Puma Biotechnology

H.C. Wainwright BIOCONNECT Virtual Conference

January 2022
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, 2020, and our Quarterly Report on Form 10-Q for the quarter ended September 30, 2021. 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*

<table>
<thead>
<tr>
<th>HER2+ Breast Cancer</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Registration</th>
<th>Approval</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Extended adjuvant</strong></td>
<td><strong>ExteneT</strong> (Phase III HER2+ EBC*)</td>
<td><strong>CONTROL</strong></td>
<td><strong>NALA</strong> (Phase III 3rd Line HER2+ MBC**)</td>
<td><strong>FB-10: T-DM1 + neratinib</strong></td>
<td><strong>TBCRC-022 (T-DM1 + neratinib)</strong></td>
</tr>
<tr>
<td>Monotherapy or combo therapy</td>
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<tr>
<td><strong>Metastatic</strong></td>
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<tr>
<td>Monotherapy or combo therapy</td>
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<tr>
<td><strong>Metastatic w/ brain mets</strong></td>
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<tr>
<td>Monotherapy or combo therapy</td>
<td></td>
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<tr>
<td><strong>HER2-mutant Breast Cancer/Solid Tumors</strong></td>
<td></td>
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<tr>
<td>Neratinib (± fulvestrant in MBC)</td>
<td></td>
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<tr>
<td><strong>Metastatic</strong></td>
<td>SUMMIT: Breast HRC+ ***</td>
<td>SUMMIT: Cervical</td>
<td>SUMMIT: exon 18 mut NSCLC</td>
<td>SUMMIT (Basket Trial)</td>
<td></td>
</tr>
</tbody>
</table>

* EBC: Early breast cancer  ** MBC: Metastatic breast cancer  *** HRC+: Hormone receptor positive
PUMA’s Pharmacy and Distributor Network

Hub Services

Patients

Sites of Care

Academic Hospitals
Community Hospitals
Physician Practices
Others (VA, DOD)

Specialty Pharmacy Network (SP)
- Acaria Health
- Accredro
- CVS
- ONCO 360
- Optum / Diplomat
- Biologics

Specialty Distributor Network (SD)
- McKesson
- ASD/Oncology Supply
- Cardinal Health
- DMS Pharmaceutical Group Inc.
~$43 Million net NERLYNX revenue in Q3’21
3,430 Ex-factory bottles were sold in Q4’21

Includes Commercial SP and SD

Q4’21 bottle count includes ~200 additional bottles due to increase in inventory
Field Structure Reduced to Adapt to Virtual Environment

Prior Field Structure

VP, Sales

Area Directors (2 total)

Regional Manager (10 total)

Clinical Specialists (71 total)

Current Field Structure

VP, Sales

Regional Director (7 total)

Clinical Specialists (42 total)
~57% of patients in Q3’21 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

<table>
<thead>
<tr>
<th>Region</th>
<th>Partner</th>
<th>Regulatory Approvals</th>
<th>Commercial Launches</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Australia / SE Asia</strong></td>
<td></td>
<td>• 2019 – Ext. Adj. in Australia, Singapore</td>
<td>• 2020 – Singapore</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• 2020 – Ext. Adj. in Brunei, Malaysia, New Zealand</td>
<td>• Q2 2021 – Malaysia</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Q3 / Q4 2021 – Brunei, New Zealand</td>
</tr>
<tr>
<td>Israel</td>
<td></td>
<td>• 2020 – Approved in Ext. Adj. and mBC</td>
<td>• 2020 – Launched</td>
</tr>
<tr>
<td>Canada</td>
<td></td>
<td>• 2019 – Ext. Adj. approved</td>
<td>• 2020 – Launched</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Q2 2021 – mBC approved</td>
<td></td>
</tr>
<tr>
<td>Latin America</td>
<td></td>
<td>• 2019 – Ext Adj in Argentina</td>
<td>• 2020 – Argentina</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• 2020 – Ext. Adj in Chile, Ecuador</td>
<td>• Q2 2021 – Chile</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• 2020 – mBC in Argentina</td>
<td>• Q4 2021 – Peru</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• 2021 – Ext Adj and mBC in Peru</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• 2021 – Expected approvals in Brazil and Mexico</td>
<td></td>
</tr>
<tr>
<td>Europe</td>
<td>Pierre Fabre</td>
<td>• 2019 – EMA approval</td>
<td>• 2019 – Germany, UK, Austria</td>
</tr>
<tr>
<td>Greater China</td>
<td></td>
<td>• 2019 – Ext. Adj. in Hong Kong</td>
<td>• 2020 – Sweden, Finland, Scotland, Switzerland</td>
</tr>
<tr>
<td>Middle East</td>
<td></td>
<td>• 2020 – Ext. Adj. in China, Taiwan</td>
<td>• Denmark</td>
</tr>
<tr>
<td>North and West Africa</td>
<td></td>
<td>• Q4 2021 – mBC in Taiwan</td>
<td>• 2020 – Hong Kong</td>
</tr>
<tr>
<td>South Africa</td>
<td></td>
<td>• Q1 2021 – China, Taiwan</td>
<td>• Q1 2021 – China</td>
</tr>
<tr>
<td>Turkey</td>
<td></td>
<td>• Q1 2021 – Greece, Czech Republic</td>
<td>• Q1 2021 – Czech Republic</td>
</tr>
<tr>
<td>South Korea</td>
<td></td>
<td>• Q4 2021 – Ext. Adj. in S. Korea</td>
<td></td>
</tr>
</tbody>
</table>
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

**HER2+ early BC**
- Received up to 1 year of adjuvant trastuzumab
- Stage I–3c
- HR (ER/PR) +/-

**STUDY ENDPOINTS**
Primary endpoint: incidence of grade ≥3 diarrhea
Secondary endpoints: frequency distribution of maximum-grade diarrhea; incidence and severity of diarrhea by loperamide exposure
CONTROL
Study Flowchart

Stage 1–3c HER2+ breast cancer
Trastuzumab-based adjuvant therapy completed within 1 year

Sequential investigational cohorts

Population

Cohort

Treatment

Analysis

Loperamide cohort
(Original protocol)

Neratinib
Loperamide prophylaxis

Final analysis
(N=137)

Budesonide cohort

Neratinib
Loperamide prophylaxis
Budesonide

Final analysis
(N=64)

Colestipol cohort

Neratinib
Loperamide prophylaxis
Colestipol

Final analysis
(N=136)

Colestipol cohort

Neratinib
Colestipol prophylaxis
Loperamide PRN

Final analysis
(N=104)

Dose-escalation cohort

Neratinib dose escalation

Final analysis
(N=60)
**CONTROL vs ExteNET: Neratinib Treatment-Emergent Diarrhea**

Loperamide prophylaxis reduces incidence and severity of diarrhea

<table>
<thead>
<tr>
<th>Treatment-emergent diarrhea incidence, n (%)</th>
<th>CONTROL¹</th>
<th>ExteNET³</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Loperamide (n=137)</td>
<td>Budesonide + loperamide (n=64)</td>
</tr>
<tr>
<td>No diarrhea</td>
<td>28 (20)</td>
<td>9 (14)</td>
</tr>
<tr>
<td>Grade 1</td>
<td>33 (24)</td>
<td>16 (25)</td>
</tr>
<tr>
<td>Grade 2</td>
<td>34 (25)</td>
<td>21 (33)</td>
</tr>
<tr>
<td>Grade 3</td>
<td>42 (31)</td>
<td>18 (28)</td>
</tr>
<tr>
<td>Grade 4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Diarrhea leading to discontinuation</td>
<td>28 (20)</td>
<td>5 (8)</td>
</tr>
<tr>
<td>Hospitalization (due to diarrhea)</td>
<td>2 (1)</td>
<td>0</td>
</tr>
<tr>
<td>Diarrhea leading to dose reduction</td>
<td>10 (7)</td>
<td>3 (5)</td>
</tr>
</tbody>
</table>

2. Ruiz-Borrego et al. SABCS 2020
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
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:

<table>
<thead>
<tr>
<th></th>
<th>N+C</th>
<th>L+C</th>
</tr>
</thead>
<tbody>
<tr>
<td>307</td>
<td>314</td>
<td></td>
</tr>
<tr>
<td>183</td>
<td>183</td>
<td></td>
</tr>
<tr>
<td>113</td>
<td>82</td>
<td></td>
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<tr>
<td>69</td>
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<td>54</td>
<td>24</td>
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<td>35</td>
<td>9</td>
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<td>20</td>
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<td>13</td>
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<td>9</td>
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<td>7</td>
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<td>2</td>
<td>2</td>
<td>1</td>
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</tbody>
</table>

Hazard ratio (95% CI) Log-rank p-value
0.76 (0.63–0.93) 0.0059

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  1

Mean PFS (months)  p-value
Neratinib + Capecitabine  8.8  0.0003
Lapatinib + Capecitabine  6.6

Restriction: 24 months

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

Mean OS (months) | Hazard ratio (95% CI) | Log-rank p-value
--- | --- | ---
Neratinib + Capecitabine | 24.0 | 0.88 (0.72–1.07) | 0.2086
Lapatinib + Capecitabine | 22.2 |

Restriction: 48 months

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

Time to intervention for CNS metastases

Overall cumulative incidence (Gray’s test): 22.8% vs 29.2%; \( p=0.043 \)

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Neratinib + Capecitabine (n=55/307)</th>
<th>Lapatinib + Capecitabine (n=75/314)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radiation therapy</td>
<td>11%</td>
<td>15%</td>
</tr>
<tr>
<td>Surgery/procedure</td>
<td>2%</td>
<td>3%</td>
</tr>
<tr>
<td>Anticancer medication</td>
<td>1%</td>
<td>1%</td>
</tr>
</tbody>
</table>
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\(^1\)

\(^1\)Roche epidemiology slides 09/18
FB-10 – Phase I/II Trial of Kadcyla (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 Kadcyla (T-DM1) + Neratinib

ORR (CR/PR): 12 of 20 (60%)

*Off TX, AE/withdrawn
+ On treatment

Days on Treatment

Dose mg/d

0 100 200 300 400 500 600 700 800

Days on Treatment

Dose mg/d

240
240
200
200
200
200
200
160
160
160
160
160
160
120
120
120
120
120
0

CR
PR
SD
PD

*
**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)*

CNS ORR = 49% (95% CI 32–66%)

18 responses
Neratinib Recently Included as a Treatment Option for Recurrent Breast Cancer CNS Metastases By NCCN® Guidelines

Guidelines updated March 2020

<table>
<thead>
<tr>
<th>Category 2A: Neratinib + Capecitabine</th>
<th>Category 2B: Neratinib + Paclitaxel</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TBCRC 022</strong></td>
<td><strong>NEfERT-T</strong>3,4</td>
</tr>
<tr>
<td>A Phase II Trial of Neratinib and Capecitabine for Patients with HER2+ Breast Cancer Brain Metastases (NCT01494662)</td>
<td>Randomized, Multi-Center, International Study of HER2-Directed Therapy in 1st-line mBC (NCT00915018)</td>
</tr>
</tbody>
</table>

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Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Central Nervous System Cancers V.1.2018. © National Comprehensive Cancer Network, Inc. 2018. All rights reserved. Accessed [March 20, 2018]. To view the most recent and complete version of the guideline, go online to NCCN.org

Current SUMMIT ‘Basket’ Trial: Study Design

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

Primary endpoint
- Objective response rate at first post-baseline tumor assessment (ORRfirst)

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
- ORRfirst, ORR, CBR: associated 95% CI
- Median PFS: Kaplan-Meier estimate with 95% CI

ClinicalTrials.gov Identifier NCT01953926
SUMMIT
Breast Cancer Cohort
Characteristics of HER2-mutant breast cancer

**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

Current SUMMIT breast cancer cohorts

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

**HER2-mutant MBC**

- HR+/HER2-negative MBC (with prior CDK4/6i)
  - Non-randomized
  - Treatment assignment: Neratinib + Fulvestrant + Trastuzumab

- HR+/HER2-negative MBC (with prior CDK4/6i)
  - Randomized
  - R 1:1:1
  - Treatment assignment:
    - Neratinib + Fulvestrant + Trastuzumab
    - Fulvestrant + Trastuzumab
    - Fulvestrant
    - Neratinib + Trastuzumab

**Triple-negative breast cancer**

- **Design:** Simon 2-stage
  - If ≥1 response in first evaluable 7 patients, expand cohort to Stage 2 (N=18)
  - If ≥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>

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<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

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

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

^aObjective 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; ^bKaplan-Meier analysis

^cClinical 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

#### Characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>(N+F+T, n=7)</th>
<th>(F+T, n=7)</th>
<th>(F, n=7)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Objective response (confirmed CR/PR)</strong>&lt;sup&gt;a&lt;/sup&gt;, n (%)</td>
<td>2 (28.6)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>CR</td>
<td>1 (14.3)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>PR</td>
<td>1 (14.3)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Best overall response</strong>&lt;sup&gt;c&lt;/sup&gt;, n (%)</td>
<td>3 (42.9)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Median DOR</strong>&lt;sup&gt;b&lt;/sup&gt;, months (95% CI)</td>
<td>NE</td>
<td>NE</td>
<td>NE</td>
</tr>
<tr>
<td><strong>Clinical benefit</strong>&lt;sup&gt;c&lt;/sup&gt;, n (%)</td>
<td>2 (28.6)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Median PFS</strong>, months (95% CI)</td>
<td>6.2 (2.1–NE)</td>
<td>3.9 (1.9–4.1)</td>
<td>4.1 (1.6–4.1)</td>
</tr>
<tr>
<td><strong>Median duration of treatment</strong>, months (range)</td>
<td>5.0 (0.7–13.2)</td>
<td>3.5 (0.8–4.1)</td>
<td>2.1 (0.7–4.1)</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Baseline characteristics</th>
<th>TNBC (N+T, n=18)</th>
<th>Efficacy</th>
<th>TNBC (N+T, n=18)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ECOG performance status, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>9 (50.0)</td>
<td><strong>Objective response (confirmed CR/PR)</strong>&lt;sup&gt;a&lt;/sup&gt;, n (%)</td>
<td>6 (33.3)</td>
</tr>
<tr>
<td>1</td>
<td>9 (50.0)</td>
<td>CR</td>
<td>1 (5.6)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PR</td>
<td>5 (27.8)</td>
</tr>
<tr>
<td><strong>Histological type, n (%)</strong></td>
<td></td>
<td><strong>Best overall response (confirmed or unconfirmed PR or CR), n (%)</strong></td>
<td>7 (38.9)</td>
</tr>
<tr>
<td>Lobular</td>
<td>3 (16.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ductal</td>
<td>7 (38.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mixed Ductal and Lobular</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>8 (44.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Median number of prior anti-cancer regimens (range)</strong></td>
<td>3.5 (1–7)</td>
<td><strong>Median DOR</strong>&lt;sup&gt;b&lt;/sup&gt;, months (95% CI)</td>
<td>NE</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Clinical benefit</strong>&lt;sup&gt;c&lt;/sup&gt;, n (%)</td>
<td>7 (38.9)</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Median PFS, months (95% CI)</strong></td>
<td>6.2 (2.1–8.2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Median duration of treatment, months (range)</strong></td>
<td>4.4 (0.3–15.4)</td>
</tr>
</tbody>
</table>

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

**HER2 mutation category**
- Kinase domain hotspot
- Exon 20 insertion
- Extracellular domain hotspot
- Exon 19 deletion
- Transmembrane domain hotspot

**Evaluation modality**
- RECIST
- Modified PERCIST
- New non-target lesion
- Not evaluable

**Best overall response**
- CR
- PR
- SD
- PD

- Maximum change in tumor volume from baseline (%)
- Non-randomized HR+ Prior CDK4/6i N+F+T
- Randomized HR+ Prior CDK4/6i N+F+T
- Randomized HR+ Prior CDK4/6i F+T
- Randomized HR+ Prior CDK4/6i F
- TNBC N+T

**Histology**
- CR
- PR
- SD
- PD
Conclusions/Next Steps

- The combination of N+F+T demonstrated encouraging clinical activity in patients with heavily pretreated HR+, HER2-negative, HER2-mutant MBC who had previously received CDK4/6:
  - Objective response rate 42.4% (1 CR and 13 PRs); median PFS 7.0 months, n=33

- Following guidance from the Independent Data Monitoring Committee, the F+T and F arms of SUMMIT were closed

- Following closure of the F+T and F arms of the randomized cohort, additional patients with HR+, HER2-negative, HER2-mutant MBC and prior CDK4/6i have been enrolled, totaling n=50 who have received N+F+T
  - Safety and efficacy outcomes of these 50 patients will be evaluated and discussed with the FDA in 2022

- The N+T combination showed promising clinical activity in heavily pretreated HER2-mutant TNBC:
  - Objective response rate 33.3% (1 CR and 5 PRs); median PFS 6.2 months
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 HER2mut 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

<table>
<thead>
<tr>
<th>HER2-mutation category</th>
<th>Best response (REIST v1.1)</th>
<th>Histology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-hotspot</td>
<td>Partial response</td>
<td>Squamous cell carcinoma</td>
</tr>
<tr>
<td>ECD and KD hotspot</td>
<td>Stable disease</td>
<td>Adenocarcinoma</td>
</tr>
<tr>
<td>Extracellular domain hotspot</td>
<td>Progressive disease</td>
<td>Endocervical adenocarcinoma</td>
</tr>
<tr>
<td>Kinase domain hotspot</td>
<td>Not evaluable</td>
<td></td>
</tr>
<tr>
<td>Transmembrane domain hotspot</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

![Graph showing best change from baseline (%) for different HER2-mutation categories and histologies.]

Gynecologic Oncology, 2020
Neratinib Monotherapy Results Published in Gynecologic Oncology
SUMMIT (PUMA-NER-5201) Basket Trial

*EGFR* exon 18 lung cancer cohort update
**EGFR Exon 18-Mutant Lung Cancer Cohort Receiving Neratinib Monotherapy:** Baseline Demographics and Patient Characteristics

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>Safety/Efficacy evaluable patients (n=11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median (range), years</td>
<td>67 (56-83)</td>
</tr>
<tr>
<td>&lt;65 years, n (%)</td>
<td>4 (36)</td>
</tr>
<tr>
<td>≥65 years, n (%)</td>
<td>7 (64)</td>
</tr>
<tr>
<td>Gender, n (%)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>5 (45)</td>
</tr>
<tr>
<td>Male</td>
<td>6 (55)</td>
</tr>
<tr>
<td>ECOG performance status, n (%)</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>5 (45)</td>
</tr>
<tr>
<td>1</td>
<td>6 (55)</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td></td>
</tr>
<tr>
<td>Black or African American</td>
<td>1 (9)</td>
</tr>
<tr>
<td>White</td>
<td>10 (91)</td>
</tr>
<tr>
<td>Median number of prior therapies in metastatic/locally advanced setting (range)</td>
<td></td>
</tr>
<tr>
<td>Prior checkpoint inhibitor, n (%)</td>
<td></td>
</tr>
<tr>
<td>Prior chemotherapy, n (%)</td>
<td></td>
</tr>
<tr>
<td>Prior tyrosine kinase inhibitor, n (%)</td>
<td>10 (91)</td>
</tr>
<tr>
<td>gefitinib/erlotinib (reversible 1st gen EGFR TKI)</td>
<td>7 (58)</td>
</tr>
<tr>
<td>osimertinib (irreversible EGFR T790M TKI)</td>
<td>3 (25)</td>
</tr>
<tr>
<td>afatinib (irreversible pan-HER TKI)</td>
<td>2 (17)</td>
</tr>
</tbody>
</table>

Data cut-off: 21-Aug-2020
## EGFR Exon 18-Mutant Lung Cancer Cohort Receiving Neratinib Monotherapy: Efficacy Summary

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

- 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.
- Kaplan-Meier analysis in safety population.
- 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 \textit{EGFR} Exon 18 Mutations (G719X)

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

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.

Milestones for Neratinib in EGFR Exon 18-Mutant Lung Cancer Cohort in SUMMIT Study

- The success criteria for the 1st stage and 2nd stage of the Simon’s 2-stage design has been met
  - Enrollment in the 2nd stage is continuing up to a total of 30 patients

- Anticipate presentation of additional data from SUMMIT in patients with EGFR exon 18-mutant lung cancer in the first half of 2022

- Anticipate scheduling meeting with FDA to discuss potential accelerated approval strategy for patients with EGFR exon 18-mutant lung cancer who have been treated with a prior EGFR TKIs in 2022
Puma – Expected Milestones

- Conduct pre-NDA meeting with the FDA to discuss accelerated approval of neratinib in HER2-mutated HR+ breast cancer (H1 2022)

- 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 (H1 2022)

- Conduct 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 Kadcyla + neratinib in patients with HER2+ breast cancer with brain metastases who have previously been treated with Kadcyla (H2 2022)

- Report Phase II data from SUMMIT trial in cervical cancer patients with HER2 mutations (H2 2022)
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  
   – 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

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

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  
Former CFO, Myriad Genetics

Adrian Senderowicz, M.D.  
SVP & 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
Currently trading on NASDAQ: PBYI

Cash, cash equivalents and marketable securities at September 30, 2021: ~$87.5 million

Cash burn in Q3 2021: ~$21.4 million

Note purchase agreement (July 2021)
  - Fund managed by Athyrium Capital Management
  - New agreement for $125 million replaces loan of $100 million
  - $100 million drawn down to repay loan from Oxford Finance
  - Provides increased cash flexibility, improved short-term cash flow, ongoing clinical funding

Shares issued and outstanding: 40.9 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
- 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®
- Large initial market opportunity with additional label expansion potential