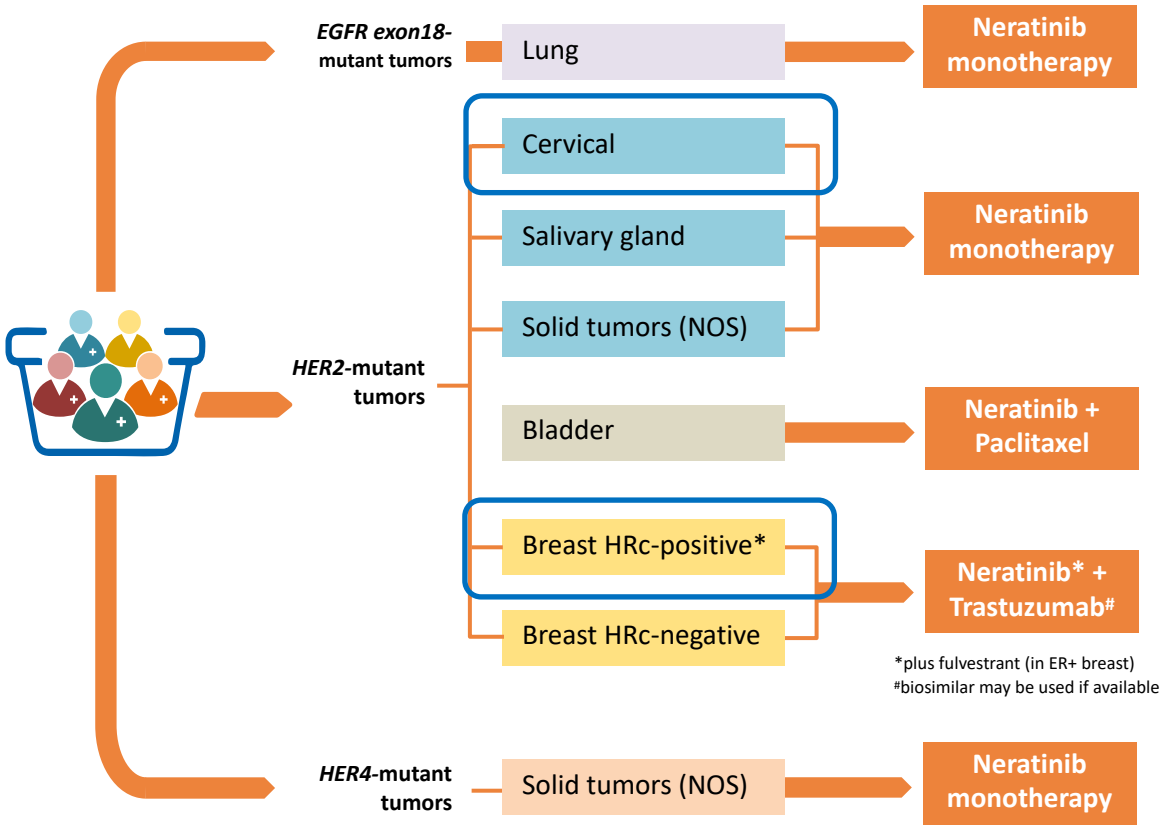
Puma Biotechnology
SUMMIT Trial
Update on Regulatory Strategy

November 6, 2019

Forward-Looking Safe Harbor Statement

This presentation contains forward-looking statements, including statements regarding ongoing clinical studies and potential regulatory approvals for NERLYNX®. All statements other than historical facts are forward–looking statements and are based on the current expectations, forecasts and assumptions of Puma Biotechnology, Inc. ("Puma"). Forward–looking statements involve risks and uncertainties that could cause Puma's actual results to differ materially from the anticipated results and expectations expressed in these forward-looking statements. These risk and uncertainties are identified in Puma's Annual Report on Form 10-K for the year ended December 31, 2018 and any subsequent documents Puma files with the Securities and Exchange Commission. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof, and you should not rely on these forward-looking statements as representing Puma's views as of any date subsequent to the date of this presentation. Puma assumes no obligation to update these forward-looking statements, except as required by law.

Current SUMMIT 'Basket' Trial: Study Design



*plus fulvestrant (in ER+ breast)
#biosimilar may be used if available

EGFR, HER2 or _HER4_ mutations
(documented by local testing)

Primary endpoint
- Objective response rate at first post-baseline tumor assessment (ORR_{first})

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_{first}, 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

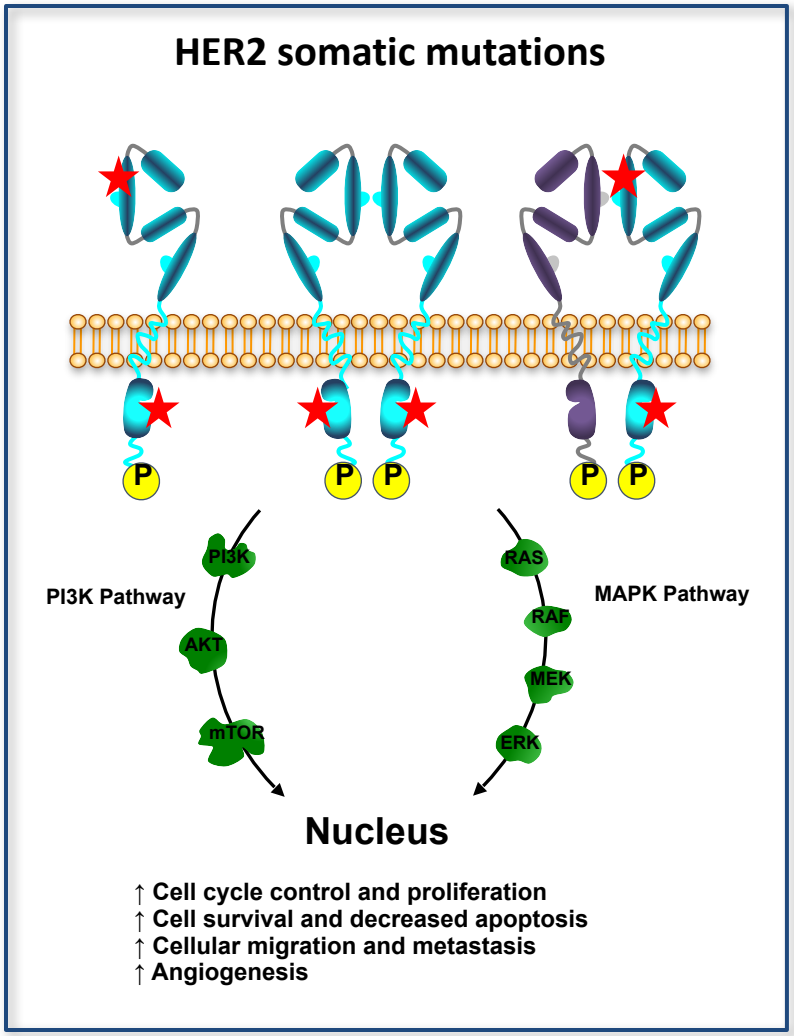
Clinical Trials.gov Identifier NCT01953926

SUMMIT

Hormone Receptor Positive Breast Cancer Cohort

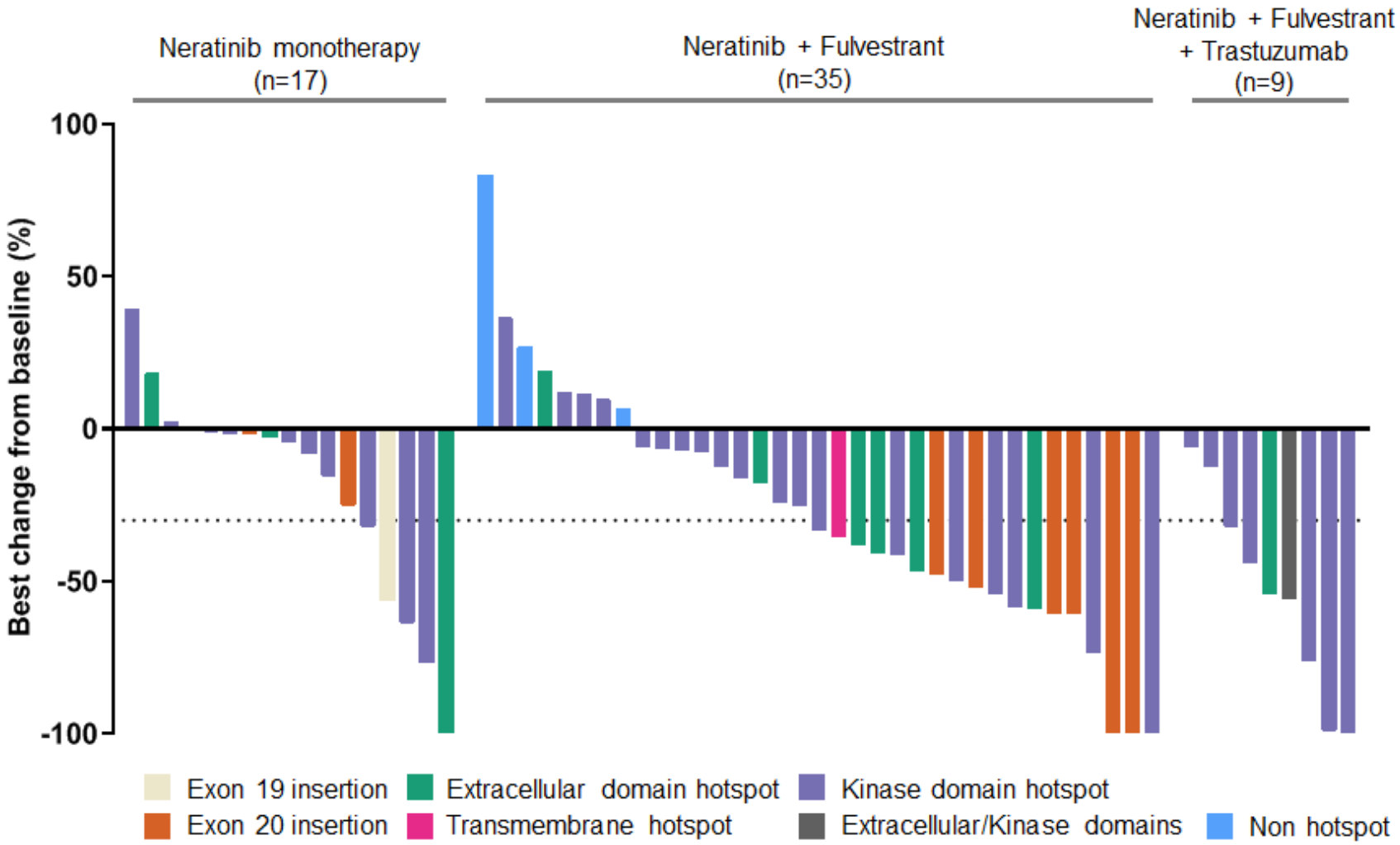
Somatic Mutations in HER2 (ERBB2) in Hormone Receptor Positive Breast Cancer

- **Incidence:**
  - 7-9%, pre-treated ER+ MBC[1]
- **Tumor characteristics:**
  - usually mutually exclusive to HER2 amplifications
- **Preclinical evidence of oncogenic activity:**
  - constitutive activation of intracellular kinase and downstream signaling pathways[2]
  - increased cell proliferation and tumor growth[2]
  - Cross-talk occurs between ER and HER2 mutation (modified SUMMIT trial to add fulvestrant to ER positive patients)
  - HER2 amplification seen as potential mechanism of resistance to neratinib plus fulvestrant (modified SUMMIT trial to add trastuzumab to neratinib plus fulvestrant in ER positive patients)

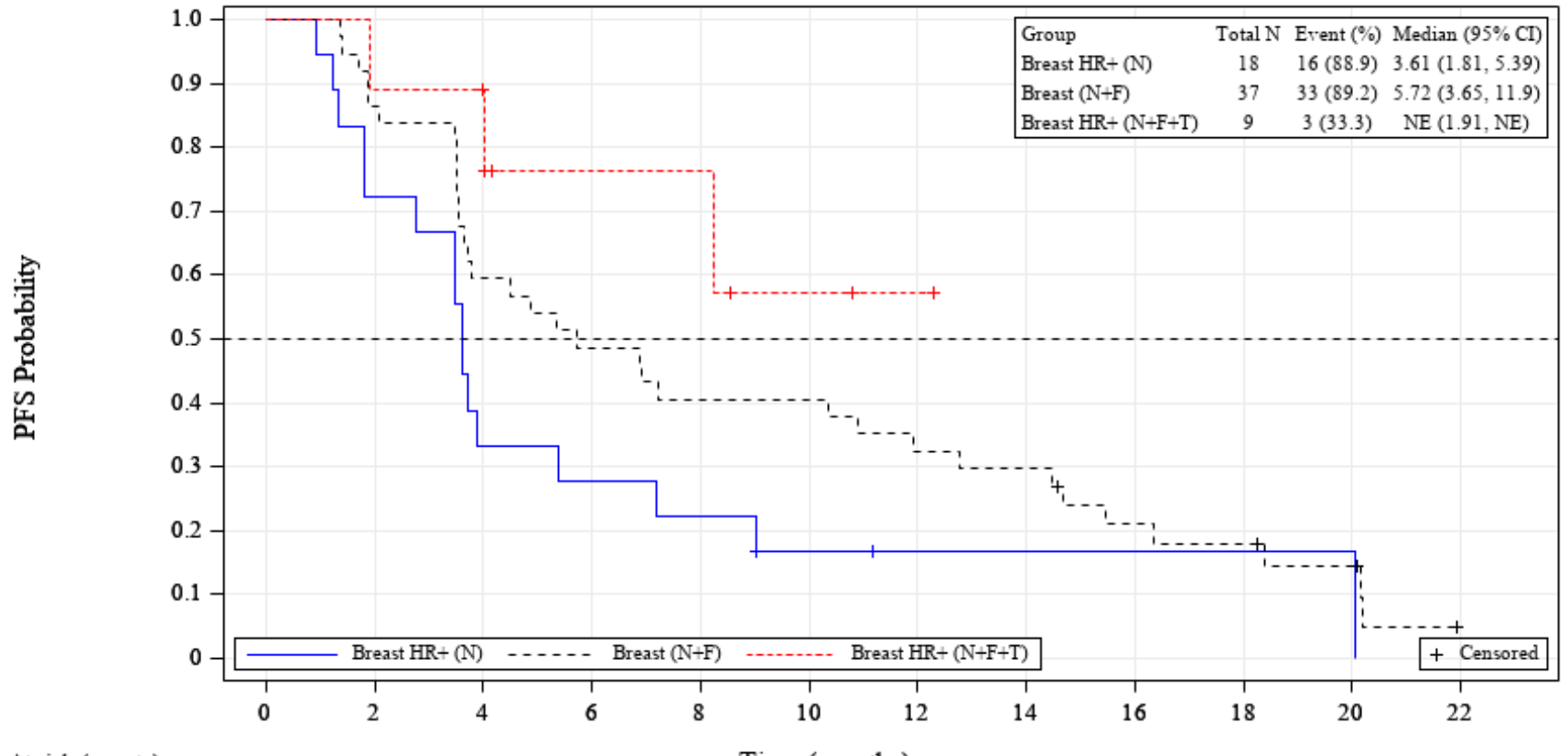


[1]Wagle et al, ASCO 2016; [2]Bose et al, Cancer Disc. 2013

Maximal Change in Tumor in RECIST Measurable HR positive/HER2-negative, HER2mut MBC Subjects Receiving Neratinib Monotherapy, N+F, or N+F+T and Grouped by Treatment Type and HER2mut Type



Kaplan Meier Plot of Progression Free Survival for Breast Cancer Cohorts in SUMMIT (Efficacy Evaluable Population - HR positive/HER2-negative, HER2mut MBC Cohort and with RECIST Tumor Assessment)



At risk (events)												
Breast HR+ (N)	18 (0)	13 (5)	6 (12)	5 (13)	4 (14)	2 (15)	1 (15)	1 (15)	1 (15)	1 (15)	1 (15)	0 (16)
Breast (N+F)	37 (0)	32 (5)	22 (15)	18 (19)	15 (22)	15 (22)	12 (25)	11 (26)	7 (29)	6 (30)	4 (31)	0 (33)
Breast HR+ (N+F+T)	9 (0)	8 (1)	7 (1)	4 (2)	4 (2)	2 (3)	1 (3)	0 (3)				

Proposed Amendment to Breast Cancer Cohort in SUMMIT for HR positive/HER2-negative, HER2mut MBC Cohort to Support Accelerated Approval

***HER2* mutations**
(documented by local testing)

Primary endpoint
- Objective response rate

Secondary endpoints
- DOR

Simon 2-stage design

Proposed assessment criteria consistent with original 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

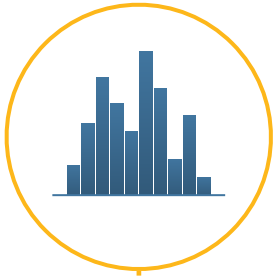
Tumor assessments
- RECIST v1.1 (primary criteria)

Puma to schedule pre NDA meeting with FDA after initial Simon 2 stage results to discuss potential for accelerated approval (anticipated Q4 2020-Q2 2021)

SUMMIT

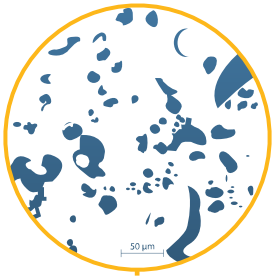
Cervical Cancer Cohort

Characteristics of *HER2* Mutant Cervical Cancer



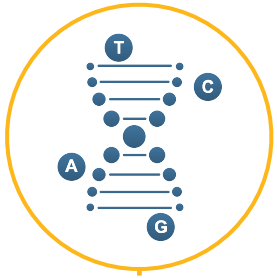
Incidence

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



Histology

- Enriched in adenocarcinomas
- High occurrence in HPV+ tumors

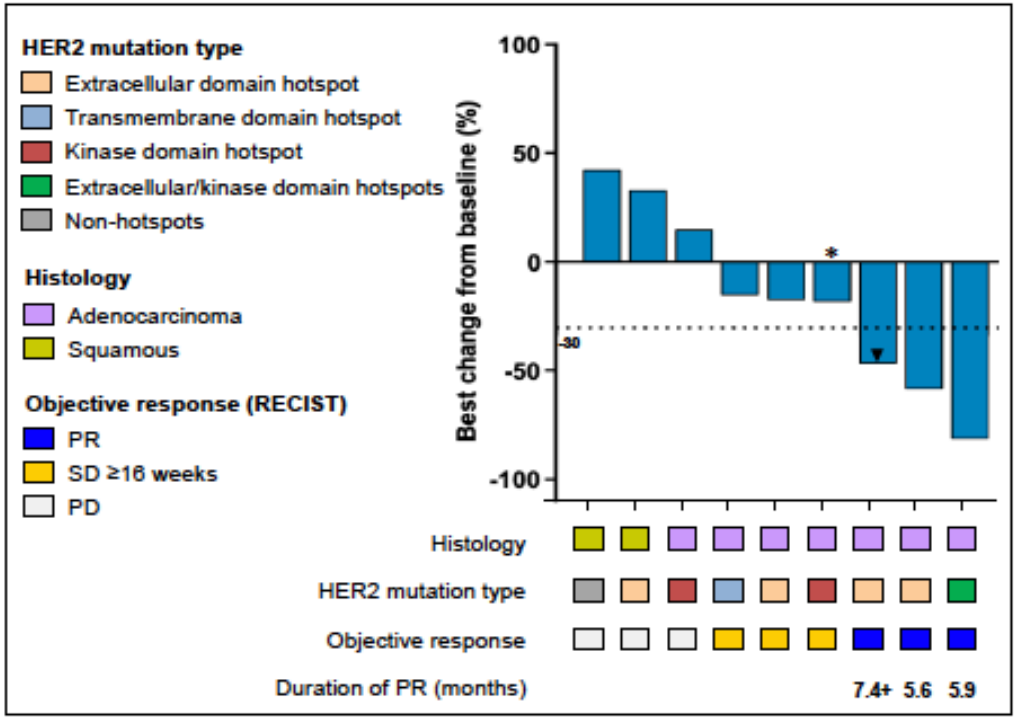


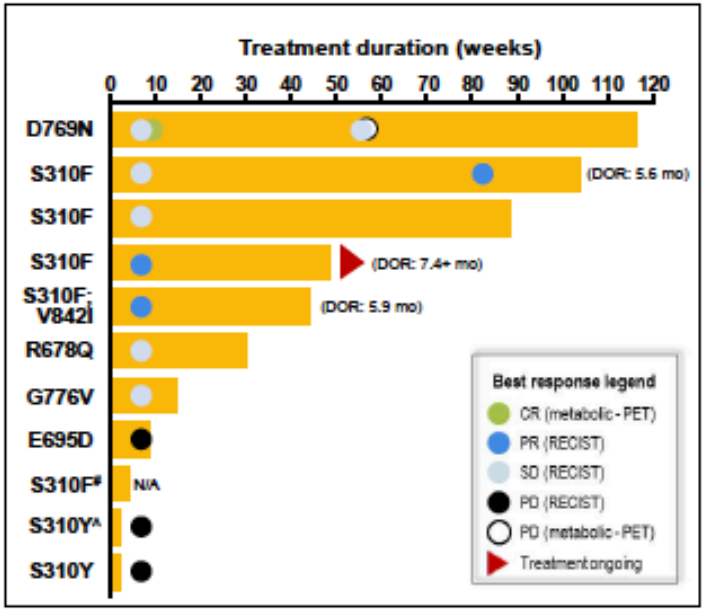
Genomics

- Most common HER2^{mut} is S310 extracellular domain hotspot mutation
- Usually exclusive to HER2 amplifications
- Most common co-mutations include TP53, PIK3CA

Neratinib Monotherapy Results Presented at SGO Meeting

Best change in tumor and treatment duration





2 patients did not have a measurable post-baseline tumor assessment
Patient died prior to first post-baseline baseline scan
^ Tumor lesions were not measurable on post-baseline scan; evaluated as PD due to development of new lesion

▼ *Treatment ongoing*
∗ *Confirmed complete metabolic response (per PET response criteria)*

HAWAII FIVE-O SGO 50TH ANNUAL MEETING ON WOMEN'S CANCER

Society of Gynecologic Oncology

Celebrating 50 Years of SGO Since 1969

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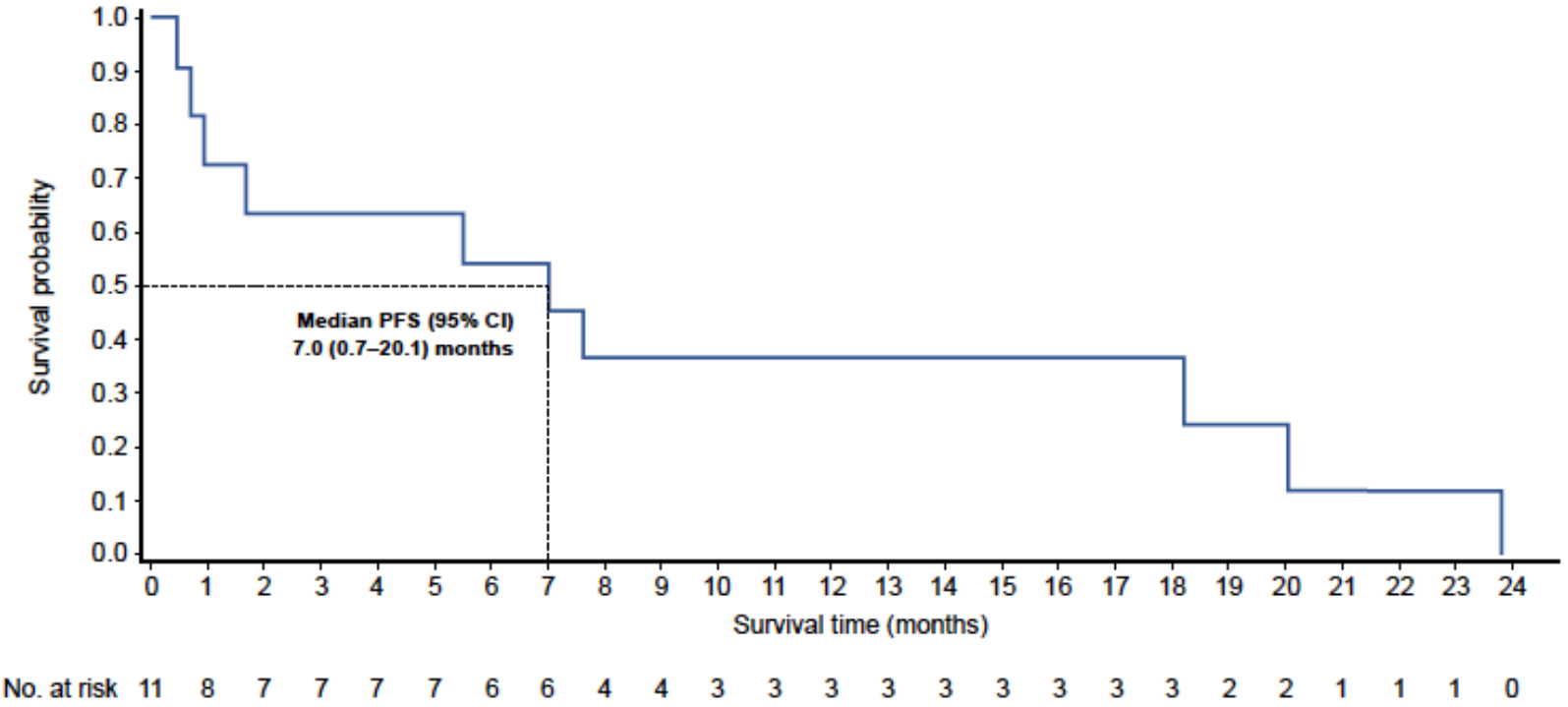
Neratinib Monotherapy Results Presented at SGO Meeting

Progression-free survival (n=11)



HAWAII FIVE-O SGO 50TH ANNUAL MEETING ON WOMEN'S CANCER

Society of Gynecologic Oncology

Celebrating 50 Years of SGO Since 1969

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Path Forward

- SUMMIT study to enroll additional patients with HER2 mutated cervical cancer

- Monotherapy data can be used to file for accelerated approval
  - Overall response rate
  - Duration of response

- Puma to schedule pre NDA meeting with FDA (anticipated Q4 2020-Q2 2021)

HER-Seq (PUMA-NER-9501): *HER2* mutation screening protocol

Why HER-Seq?

1 **Rarity of *HER2* mutation warrants an active screening program**

2 **Lack of access to genomic testing**
- Ex-US regions

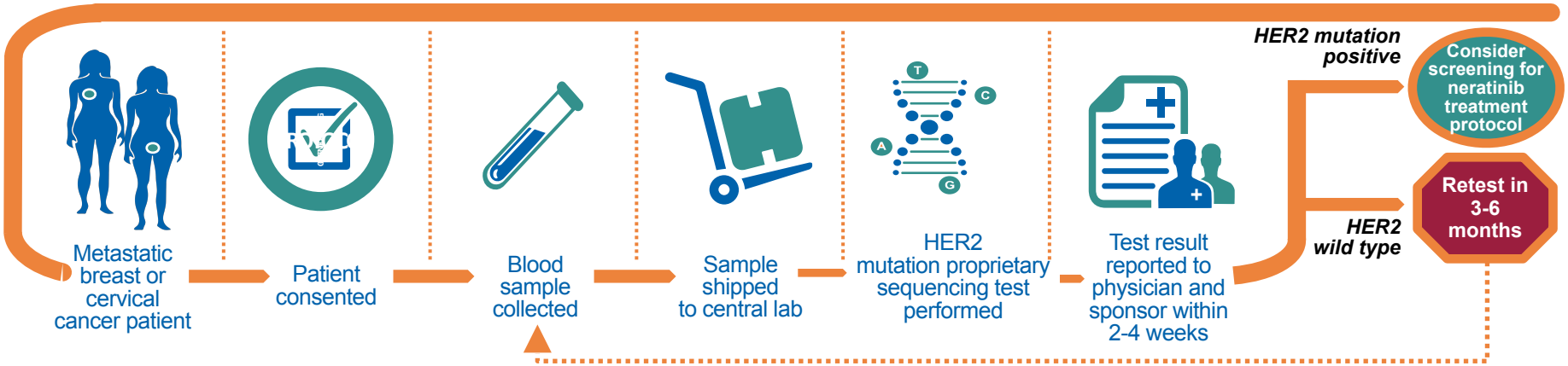
3 **Liquid biopsy is non-invasive and convenient**
- Also facilitates repeat sampling

4 **Tracked by Puma from clinical presentation to neratinib trial eligibility**

HER-Seq fills a need for inexpensive, high-throughput *HER2* genomic sequencing

HER-Seq (PUMA-NER-9501) Study Protocol

HER-Seq: A Blood-based Screening Study to Identify Patients with *HER2* Mutations for Enrollment into SUMMIT (initiated December 2018)



PRIMARY OBJECTIVE:

To identify patients with *HER2* mutations who may be eligible for screening into the SUMMIT 'basket' trial or other disease-specific neratinib treatment protocol.

Key Inclusion Criteria

- of informed consent.
- Histologically-confirmed metastatic breast or cervical cancer
- ECOG status of 0 to 2
- Provide written, informed consent to participate in the study and for circulating tumor DNA screening
- Must provide blood sample(s) for *HER2* mutation testing

Key Exclusion Criteria

- Patients with known HER2+ or *HER2*-amplified tumors
- Patients who have received neratinib or any other prior EGFR/HER2 tyrosine kinase inhibitor

Clinical trials.gov NCT: NCT03786107

HER-Seq Trial

- Currently open at ~15 sites
  - Being expanded to other SUMMIT sites
- Utilizes proprietary next generation sequencing assay for HER2 mutations
- Screening Goals:
  Breast cancer: Screen 2500 patients
  Cervical cancer: Screen 1200 patients
- Patients with HER2 mutations identified through HER-Seq will be considered for enrollment in SUMMIT

SUMMIT Trial

Proposed Registration Pathway

- ✓ Meet with FDA to discuss registration pathway in HR-positive, HER2 negative HER2 mutated breast cancer and HER2 mutated cervical cancer
- Modify SUMMIT trial to expand HER2 mutated breast cancer cohort
- Continue to enroll HER2 mutated cervical cancer cohort
- Expand HER-Seq to expedite enrollment in SUMMIT
- Puma R&D budget decrease due to declines in expenses associated with ExteNET, NALA, CONTROL will open up opportunity to expand SUMMIT
- Meet with FDA for pre-NDA meeting anticipated Q4 2020-Q2 2021