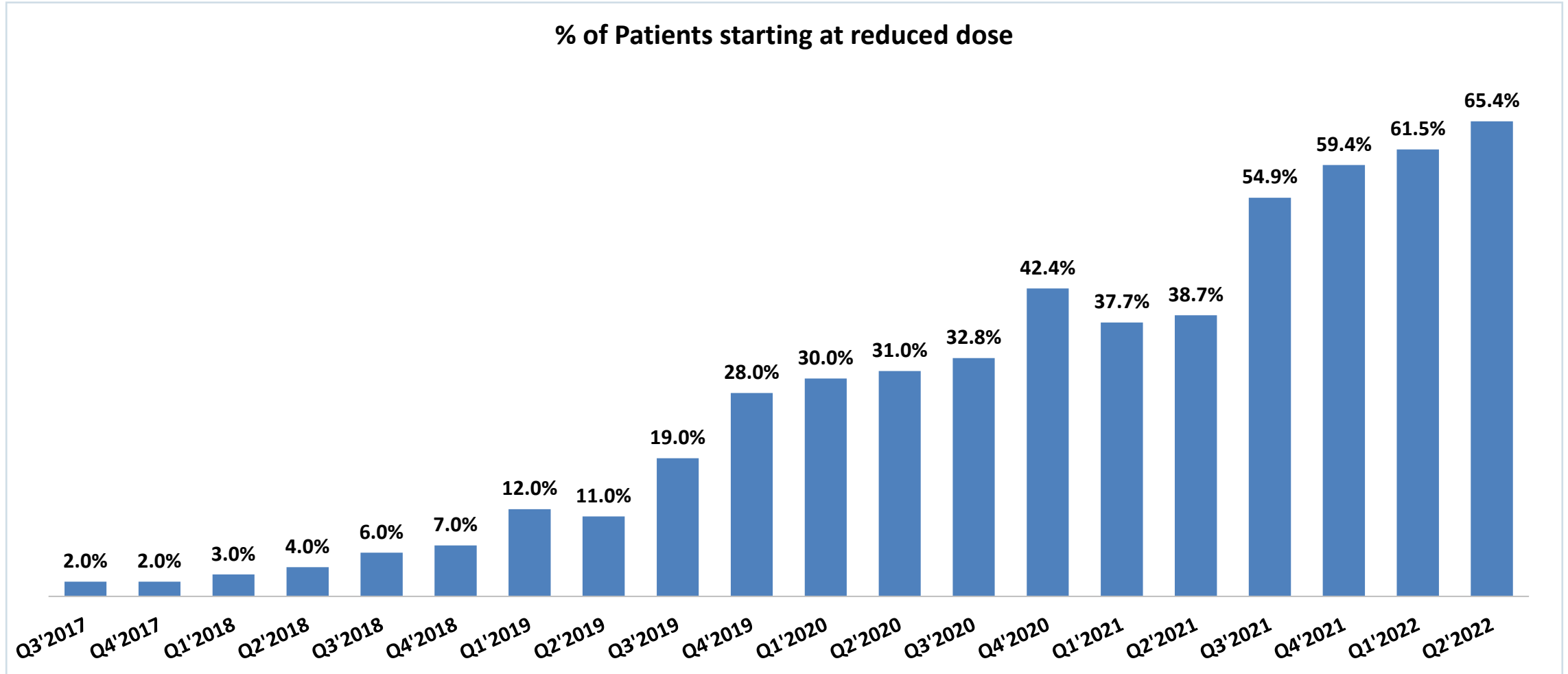


# 3,200 Ex-factory bottles were sold in Q2'22



Includes Commercial SP and SD







# ~65% of patients in Q2'22 started at a reduced dose\* \*\*



\*Reduced dose defined as fewer than 6 pills per day

\*\* FDA approved dose-escalation label supplement in June 2021

# Rest of World Partnerships – Timelines

Region	Partner	Regulatory Approvals	Commercial Launches
Australia / SE Asia	 Specialised Therapeutics	<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>• <b>Q2 2022 – Ext. Adj. in the Philippines</b></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	 MEDISON Driving Innovative Healthcare	<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	 Knight	<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	 PINT PHARMA	<ul style="list-style-type: none"> <li>• 2019 – Ext Adj in Argentina</li> <li>• 2020 – Ext. Adj in Chile, Ecuador</li> <li>• 2020 – mBC in Argentina</li> <li>• 2021 – Ext Adj and mBC in Peru; mBC in Chile</li> <li>• Q4 2021 – Ext. Adj. in Brazil</li> <li>• Q1 2022 – Ext. Adj. in Mexico</li> <li>• <b>Q3 2022 – mBC in Ecuador</b></li> </ul>	<ul style="list-style-type: none"> <li>• 2020 – Argentina</li> <li>• Q2 2021 – Chile</li> <li>• Q4 2021 – Peru</li> </ul>
Europe Greater China Middle East North and West Africa South Africa Turkey	 Pierre Fabre	<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> </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>• <b>Q3 2022 – Spain</b></li> </ul>
South Korea	 BIXINK THERAPEUTICS	<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>

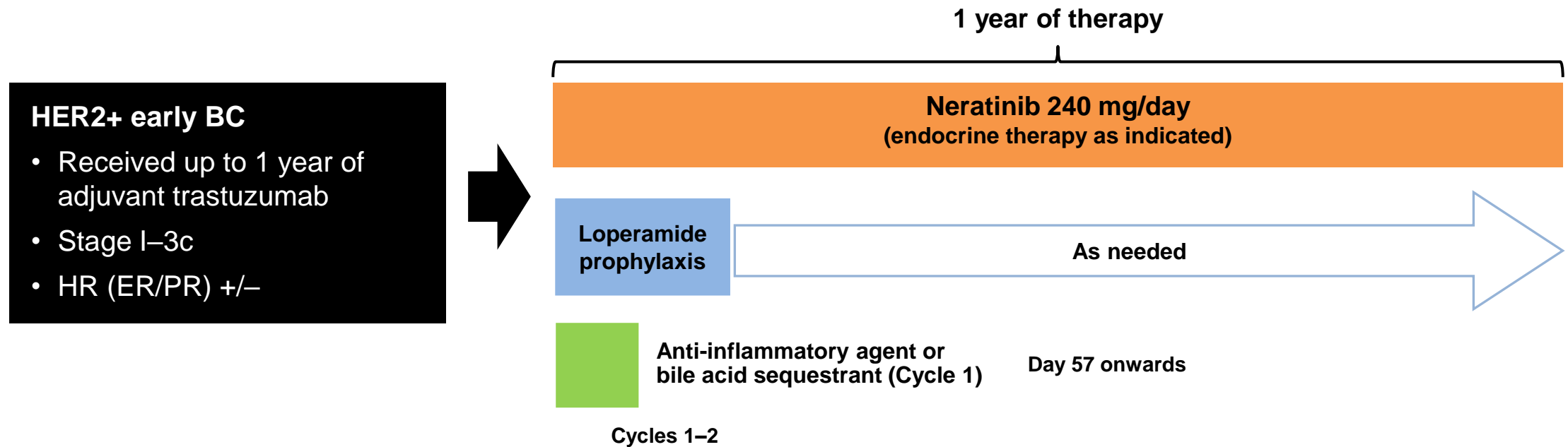


# Puma Financial Guidance for 2022

- NERLYNX revenue guidance: \$180 to \$190 million
- NERLYNX royalty guidance: \$27 to \$30 million
- Net income guidance: \$6 to \$7 million

# CONTROL Study Design

Phase 2 trial to characterize the incidence and severity of diarrhea in patients with HER2+ early breast cancer treated with neratinib and loperamide prophylaxis ± an investigational agent



## STUDY ENDPOINTS

Primary endpoint: incidence of grade  $\geq 3$  diarrhea

Secondary endpoints: frequency distribution of maximum-grade diarrhea; incidence and severity of diarrhea by loperamide exposure

# CONTROL vs ExteNET: Neratinib Treatment-Emergent Diarrhea

## Loperamide prophylaxis reduces incidence and severity of diarrhea

	CONTROL <sup>1</sup>					ExteNET <sup>3</sup>
	Loperamide (n=137)	Budesonide + loperamide (n=64)	Colestipol + loperamide (n=136)	Colestipol + loperamide prn (n=104)	Neratinib dose escalation + loperamide prn (n=60) <sup>2</sup>	Loperamide prn (n=1408)
<b>Treatment-emergent diarrhea incidence, n (%)</b>						
No diarrhea	28 (20)	9 (14)	23 (17)	5 (5)	1 (2)	65 (5)
Grade 1	33 (24)	16 (25)	38 (28)	34 (33)	24 (40)	323 (23)
Grade 2	34 (25)	21 (33)	47 (35)	32 (31)	27 (45)	458 (33)
Grade 3	42 (31)	18 (28)	28 (21)	33 (32)	8 (13)	561 (40)
Grade 4	0	0	0	0	0	1 (<1)
Diarrhea leading to discontinuation	28 (20)	5 (8)	5 (4)	8 (8)	2 (3)	237 (17)
Hospitalization (due to diarrhea)	2 (1)	0	0	0	0	20 (1)
Diarrhea leading to dose reduction	10 (7)	3 (5)	10 (7)	12 (12)	2 (3)	372 (26)

1. Barcenas et al. *Annals of Oncology*, 2020

2. Ruiz-Borrego et al. SABCS 2020 3. Chan et al. *Lancet Oncology* 2016

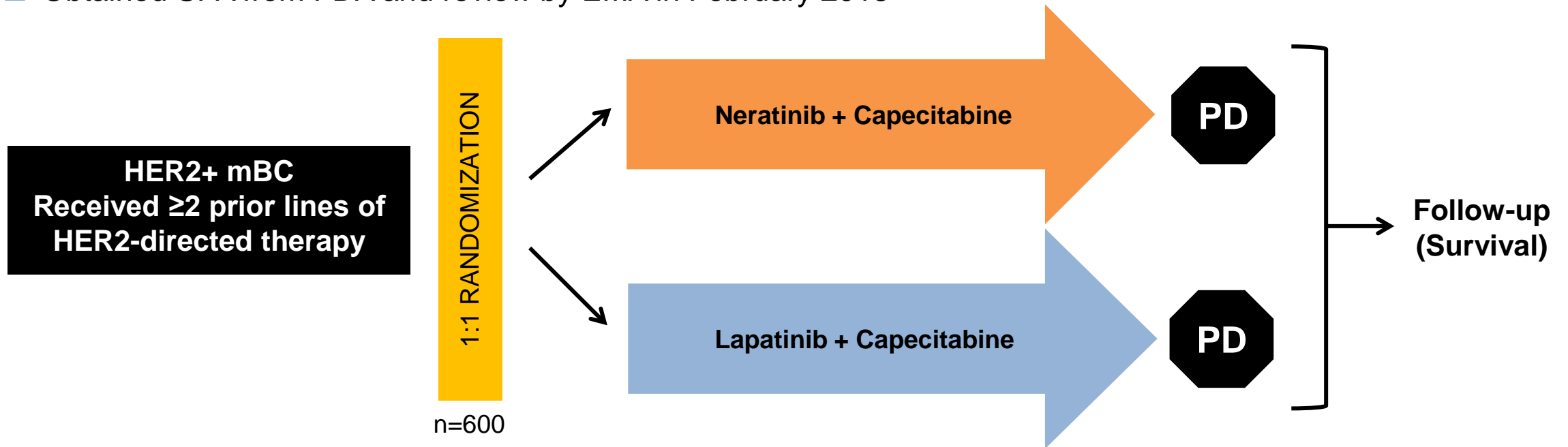
# NERLYNX<sup>®</sup> Extended Adjuvant HER2+ Breast Cancer Market Size

- 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

# Phase III Trial – Third-Line HER2+ MBC (NALA) Study Design

- 3rd- or later-line therapy for patients with HER2+ mBC
- Patients with asymptomatic CNS metastatic disease are eligible
- Obtained SPA from FDA and review by EMA in February 2013



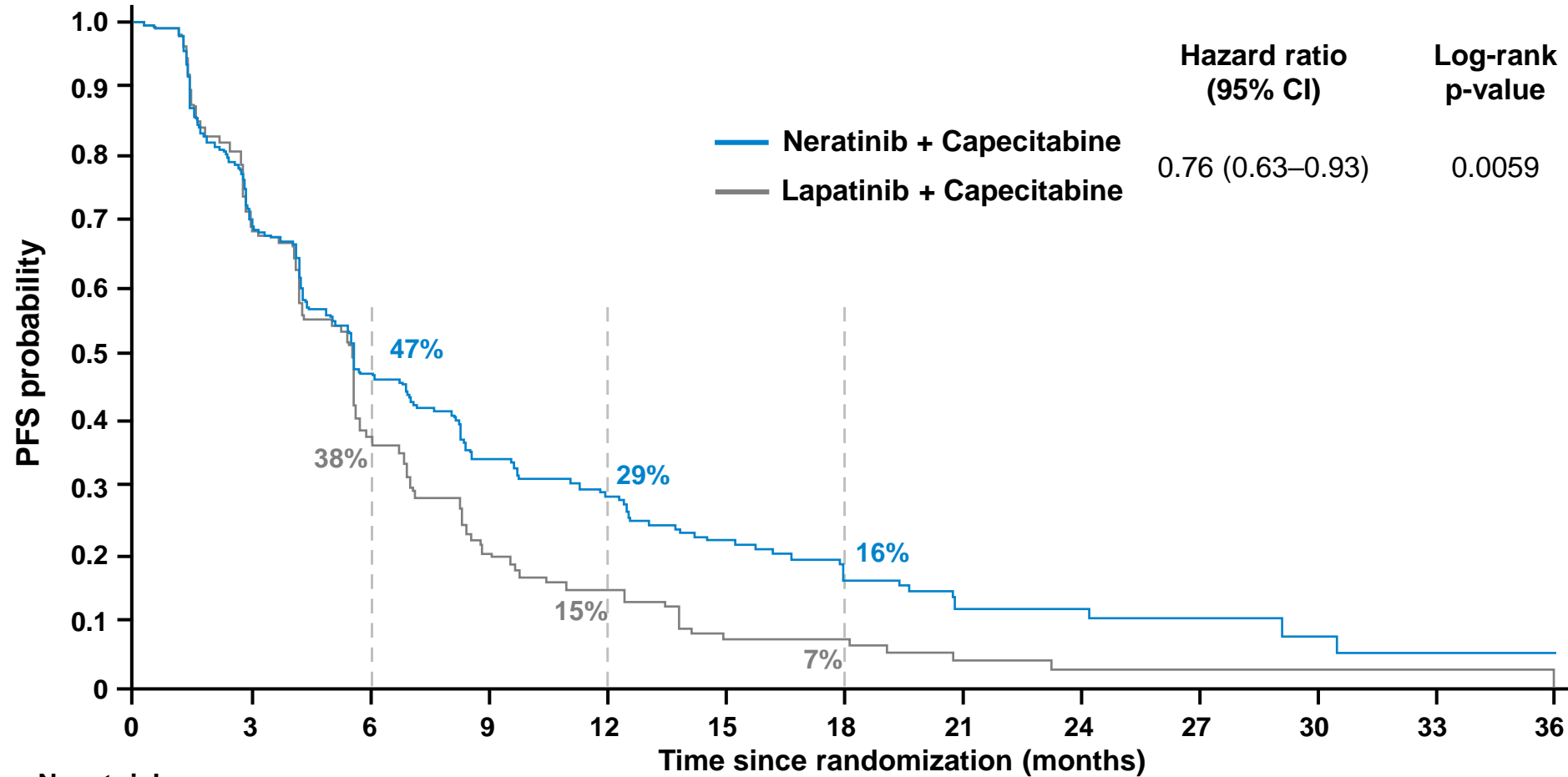
## STUDY OBJECTIVES

Co-Primary: PFS (central) and OS

Secondary: PFS (local), ORR, DoR, CBR, time to intervention for CNS metastases, safety, health outcomes

# Phase III Trial – Third-Line HER2+ MBC (NALA): Study Results

## Centrally Confirmed PFS (co-primary endpoint)



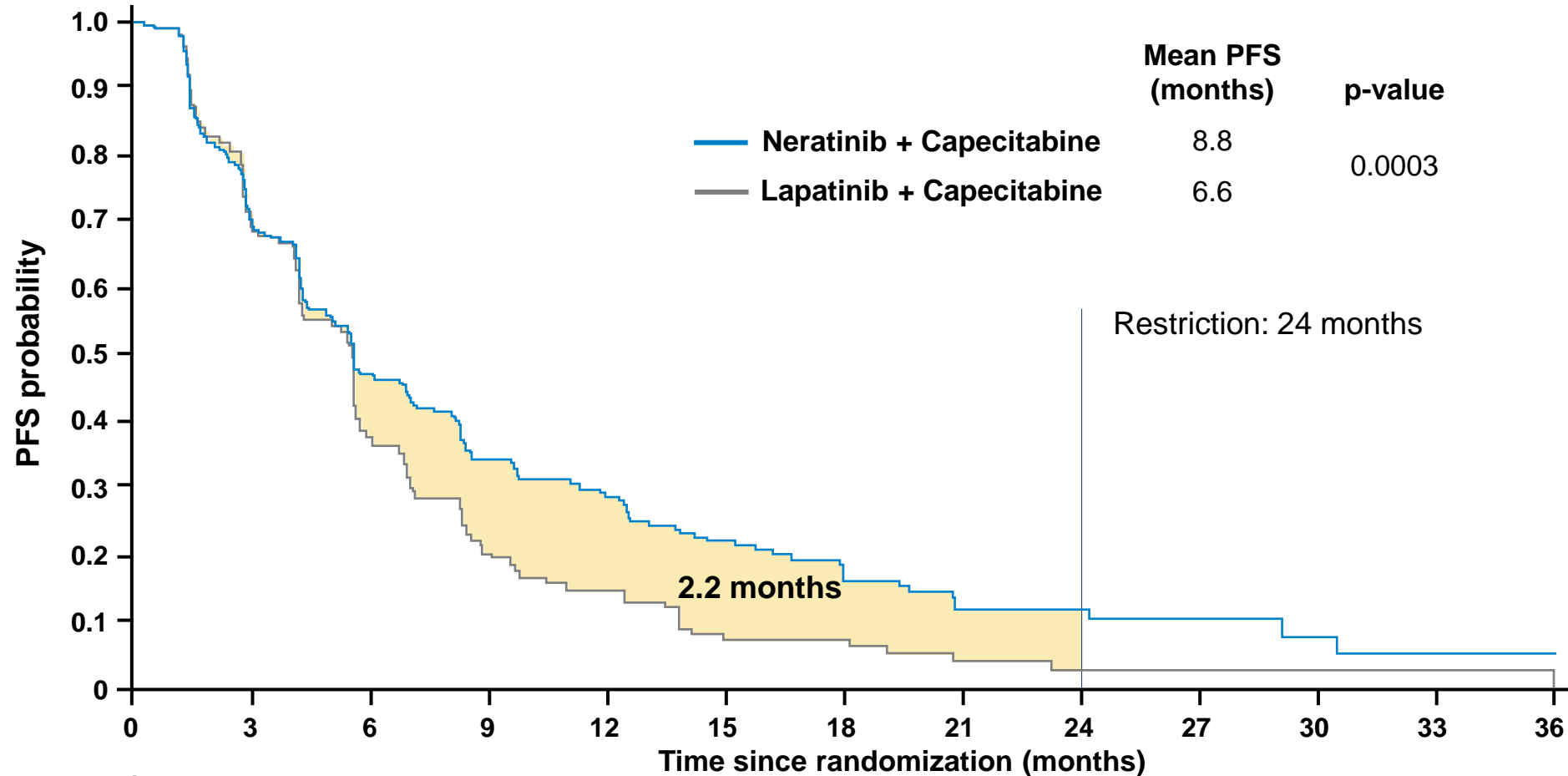
No. at risk:

N+C	307	183	113	69	54	35	20	13	9	7	3	2	2
L+C	314	183	82	39	24	9	8	3	2	2	2	2	1

Saura et al. ASCO 2019 Oral Session: Breast Cancer – Metastatic. Abstract 10002. Presented Tuesday, June 4, 2019

# Phase III Trial – Third-Line HER2+ MBC (NALA): Study Results

## Prespecified restricted means analysis – PFS



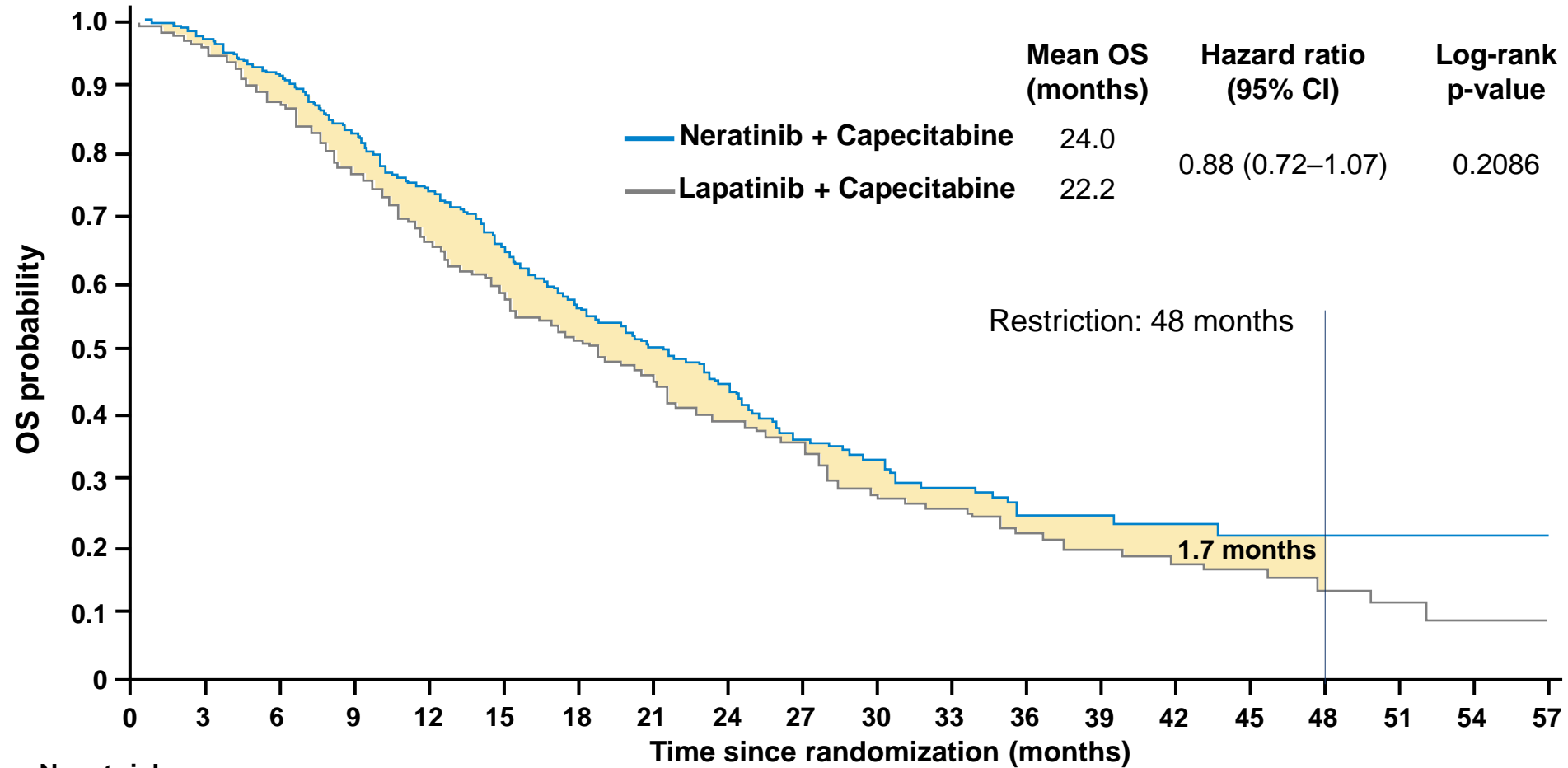
No. at risk:

N+C	307	183	113	69	54	35	20	13	9	7	3	2	2
L+C	314	183	82	39	24	9	8	3	2	2	2	2	1

Saura et al. ASCO 2019 Oral Session: Breast Cancer – Metastatic. Abstract 10002. Presented Tuesday, June 4, 2019

# Phase III Trial – Third-Line HER2+ MBC (NALA): Study Results

## OS (co-primary endpoint)



No. at risk:

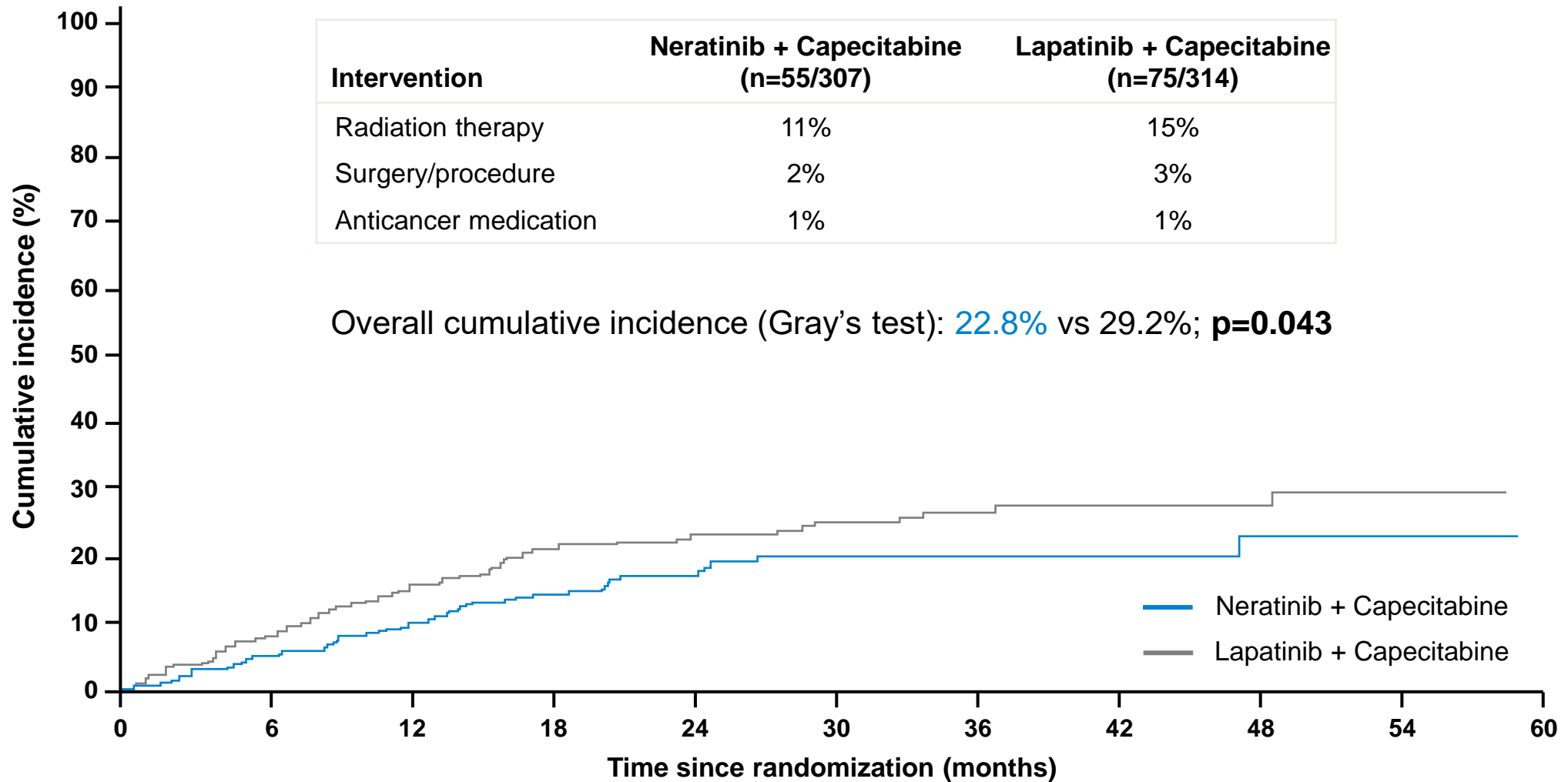
N+C	307	294	275	244	220	182	142	112	82	64	47	34	28	18	15	13	6	4	2	1
L+C	314	303	273	240	208	170	132	107	84	67	47	36	27	22	17	12	8	4	3	1

Saura et al. ASCO 2019 Oral Session: Breast Cancer – Metastatic. Abstract 10002. Presented Tuesday, June 4, 2019



# Phase III Trial – Third-Line HER2+ MBC (NALA): Study Results

## Time to intervention for CNS metastases



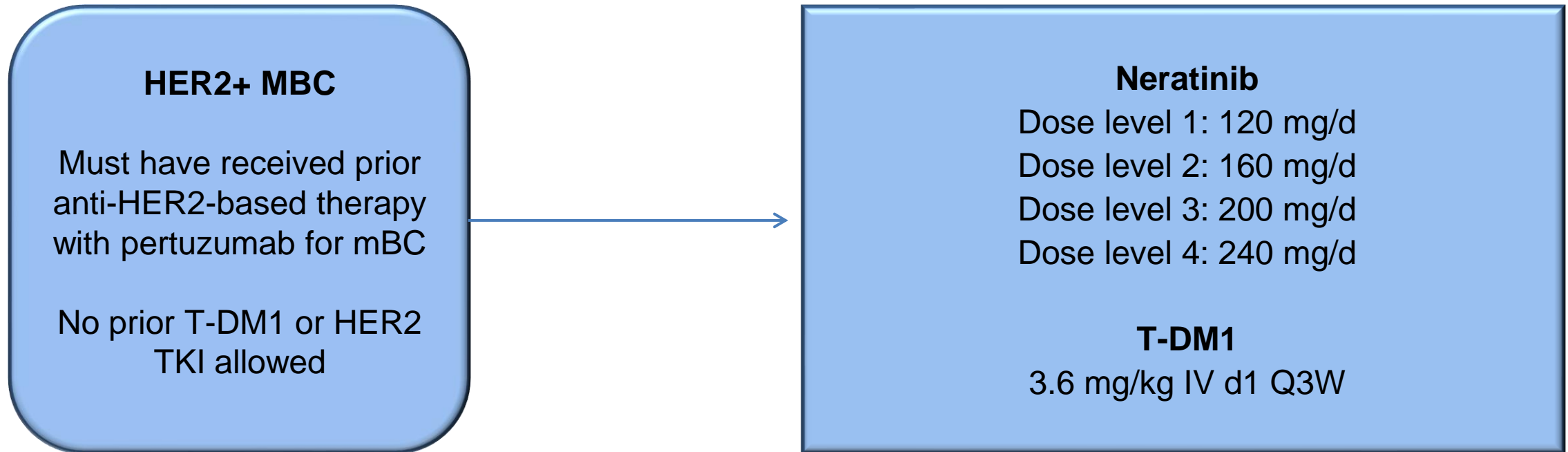
Saura et al. ASCO 2019 Oral Session: Breast Cancer – Metastatic. Abstract 10002. Presented Tuesday, June 4, 2019

# Third-Line HER2+ MBC Market Size

- Approximately 6,400 patients (US) with third-line HER2+ metastatic breast cancer and 4,700 patients (US) with fourth-line HER2+ metastatic breast cancer<sup>1</sup>

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

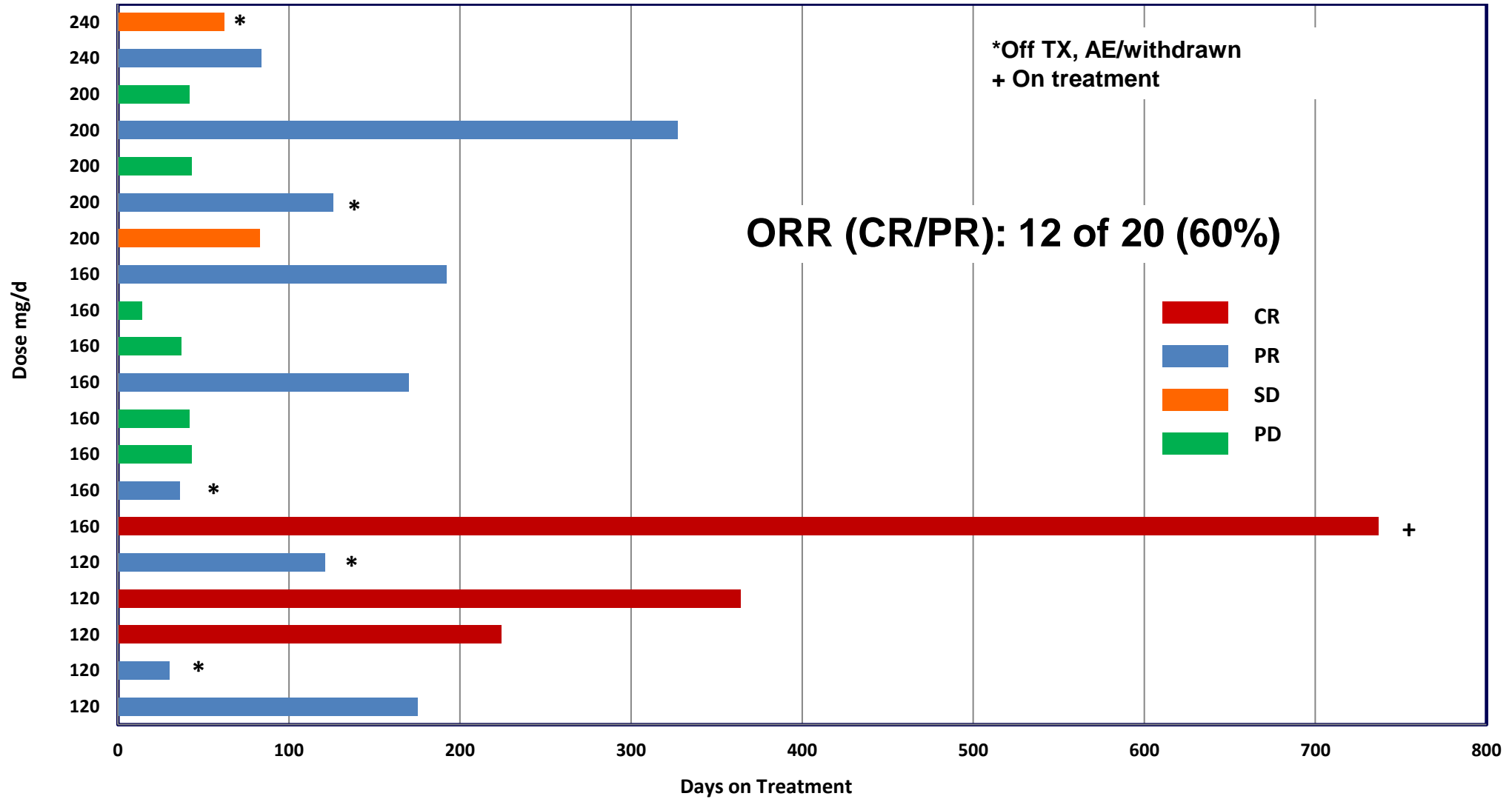
# FB-10 – Phase I/II Trial of Kadcylya (T-DM1) + Neratinib



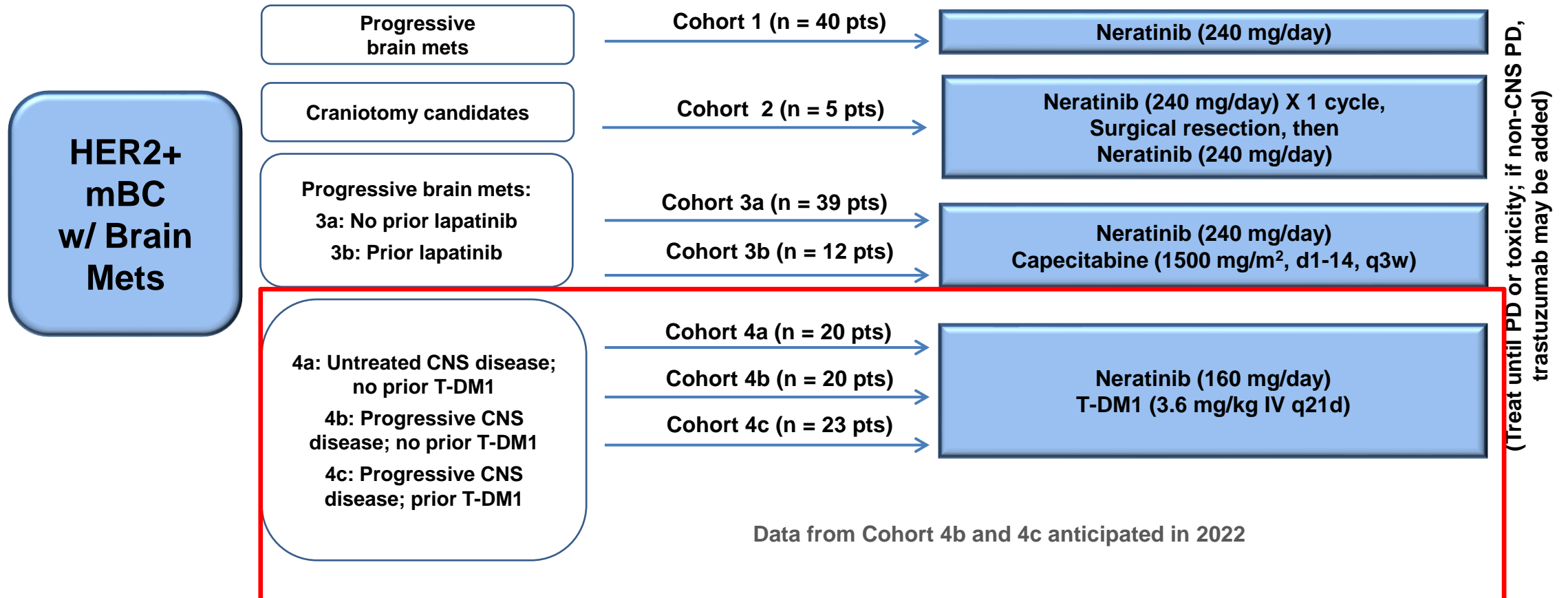
**Primary endpoint:** Phase I: Recommended dose of neratinib when given with T-DM1; Phase 2: Objective response rate (CR/PR)

**Secondary endpoint:** Clinical benefit rate (CR/PR/SD), PFS, PK, tumor biopsy for PDX model (optional)

# FB-10 – Phase I/II Trial of Kadcylya (T-DM1) + Neratinib



# TBCRC 022: Phase II Trial of HKI-272 (Neratinib) for Patients with HER2+ Breast Cancer and Brain Metastases



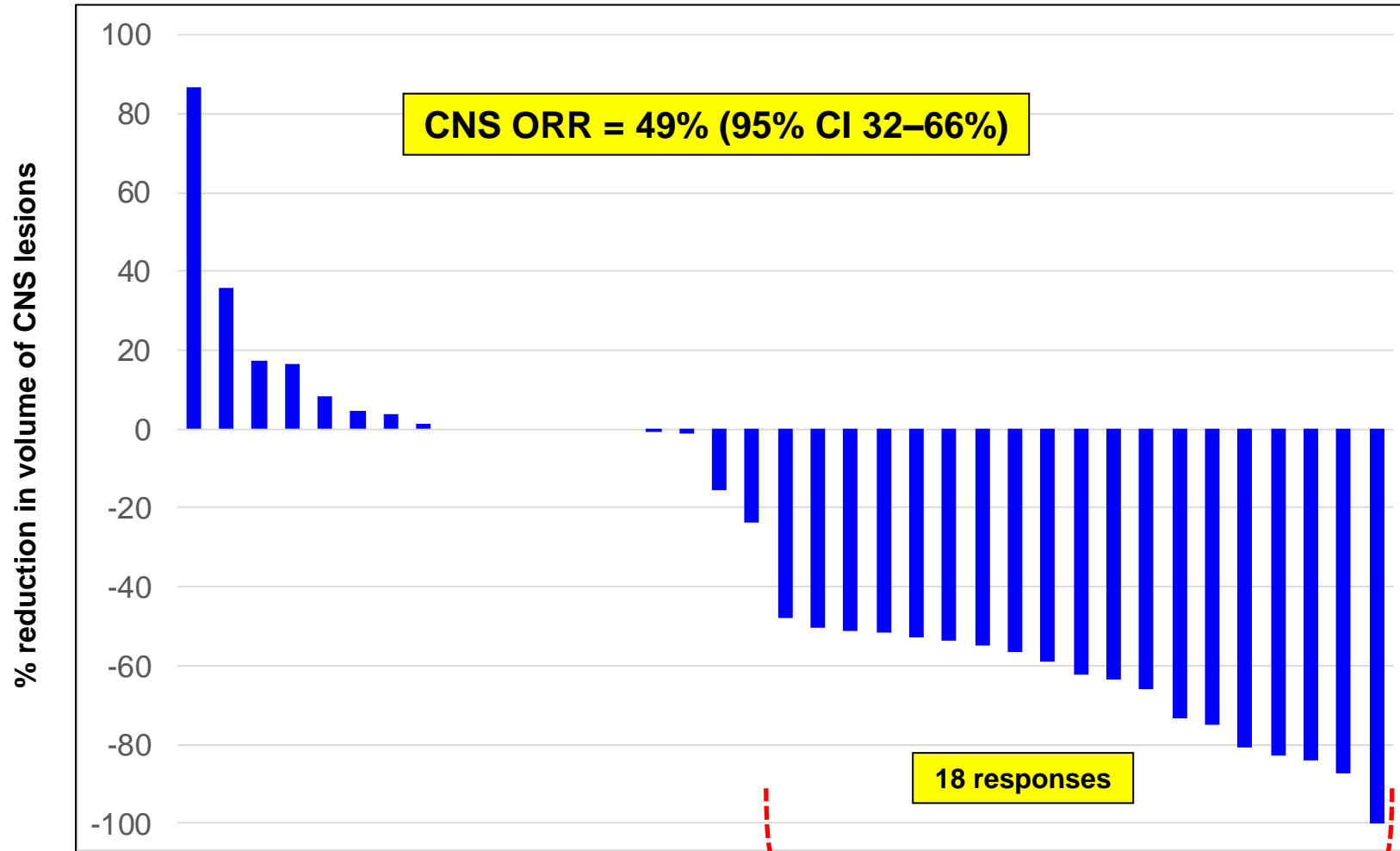
**Primary endpoint:** ORR in CNS: Cohort 1 ≥5 pts (12.5%); Cohort 3a ≥9 pts (25.7%); Cohort 3b ≥2 pts (8%); Cohort 2 PFS

**Secondary endpoints:** ORR in non-CNS, PFS, OS

# TBCRC-022 Cohort 3a

## CNS Response

Best Volumetric Response (n=31)\*



# Neratinib Included as a Treatment Option for Recurrent Breast Cancer CNS Metastases By NCCN<sup>®</sup> Guidelines<sup>1</sup>

## Guidelines updated March 2020

### Category 2A: Neratinib + Capecitabine

#### TBCRC 022<sup>2</sup>

A Phase II Trial of Neratinib and Capecitabine for Patients with HER2+ Breast Cancer Brain Metastases (NCT01494662)

### Category 2B: Neratinib + Paclitaxel

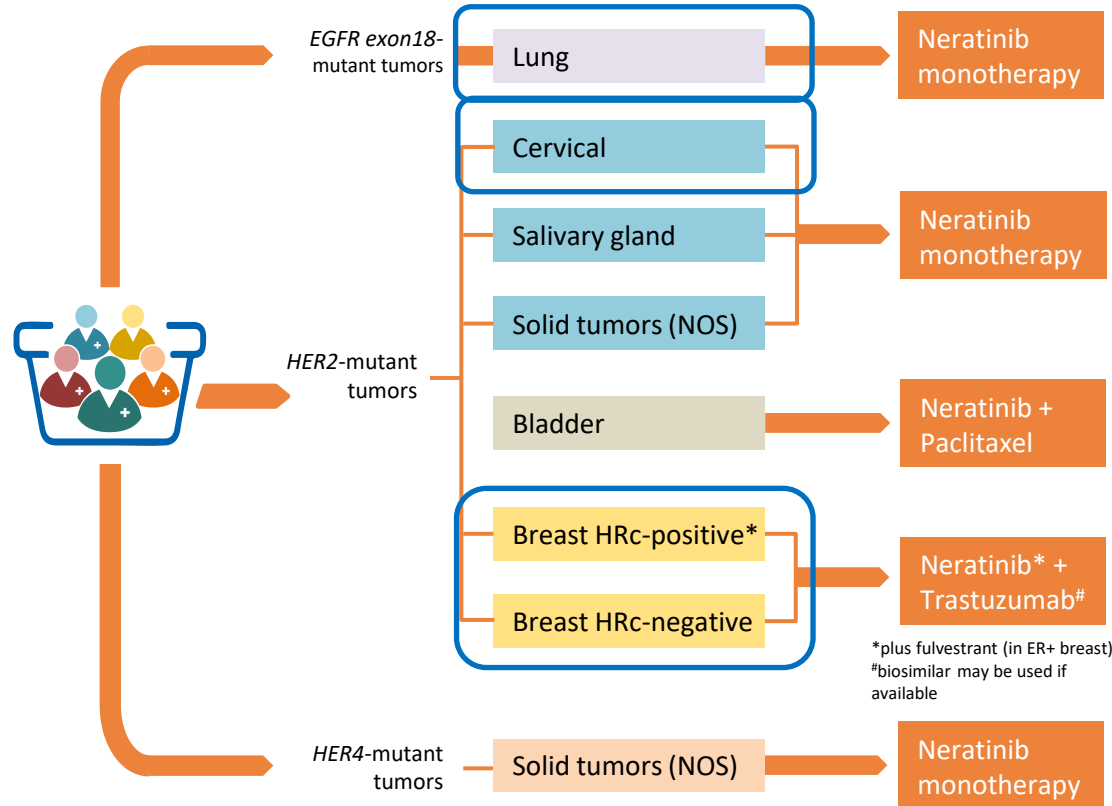
#### NEfERT-T<sup>3,4</sup>

Randomized, Multi-Center, International Study of HER2-Directed Therapy in 1st-line mBC (NCT00915018)

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1. NCCN Guidelines v 1.2018. Central Nervous System Cancers.
2. Freedman RA, et al. Presented at ASCO Annual Meeting, 2017. Abstract 1005
3. Awada A, et al. *Poster Presentation at ASCO Annual Meeting, 2015. #610.*
4. Awada A, et al. *JAMA Oncol.* 2016;2:1557-1564.

# Current SUMMIT 'Basket' Trial: Study Design



EGFR, HER2 or HER4 mutations  
(documented by local testing)

## Primary endpoint

- Objective response rate at first post-baseline tumor assessment (ORR<sub>first</sub>)

## Secondary endpoints

- ORR (confirmed)
- Clinical benefit rate (CBR)
- Progression-free survival (PFS)
- Safety
- Biomarkers

## Simon 2-stage design

- If ≥1 response in first evaluable 7 patients, expand cohort to Stage 2 (N=18)
- If ≥4 responses in Stage 2, expand or breakout

## Tumor assessments

- RECIST v1.1 (primary criteria)
- PET response criteria (RECIST non-evaluable)

## Statistical methods

- ORR<sub>first</sub>, ORR, CBR: associated 95% CI
- Median PFS: Kaplan-Meier estimate with 95% CI

## Key Inclusion Criteria

- Histologically confirmed cancers for which no curative therapy exists
- Documented EGFR exon 18, HER2 or HER4 mutation
- ECOG status of 0 to 2
- RECIST 1.1 evaluable disease (measurable or non-measurable disease): if RECIST non-measurable, evaluable by other accepted criteria

## Key Exclusion Criteria

- Prior treatment with any pan-HER TKI (eg, lapatinib, afatinib, dacomitinib, neratinib)
- Patients who are receiving any other anticancer agents
- Symptomatic or unstable brain metastases
- Women who are pregnant or breast-feeding



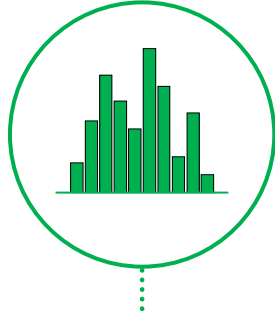
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# SUMMIT

## Breast Cancer Cohort

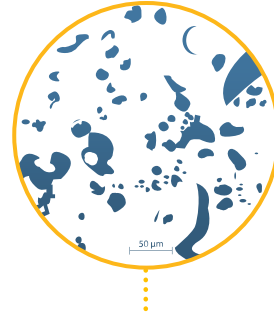


# Characteristics of *HER2*-mutant breast cancer<sup>1–8</sup>



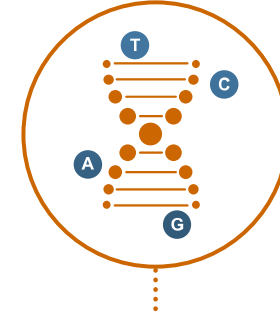
## Incidence

- 2% Primary breast cancers
- 2–4% MBC
- 8% ER+ MBC
- Up to 15% in metastatic ILC



## Histology

- Predominantly in hormone receptor-positive (luminal-A) and *HER2*-negative tumors
- Represented in all histology subtypes but enriched in lobular carcinoma



## Genomics

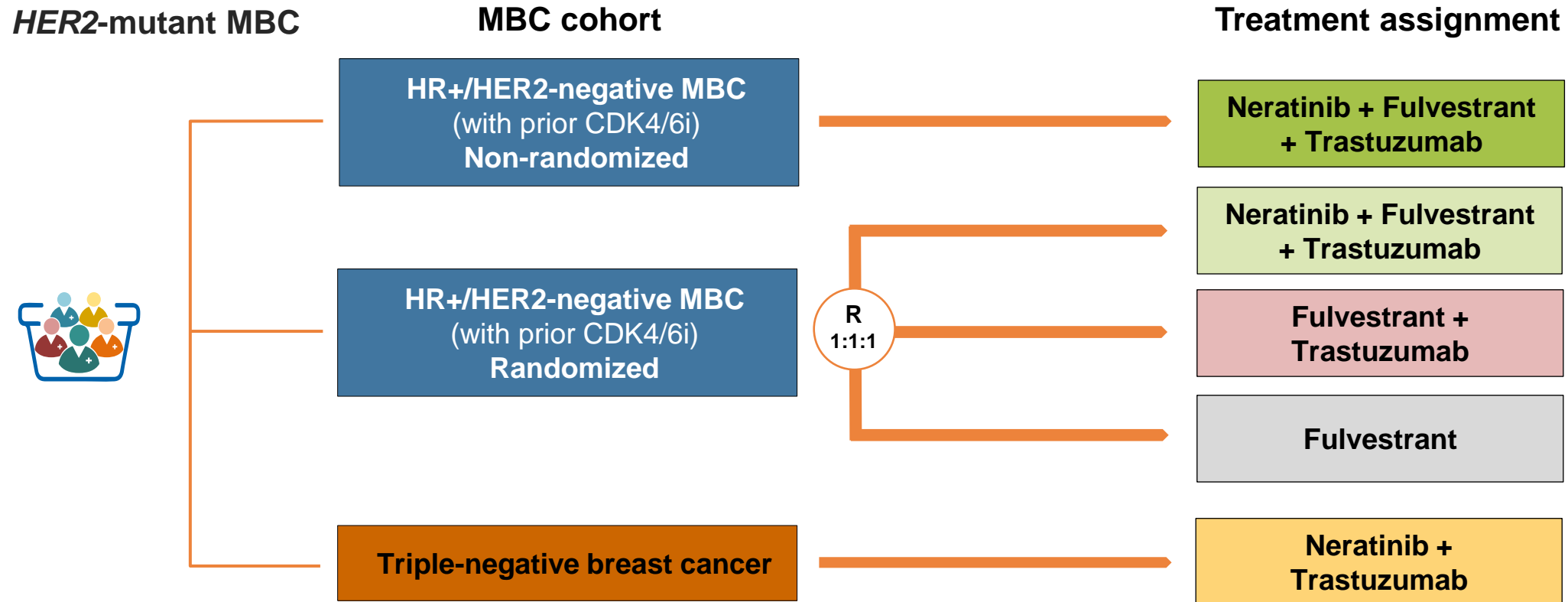
- Occur across multiple domains of the protein (KD, ECD, TMD)
- Most common variants:
  - SNVs in KD
  - *Exon 20* insertions
  - S310F/Y in ECD
- Common co-mutations include *TP53*, *PIK3CA*, *ERBB3* and *CDH1*

Abbreviations: ECD, extracellular domain; ILC, invasive lobular carcinoma; KD, kinase domain; MBC, metastatic breast cancer; SNV, single nucleotide variant; TMD, transmembrane domain

1. Bose et al. *Cancer Discovery* 2013; 2. Razavi et al. *Cancer Cell* 2018; 3. Nayar et al. *Nat Genet* 2019;51; 4. Croessmann et al. *Clin Cancer Res* 2019  
5. Hyman et al. *Nature* 2018; 6. Smyth et al. *Cancer Discov* 2020; 7. Ma et al. *Clin Cancer Res* 2017; 8. Jhaveri et al. *SABCS* 2020

# Current SUMMIT breast cancer cohorts

- Added inclusion criteria for HR+ cohort to reflect current standard of care: prior CDK4/6 inhibitor therapy



- **Design:** Simon 2-stage
  - If  $\geq 1$  response in first evaluable 7 patients, expand cohort to Stage 2 (N=18)
  - If  $\geq 4$  responses in Stage 2, expand up to 50 patients
- **Primary endpoint:** HR+: confirmed objective response rate (ORR, RECIST v1.1)<sup>a</sup>; TNBC: ORR at first post-baseline tumor assessment (ORR<sub>first</sub>), RECIST v1.1 or modified PERCIST
- **Key secondary endpoint:** Confirmed ORR<sup>b</sup>

<sup>a</sup>ORR by independent review was a primary endpoint in the randomized HR+ cohorts  
<sup>b</sup>ORR by investigator review was a secondary endpoint in the randomized HR+ cohorts

# HR+ non-randomized N+F+T w prior CDK4/6i: Efficacy findings

Characteristics	Non-randomized (N+F+T, n=26)
<b>Objective response (confirmed CR/PR)<sup>a</sup>, n (%)</b>	12 (46.2)
CR	0
PR	12 (46.2)
<b>Best overall response (confirmed or unconfirmed PR or CR), n (%)</b>	15 (57.7)
<b>Median DOR<sup>b</sup>, months (95% CI)</b>	14.4 (6.4–NE)
<b>Clinical benefit<sup>c</sup>, n (%)</b>	15 (57.7)
<b>Median PFS, months (95% CI)</b>	8.2 (4.0–15.1)
<b>Median duration of treatment, months (range)</b>	8.7 (1.0–22.1)

Data cut-off: 10 September 2021. Tumor response based on: investigator tumor assessments (RECIST v1.1) for HR+ cohorts

CR, confirmed response; PR, partial response; CI, confidence interval; DOR, duration of response; NE, not estimable; PFS, progression-free survival

<sup>a</sup>Objective response defined as either a complete or partial response that is confirmed no less than 4-weeks after the criteria for response are initially met; <sup>b</sup>Kaplan-Meier analysis

<sup>c</sup>Clinical benefit is defined as confirmed CR or PR or stable disease (SD) for ≥24 weeks (within +/- 7-day visit window)

# HR+ randomized cohorts: Efficacy findings

## Neratinib appears to be critical for inhibition of *HER2* mutations

Randomized cohort

Characteristics	Randomized cohort		
	(N+F+T, n=7)	(F+T, n=7)	(F, n=7)
<b>Objective response (confirmed CR/PR)<sup>a</sup>, n (%)</b>	2 (28.6)	0	0
CR	1 (14.3)	0	0
PR	1 (14.3)	0	0
<b>Best overall response (confirmed or unconfirmed PR or CR), n (%)</b>	3 (42.9)	0	0
<b>Median DOR<sup>b</sup>, months (95% CI)</b>	NE	NE	NE
<b>Clinical benefit<sup>c</sup>, n (%)</b>	2 (28.6)	0	0
<b>Median PFS, months (95% CI)</b>	6.2 (2.1–NE)	3.9 (1.9–4.1)	4.1 (1.6–4.1)
<b>Median duration of treatment, months (range)</b>	5.0 (0.7–13.2)	3.5 (0.8–4.1)	2.1 (0.7–4.1)

Data cut-off: 10 September 2021. Tumor response based on: investigator tumor assessments (RECIST v1.1) for HR+ cohorts

CR, confirmed response; PR, partial response; CI, confidence interval; DOR, duration of response; NE, not estimable; PFS, progression-free survival

<sup>a</sup>Objective response defined as either a complete or partial response that is confirmed no less than 4-weeks after the criteria for response are initially met; <sup>b</sup>Kaplan-Meier analysis

<sup>c</sup>Clinical benefit is defined as confirmed CR or PR or stable disease (SD) for ≥24 weeks (within +/- 7-day visit window)

# TNBC cohort: baseline characteristics and efficacy

Baseline characteristics	TNBC (N+T, n=18)
<b>ECOG performance status, n (%)</b>	
0	9 (50.0)
1	9 (50.0)
<b>Histological type, n (%)</b>	
Lobular	3 (16.7)
Ductal	7 (38.9)
Mixed Ductal and Lobular	0
Other	8 (44.4)
<b>Median number of prior anti-cancer regimens (range)</b>	3.5 (1–7)

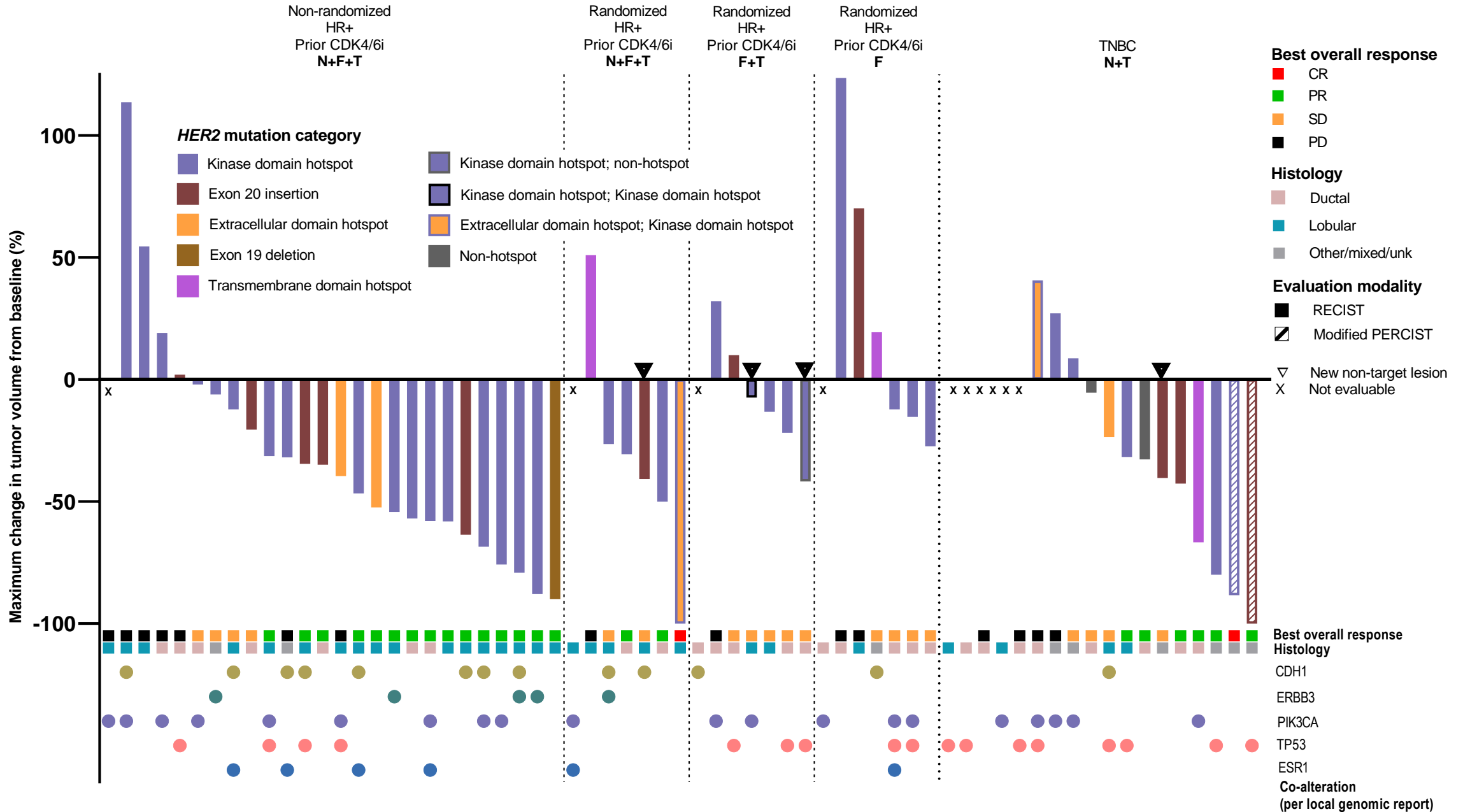
Efficacy	TNBC (N+T, n=18)
<b>Objective response (confirmed CR/PR)<sup>a</sup>, n (%)</b>	6 (33.3)
CR	1 (5.6)
PR	5 (27.8)
<b>Best overall response (confirmed or unconfirmed PR or CR), n (%)</b>	7 (38.9)
<b>Median DOR<sup>b</sup>, months (95% CI)</b>	NE
<b>Clinical benefit<sup>c</sup>, n (%)</b>	7 (38.9)
<b>Median PFS, months (95% CI)</b>	6.2 (2.1–8.2)
<b>Median duration of treatment, months (range)</b>	4.4 (0.3–15.4)

Data cut-off: 10 September 2021. Tumor response based on: investigator tumor assessments (RECIST v1.1 or modified PERCIST for TNBC cohort; TNBC cohort analysis ongoing CR, confirmed response; PR, partial response; CI, confidence interval; DOR, duration of response; NE, not estimable; PFS, progression-free survival

<sup>a</sup>Objective response defined as either a complete or partial response that is confirmed no less than 4-weeks after the criteria for response are initially met; <sup>b</sup>Kaplan-Meier analysis

<sup>c</sup>Clinical benefit is defined as confirmed CR or PR or stable disease (SD) for ≥24 weeks (within +/- 7-day visit window)

# Change in tumor size (target lesion) and characteristics



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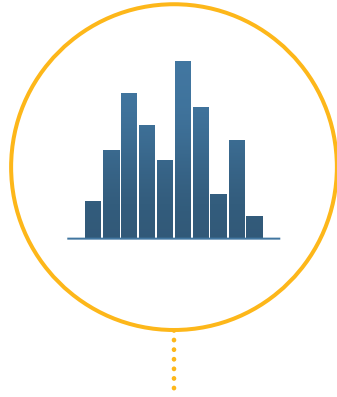
# SUMMIT

## Cervical Cancer Cohort





# Characteristics of *HER2*-Mutant Cervical Cancer



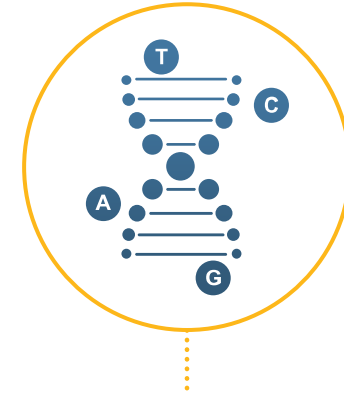
## Incidence

- 5% metastatic cervical cancers
- May be negatively prognostic for survival



## Histology

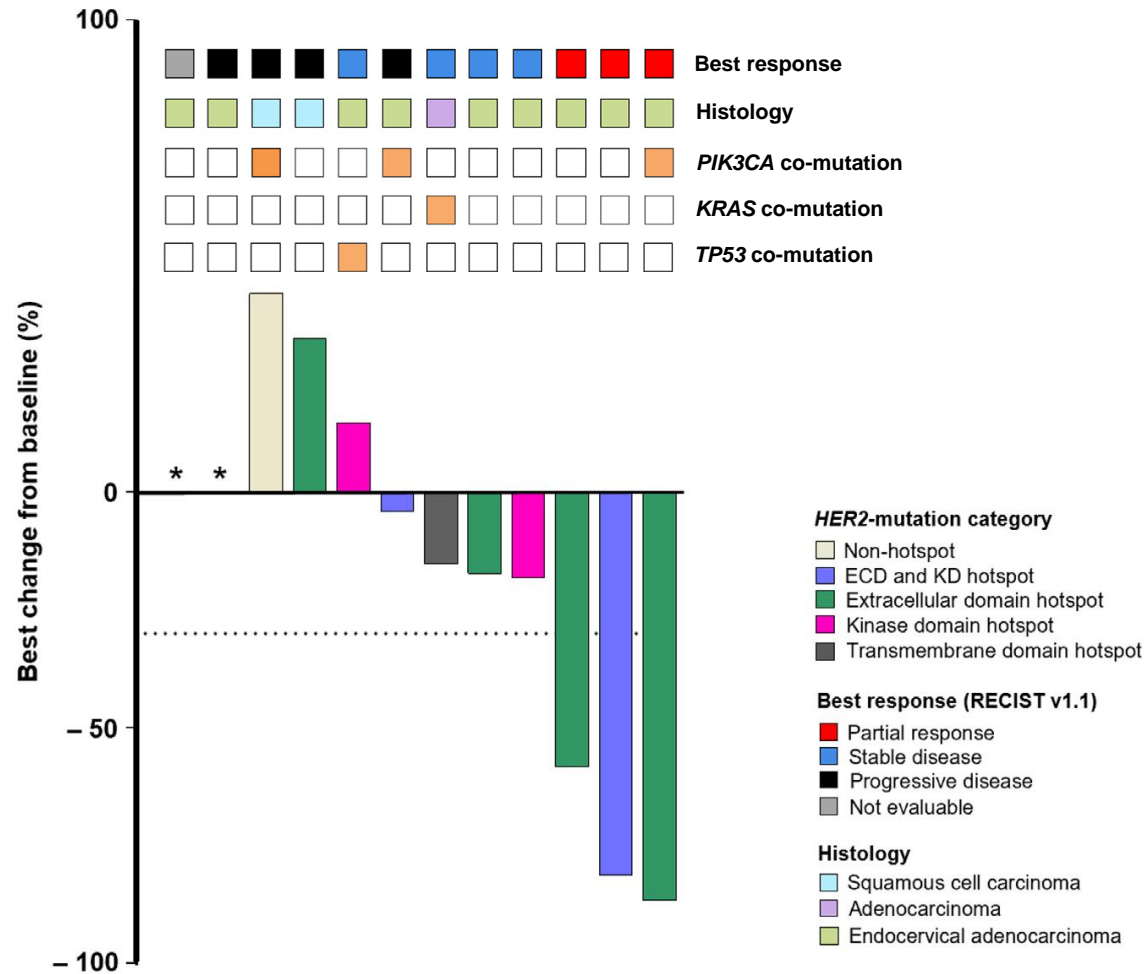
- Enriched in adenocarcinomas
- High occurrence in HPV+ tumors



## Genomics

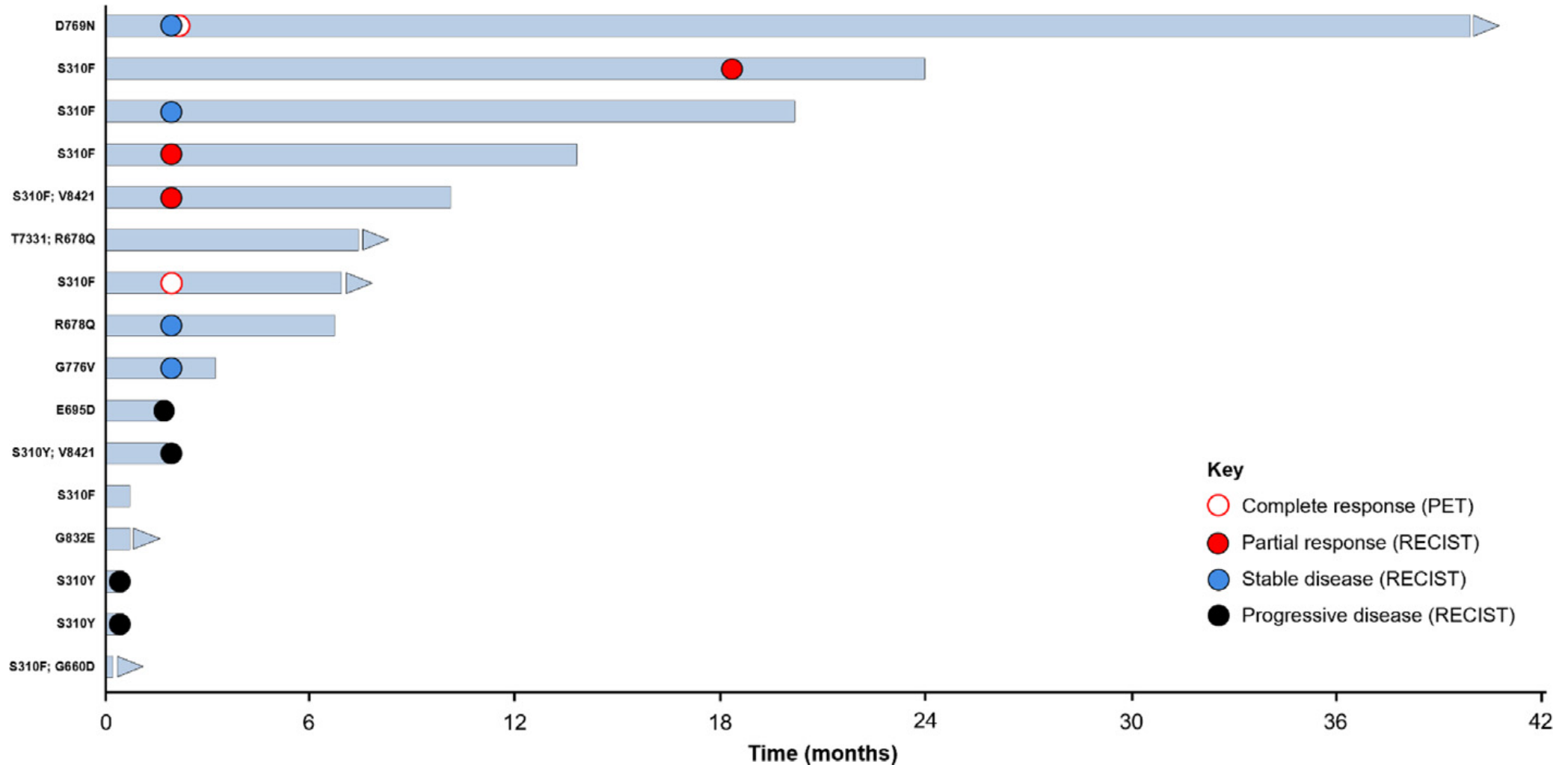
- Most common *HER2*<sup>mut</sup> is S310 extracellular domain hotspot mutation
- Usually exclusive to *HER2* amplifications
- Most common co-mutations include *TP53*, *PIK3CA*

# Neratinib Monotherapy Results Published in Gynecologic Oncology



Gynecologic Oncology, 2020

# Neratinib Monotherapy Results Published in Gynecologic Oncology



Gynecologic Oncology, 2020

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# SUMMIT (PUMA-NER-5201) Basket Trial

*EGFR* exon 18 lung cancer cohort update



# EGFR Exon 18-Mutant Lung Cancer Cohort Receiving Neratinib Monotherapy: Efficacy Summary

Parameter	Efficacy evaluable patients (n=11)	TKI Pre-Treated (n=10)
Objective response (confirmed), <sup>a</sup> n	<b>4</b>	<b>4</b>
CR	0	0
PR	4	4
Objective response rate, % (95% CI)	<b>36 (11–69)</b>	<b>40 (12–74)</b>
Best overall response, n	<b>6</b>	<b>6</b>
CR	0	0
PR	6	6
Best overall response rate, % (95% CI)	<b>54 (23–83)</b>	<b>60 (26–88)</b>
Median DOR, <sup>b</sup> months (95% CI)	<b>7.5 (4.0–NE)</b> <b>(1.9*, 4.0, 7.5, 9.2*)</b>	<b>7.5 (4.0–NE)</b> <b>(1.9*, 4.0, 7.5, 9.2*)</b>
Clinical benefit, <sup>c</sup> n	<b>8</b>	<b>8</b>
CR or PR	4	4
SD ≥16 weeks	4	4
Clinical benefit rate, % (95% CI)	<b>73 (39–94)</b>	<b>80 (44–97)</b>
Median PFS time to event, months (95% CI)	<b>6.9<sup>b</sup> (2.1–NA)</b>	<b>9.1 (3.7–NA)</b>

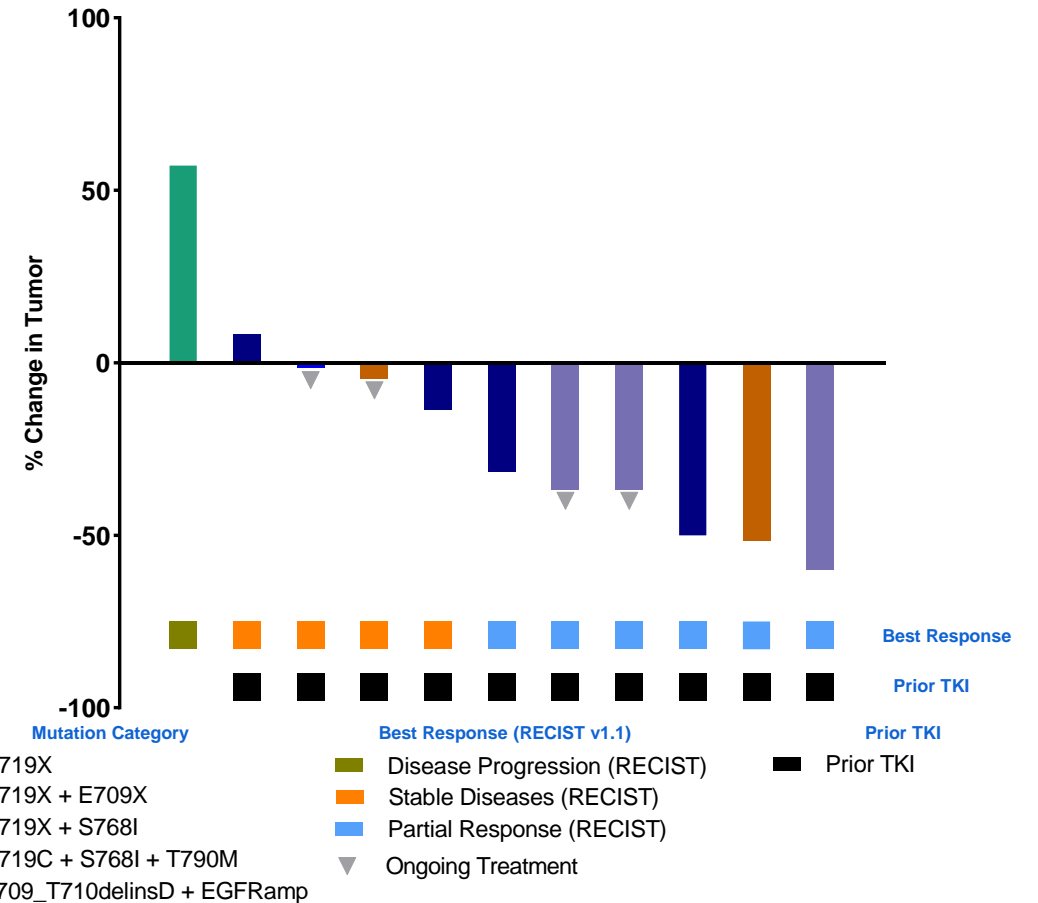
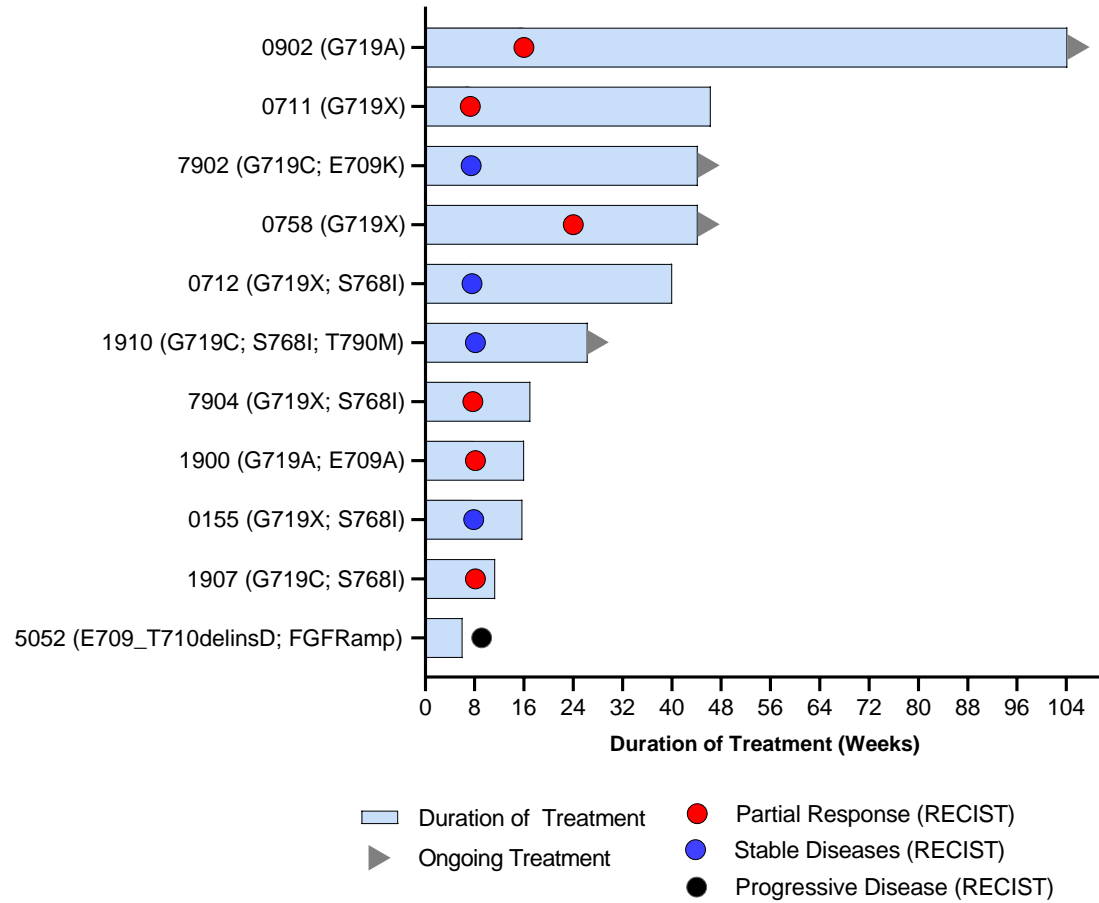
<sup>a</sup> Objective response rate (ORR) is defined as either a complete or partial response that is confirmed no less than 4-weeks after the criteria for response are initially met

<sup>b</sup> Kaplan-Meier analysis in safety population. <sup>c</sup> Clinical benefit rate (CBR) is defined as confirmed CR or PR or stable disease (SD) for ≥16 weeks (within +/- 7-day visit window)

DOR, duration of response; PFS, progression-free survival, \* response ongoing

Data cut-off: 21-Aug-2020

# EGFR Exon 18-Mutant Lung Cancer Cohort Receiving Neratinib Monotherapy: Treatment Duration, Best Response and Best Change in Tumor



Data cut-off: 21-Aug-2020

# Historical Response Rates of Afatinib in NSCLC Patients With *EGFR* Exon 18 Mutations (G719X)

**Table 3. Response Rates With Afatinib in Patients With NSCLC Harboring Uncommon Mutations**

Mutation Type	CR, n (%)	PR, n (%)	SD, n (%)	PD, n (%)	DCR, n (%)	ORR, n (%)	DoR, Mo (95% CI)
<b>EGFR TKI-naïve patients</b>							
Major uncommon mutation (n = 110)	5 (4.5)	61 (55.5)	35 (31.8)	9 (8.2)	101 (91.8)	66 (60.0)	17.1 (11.0-20.8)
TKI-naïve patients → G719X (n = 55)	4 (7.3)	31 (56.4)	16 (29.1)	4 (7.3)	51 (92.7)	35 (63.4)	17.1 (10.3-22.0)
L861Q (n = 47)	0 (0.0)	28 (59.6)	14 (29.8)	5 (10.6)	42 (89.4)	28 (59.6)	13.8 (7.4-20.6)
S768I (n = 8)	1 (12.5)	4 (50.0)	3 (37.5)	0 (0.0)	8 (100.0)	5 (62.5)	NR (15.9-NR)
Compound (n = 35)	0 (0.0)	27 (77.1)	5 (14.3)	3 (8.6)	32 (91.4)	27 (77.1)	16.6 (13.8-18.7)
With major uncommon mutation (n = 23)	0 (0.0)	18 (78.3)	4 (17.4)	1 (4.3)	22 (95.7)	18 (78.3)	17.1 (14.7-NR)
Exon 20 insertion (n = 70)	2 (2.9)	15 (21.4)	41 (58.6)	12 (17.1)	58 (82.9)	17 (24.3)	11.9 (5.4-26.7)
T790M (n = 25)	0 (0.0)	6 (24.0)	13 (52.0)	6 (24.0)	19 (76.0)	6 (24.0)	4.7 (3.8-11.0)
Others (n = 23)	0 (0.0)	15 (65.2)	5 (21.7)	3 (13.0)	20 (87.0)	15 (65.2)	9.0 (3.5-11.9)
<b>EGFR TKI-pretreated patients</b>							
Major uncommon mutation (n = 32)	0 (0.0)	8 (25.0)	14 (43.8)	10 (31.3)	22 (68.8)	8 (25.0)	4.9 (2.0-18.0)
TKI-pre-treated patients → G719X (n = 19)	0 (0.0)	2 (10.5)	10 (52.6)	7 (36.8)	12 (63.2)	2 (10.5)	10.0 (2.0-18.0)
L861Q (n = 11)	0 (0.0)	5 (45.5)	3 (27.3)	3 (27.3)	8 (72.7)	5 (45.5)	4.4 (4.3-8.4)
S768I (n = 2)	0 (0.0)	1 (50.0)	1 (50.0)	0 (0.0)	2 (100.0)	1 (50.0)	NR
Compound (n = 21)	0 (0.0)	6 (28.6)	10 (47.6)	5 (23.9)	16 (76.2)	6 (28.6)	16.7 (9.9-21.8)
With major uncommon mutation (n = 8)	0 (0.0)	3 (37.5)	3 (37.5)	2 (25.0)	6 (75.0)	3 (37.5)	16.7 (9.9-16.7)
Exon 20 insertion (n = 21)	0 (0.0)	3 (14.3)	9 (42.9)	9 (42.9)	12 (57.1)	3 (14.3)	3.7 (2.7-10.1)
T790M (n = 64)	0 (0.0)	12 (18.8)	31 (48.4)	21 (32.8)	43 (67.2)	12 (18.8)	6.1 (2.6-7.9)
Others (n = 25)	0 (0.0)	9 (36.0)	8 (32.0)	8 (32.0)	17 (68.0)	9 (36.0)	6.3 (0.8-11.3)

CI, confidence interval; CR, complete response; DCR, disease control rate; DoR, duration of response; PD, progressive disease; ORR, overall response rate; PR, partial response; SD, stable disease; TKI, tyrosine kinase inhibitor; NR, not reported.

# Puma – Expected Milestones

- Report Phase II data from cohort of patients in SUMMIT basket trial of neratinib in non-small cell lung cancer patients with *EGFR* exon 18 mutations (H2 2022)
- Conduct a meeting with the FDA to discuss the registration pathway of neratinib in HER2-mutated HR-positive breast cancer (H2 2022)
- Conduct a meeting with the FDA to discuss the potential for an accelerated approval pathway for neratinib in non-small cell lung cancer patients with *EGFR* exon 18 mutations who have been previously treated with an EGFR tyrosine kinase inhibitor (2022)
- Report Phase II TBCRC-022 trial from Cohort 4B and 4C of the combination of Kadcylla + neratinib in patients with HER2+ breast cancer with brain metastases who have previously been treated with Kadcylla (H2 2022)
- Report Phase II data from SUMMIT trial in cervical cancer patients with HER2 mutations (H2 2022)



# Intellectual Property

- 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 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

# 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, Pharma.D.

**Chief Scientific Officer**

– *Proteolix, Novacea, Genentech*

## Douglas Hunt

**Senior Vice President, Regulatory Affairs**

– *ArmaGen, Baxter Healthcare, Amgen*

# Board of Directors

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*Chairman, Chief Executive Officer, President, Founder, Puma Biotechnology, Inc.*

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*Chief Medical Officer, ESSA Pharmaceuticals; NanoString; Cleave Biosciences; Nodality; Amgen; Biogen; SmithKline*

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*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: PBYY
- Cash, cash equivalents and marketable securities at June 30, 2022: ~\$60.8 million
- Net income in Q2 2022: ~\$9.4 million
- Cash burn in Q2 2022: ~\$14 million
- 2022 Guidance
  - 2022 NERLYNX revenue guidance: \$180 to \$190 million
  - 2022 NERLYNX royalty guidance: \$27 to \$30 million
  - 2022 net income guidance: \$6 to \$10 million
- Private placement (March 2022)
  - 3,584,228 shares issued to Alan Auerbach and Athyrium Capital Management
- Shares issued and outstanding: 45.6 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
- Additional potential indications:
  - HER2+ metastatic breast cancer with brain metastases
  - HER2-mutated breast cancer
  - HER2-mutated cervical cancer
  - EGFR exon 18-mutated non-small cell lung cancer
  - HER2-mutated solid tumors
- Retain full U.S. commercial rights to NERLYNX<sup>®</sup>
- Large initial market opportunity with additional label expansion potential

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# Puma Biotechnology

**H.C. Wainwright 24<sup>th</sup> Annual Global Investment Conference**

September 2022

