Puma Biotechnology

H.C. Wainwright 24th 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**

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

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

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

Specialty Distributor Network (SD)
- McKesson
- ASD/Oncology Supply
- Cardinal Health
- DMS Pharmaceutical Group Inc.

Hub Services

Patients

Sites of Care
- Academic Hospitals
- Community Hospitals
- Physician Practices
- Others (VA, DOD)
~$51 Million net NERLYNX revenue in Q2'22
3,200 Ex-factory bottles were sold in Q2’22

Bottles Sold (SP + SD) by Quarter

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

<table>
<thead>
<tr>
<th>Region</th>
<th>Partner</th>
<th>Regulatory Approvals</th>
<th>Commercial Launches</th>
</tr>
</thead>
</table>
| **Australia / SE Asia** | [Specialised Therapeutics](#) | • 2019 – Ext. Adj. in Australia, Singapore  
• 2020 – Ext. Adj. in Brunei, Malaysia, New Zealand  
• Q2 2022 – Ext. Adj. in the Philippines | • 2020 – Singapore  
• Q2 2021 – Malaysia  
• Q3 / Q4 2021 – Brunei, New Zealand |
| **Israel**      | [MEDISON](#) | • 2020 – Approved in Ext. Adj. and mBC                                               | • 2020 – Launched                     |
| **Canada**      | [Knight](#) | • 2019 – Ext. Adj. approved  
• Q2 2021 – mBC approved                                                      | • 2020 – Launched                     |
| **Latin America** | [PINT PHARMA](#) | • 2019 – Ext Adj in Argentina  
• 2020 – Ext. Adj in Chile, Ecuador  
• 2020 – mBC in Argentina  
• 2021 – Ext Adj and mBC in Peru; mBC in Chile  
• Q4 2021 – Ext. Adj. in Brazil  
• Q1 2022 – Ext. Adj. in Mexico  
• Q3 2022 – mBC in Ecuador | • 2020 – Argentina  
• Q2 2021 – Chile  
• Q4 2021 – Peru |
| **Europe**      | [Pierre Fabre](#) | • 2019 – EMA approval  
• 2019 – Ext. Adj. in Hong Kong  
• 2020 – Ext. Adj. in China, Taiwan  
• Q4 2021 – mBC in Taiwan | • 2019 – Germany, UK, Austria  
• 2020 – Sweden, Finland, Scotland, Switzerland, Denmark  
• 2020 – Hong Kong  
• Q1 2021 – China (added to 2021 NRDL), Taiwan  
• Q1 2021 – Greece, Czech Republic  
• Q1 2022 – Ireland  
• Q3 2022 – Spain |
| **Greater China** | [BIXINK](#) | • Q4 2021 – Ext. Adj. in S. Korea                                                      | • Q1 2022 – Launched                  |
| **Middle East** |           |                                                                                      |                                       |
| **North and West Africa** |          |                                                                                      |                                       |
| **South Africa** |           |                                                                                      |                                       |
| **Turkey**      |           |                                                                                      |                                       |
NERLYNX revenue guidance: $180 to $190 million

NERLYNX royalty guidance: $27 to $30 million

Net income guidance: $6 to $7 million
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 ≥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

<table>
<thead>
<tr>
<th></th>
<th>CONTROL(^1)</th>
<th>ExteNET(^3)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Loperamide ((n=137))</td>
<td>Budesonide + loperamide ((n=64))</td>
</tr>
<tr>
<td><strong>Treatment-emergent diarrhea incidence, (n) (%)</strong></td>
<td></td>
<td></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
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)

Phase III Trial – Third-Line HER2+ MBC (NALA): Study Results
Prespecified restricted means analysis – PFS

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)

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>

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

**HER2+ MBC**
Must have received prior anti-HER2-based therapy with pertuzumab for mBC

No prior T-DM1 or HER2 TKI allowed

**Neratinib**
- Dose level 1: 120 mg/d
- Dose level 2: 160 mg/d
- Dose level 3: 200 mg/d
- Dose level 4: 240 mg/d

**T-DM1**
3.6 mg/kg IV d1 Q3W

**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
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

HER2+ mBC w/ Brain Mets

- Progressive brain mets
  - Cohort 1 (n = 40 pts)
    - Neratinib (240 mg/day)

- Craniotomy candidates
  - Cohort 2 (n = 5 pts)
    - Neratinib (240 mg/day) X 1 cycle, Surgical resection, then Neratinib (240 mg/day)

- Progressive brain mets:
  - Cohort 3a (n = 39 pts)
    - Neratinib (240 mg/day)
  - Cohort 3b (n = 12 pts)
    - Capecitabine (1500 mg/m², d1-14, q3w)

- Cohort 4a (n = 20 pts)
  - Neratinib (160 mg/day)
  - T-DM1 (3.6 mg/kg IV q21d)

- Cohort 4b (n = 20 pts)
- Cohort 4c (n = 23 pts)

- Progressive brain mets: 3a: No prior lapatinib
  - Cohort 3a (n = 39 pts)

- Progressive brain mets: 3b: Prior lapatinib
  - Cohort 3b (n = 12 pts)

- Cohort 3b (n = 12 pts)
  - Neratinib (240 mg/day)

- Progressive brain mets: 4a: Untreated CNS disease; no prior T-DM1
  - Cohort 4a (n = 20 pts)

- Progressive brain mets: 4b: Progressive CNS disease; no prior T-DM1
  - Cohort 4b (n = 20 pts)

- Progressive brain mets: 4c: Progressive CNS disease; prior T-DM1
  - Cohort 4c (n = 23 pts)

**Data from Cohort 4b and 4c anticipated in 2022**
TBCRC-022 Cohort 3a
CNS Response

Best Volumetric Response (n=31)*

CNS ORR = 49% (95% CI 32–66%)

18 responses

* ASCO 2017
# Neratinib 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></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>

**NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.**

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 (e.g., 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 (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

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

- Lung
- Cervical
- Salivary gland
- Solid tumors (NOS)
- Bladder
- Breast HRc-positive*
- Breast HRc-negative

EGFR exon18-mutant tumors

HER2-mutant tumors

HER4-mutant tumors

Neratinib monotherapy
Neratinib + Paclitaxel
Neratinib* + Trastuzumab‡

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

ClinicalTrials.gov Identifier NCT01953926
SUMMIT
Breast Cancer Cohort
Characteristics of HER2-mutant breast cancer\textsuperscript{1–8}

<table>
<thead>
<tr>
<th>Incidence</th>
<th>Histology</th>
<th>Genomics</th>
</tr>
</thead>
</table>
| - 2% Primary breast cancers  
- 2–4% MBC  
- 8% ER+ MBC  
- Up to 15% in metastatic ILC | - Predominantly in hormone receptor-positive (luminal-A) and HER2-negative tumors  
- Represented in all histology subtypes but enriched in lobular carcinoma | - 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

- **HR+/HER2-negative MBC**
  - (with prior CDK4/6i)
  - Randomized

**MBC cohort**

- **Triple-negative breast cancer**

**Treatment assignment**

- Neratinib + Fulvestrant + Trastuzumab
- Neratinib + Fulvestrant + Trastuzumab
- Fulvestrant + Trastuzumab
- Fulvestrant
- Neratinib + Trastuzumab

**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)\(^a\); TNBC: ORR at first post-baseline tumor assessment (ORR\(_{\text{first}}\)), RECIST v1.1 or modified PERCIST

**Key secondary endpoint:** Confirmed ORR\(^b\)

\(^a\)ORR by independent review was a primary endpoint in the randomized HR+ cohorts
\(^b\)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)(^a), n (%)</strong></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

\(^a\)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; 
\(^b\)Kaplan-Meier analysis

\(^c\)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 \textit{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)(^a), n (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CR</td>
<td>2 (28.6)</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 (confirmed or unconfirmed PR or CR), n (%)</strong></td>
<td>3 (42.9)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Median DOR(^b), months (95% CI)</strong></td>
<td>NE</td>
<td>NE</td>
<td>NE</td>
</tr>
<tr>
<td><strong>Clinical benefit(^c), n (%)</strong></td>
<td>2 (28.6)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Median PFS, months (95% CI)</strong></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, months (range)</strong></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

\(^a\)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; \(^b\)Kaplan-Meier analysis

\(^c\)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

<table>
<thead>
<tr>
<th>ECOG performance status, n (%)</th>
<th>TNBC (N+T, n=18)</th>
<th>Median number of prior anti-cancer regimens (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>9 (50.0)</td>
<td>3.5 (1–7)</td>
</tr>
<tr>
<td>1</td>
<td>9 (50.0)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Histological type, n (%)</th>
<th>TNBC (N+T, n=18)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Lobular</td>
<td>3 (16.7)</td>
<td></td>
</tr>
<tr>
<td>Ductal</td>
<td>7 (38.9)</td>
<td></td>
</tr>
<tr>
<td>Mixed Ductal and Lobular</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>8 (44.4)</td>
<td></td>
</tr>
</tbody>
</table>

## Efficacy

<table>
<thead>
<tr>
<th>Objective response (confirmed CR/PR)&lt;sup&gt;a&lt;/sup&gt;, n (%)</th>
<th>TNBC (N+T, n=18)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR</td>
<td>6 (33.3)</td>
</tr>
<tr>
<td>PR</td>
<td>1 (5.6)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Best overall response (confirmed or unconfirmed PR or CR), n (%)</th>
<th>TNBC (N+T, n=18)</th>
</tr>
</thead>
<tbody>
<tr>
<td>7 (38.9)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Median DOR&lt;sup&gt;b&lt;/sup&gt;, months (95% CI)</th>
<th>TNBC (N+T, n=18)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NE</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical benefit&lt;sup&gt;c&lt;/sup&gt;, n (%)</th>
<th>TNBC (N+T, n=18)</th>
</tr>
</thead>
<tbody>
<tr>
<td>7 (38.9)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Median PFS, months (95% CI)</th>
<th>TNBC (N+T, n=18)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.2 (2.1–8.2)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Median duration of treatment, months (range)</th>
<th>TNBC (N+T, n=18)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.4 (0.3–15.4)</td>
<td></td>
</tr>
</tbody>
</table>

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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)
SUMMIT

Cervical Cancer Cohort
Characteristics of HER2-Mutant Cervical Cancer

<table>
<thead>
<tr>
<th>Incidence</th>
<th>Histology</th>
<th>Genomics</th>
</tr>
</thead>
<tbody>
<tr>
<td>5% metastatic cervical cancers</td>
<td>Enriched in adenocarcinomas</td>
<td>Most common HER2(\text{mut}) is S310 extracellular domain hotspot mutation</td>
</tr>
<tr>
<td>May be negatively prognostic for survival</td>
<td>High occurrence in HPV+ tumors</td>
<td>Usually exclusive to HER2 amplifications</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Most common co-mutations include TP53, PIK3CA</td>
</tr>
</tbody>
</table>
Neratinib Monotherapy Results Published in Gynecologic Oncology

Gynecologic Oncology, 2020
Neratinib Monotherapy Results Published in Gynecologic Oncology

Key:
- Complete response (PET)
- Partial response (RECIST)
- Stable disease (RECIST)
- Progressive disease (RECIST)

Gynecologic Oncology, 2020
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**

<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><strong>Objective response (confirmed), a n</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CR</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>PR</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td><strong>Objective response rate, % (95% CI)</strong></td>
<td>36 (11–69)</td>
<td>40 (12–74)</td>
</tr>
<tr>
<td><strong>Best overall response, n</strong></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><strong>Best overall response rate, % (95% CI)</strong></td>
<td>54 (23–83)</td>
<td>60 (26–88)</td>
</tr>
<tr>
<td><strong>Median DOR, b months (95% CI)</strong></td>
<td>7.5 (4.0–NE)</td>
<td>7.5 (4.0–NE)</td>
</tr>
<tr>
<td></td>
<td>(1.9*, 4.0, 7.5, 9.2*)</td>
<td>(1.9*, 4.0, 7.5, 9.2*)</td>
</tr>
<tr>
<td><strong>Clinical benefit, c n</strong></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><strong>Clinical benefit rate, % (95% CI)</strong></td>
<td>73 (39–94)</td>
<td>80 (44–97)</td>
</tr>
<tr>
<td><strong>Median PFS time to event, months (95% CI)</strong></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

Copyright 2022 Puma Biotechnology
## Historical Response Rates of Afatinib in NSCLC Patients With 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>EGFR 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 (n = 23)</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>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>EGFR TKI-pretreated 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 (n = 8)</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>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.

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 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)
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

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
Currently trading on NASDAQ: PBYI

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® – 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