Puma Biotechnology

Credit Suisse 29th Annual Virtual Healthcare Conference

November 2020

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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, 2019, Quarterly Report on Form 10-Q for the quarter ended September 30, 2020, and subsequent reports. 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>
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</thead>
<tbody>
<tr>
<td><strong>Extended adjuvant</strong></td>
<td><strong>CONTROL</strong></td>
<td>Neratinib monotherapy</td>
<td>ExteNET (Phase III HER2+ EBC*)</td>
<td>EAP/MAP</td>
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<tr>
<td><strong>Metastatic</strong></td>
<td>FB-10: T-DM1 + neratinib</td>
<td>Monotherapy or combo therapy</td>
<td>NALA (Phase III 3rd Line HER2+ MBC**)</td>
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<tr>
<td><strong>Metastatic w/ brain mets</strong></td>
<td>TBCRC-022</td>
<td>Monotherapy or combo therapy</td>
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</table>

| HER2-mutant Breast Cancer/Solid Tumors | | | | |
|--------------------------------------|---------|----------|-----------|--------------|----------|
| **Metastatic** | SUMMIT- Breast HRC+ *** | Neratinib (± fulvestrant in MBC) | SUMMIT - Cervical | SUMMIT - exon 18 mut NSCLC | SUMMIT (Basket Trial) |

* EBC: Early breast cancer
** MBC: Metastatic breast cancer
*** HRC+: Hormone receptor positive
~$49.3 Million Net NERLYNX Revenue in Q3’2020
~3,600 Ex-factory Bottles were Sold in Q3’20

Bottles Sold (SP + SD) by Quarter

Q3’2017: 675
Q4’2017: 2,137
Q1’2018: 3,517
Q2’2018: 4,799
Q3’2018: 4,936
Q4’2018: 5,538
Q1’2019: 4,452
Q2’2019: 4,791
Q3’2019: 4,696
Q4’2019: 4,935
Q1’2020: 4,035
Q2’2020: 3,728
Q3’2020: 3,611

Includes Commercial SP and SD

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~33% of Patients in Q3’20 Started at a Reduced Dose

Reduced Dose defined as fewer than 6 pills per day
## Rest of World Partnerships – Timelines

<table>
<thead>
<tr>
<th>Region</th>
<th>Partner</th>
<th>Regulatory / Launch Milestones</th>
</tr>
</thead>
</table>
| Australia / SE Asia     | Specialised Therapeutics | • March 2019 – Approved in Australia  
• December 2019 -- Approved in Singapore  
• Q2/Q3 2020 - Approved in Brunei, Malaysia, New Zealand |
| Israel                  | MEDISON           | • Q1 2020 – Launched  
• Q3 2020- Approved in metastatic breast cancer |
| Canada                  | Knight            | • July 2019 – Approved  
• September 2020- metastatic sNDS accepted by HC |
| Greater China           | CANbridge         | • November 2019 – Approved in Hong Kong  
• April 2020 – Approved in China  
• August 2020 – Approved in Taiwan |
| Latin America           | PINT PHARMA       | • Q1 2020 – Argentina-Launched  
• Q2 2020 – Approved in Chile  
• Q3 2020 – Approved in Ecuador  
• 2021 – Expected approvals in Brazil, Colombia, Mexico, Peru |
| Europe                  | Pierre Fabre      | • Q4 2019 – Germany-Launched  
• Q4 2019 – United Kingdom-Launched  
• Q4 2019 – Austria-Launched  
• Q1 2020 – Sweden Launched  
• Q1 2020 – Approved in Switzerland  
• Q4 2020 – Planned launch in Finland |
| Middle East             |                  |                                                                                                           |
| North and West Africa   |                  |                                                                                                           |
| South Africa            |                  |                                                                                                           |
| Turkey                  |                  |                                                                                                           |
| South Korea             | BIXINK            | • October 2020 – NDA Filed                                                                                         |
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
Stage 1-3c HER2+ breast cancer
Trastuzumab-based adjuvant therapy completed within 1 year

Sequential investigational cohorts

Population
Cohort
Treatment
Analysis

Loperamide cohort
Budesonide cohort
Colestipol cohort
Colestipol cohort
Dose escalation cohort

Neratinib
Loperamide prophylaxis

Neratinib
Loperamide prophylaxis
Budesonide

Neratinib
Loperamide prophylaxis
Colestipol

Neratinib
Colestipol prophylaxis
Loperamide PRN

Preliminary analysis (N=137)
Preliminary analysis (N=64)
Preliminary analysis (N=136)
Preliminary analysis (N=104)
Currently enrolling

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**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>ExteNET²</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>

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 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)

Neratinib + Capecitabine
Lapatinib + Capecitabine

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

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)

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**
Approximately 6,400 patients (US) with third-line HER2+ metastatic breast cancer and 4,700 patients (US) with fourth line HER2 positive metastatic breast cancer\(^1\)

\(^1\)Roche epidemiology slides 09/18
NALA - HER2+ MBC Phase III Trial

Neratinib + capecitabine in third-line patients

 ✓ Filed sNDA for U.S. FDA approval (June 2019)

 ✓ sNDA accepted by U.S. FDA (September 2019)

 ✓ Approved in February 2020, two months before anticipated PDUFA Date (April 2020)
FB-10 - Phase I/II trial of Kadcyla (T-DM1) plus 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)

**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

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FB-10 - Phase I/II Trial of Kadcyla (T-DM1) plus Neratinib

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

Days on Treatment

Days on Treatment

Dose mg/d

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

*Off TX, AE/withdrawn
+ On treatment

CR
PR
SD
PD

ASCOR 2018
TBCRC 022: A Phase II Trial of HKI-272 (Neratinib) and Capecitabine for Patients with Human Epidermal Growth Factor Receptor 2 (HER2)-Positive 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

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

**Guidelines updated March 2020**

**Category 2A:**
Neratinib + Capecitabine

TBCRC 022

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

**Category 2B:**
Neratinib + Paclitaxel

NEfERT-T³,⁴

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

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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

**Clinical Trials.gov Identifier NCT01953926**

**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

**EGFR exon18-mutant tumors**
- Lung
- Cervical
- Salivary gland
- Solid tumors (NOS)
- Bladder

**HER2-mutant tumors**
- Breast HRc-positive*
- Breast HRc-negative

**HER4-mutant tumors**
- Solid tumors (NOS)

**Neratinib**
- Monotherapy
- + Paclitaxel

**Neratinib**
- * + Trastuzumab#

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

- **Tumor characteristics:**
  - usually mutually exclusive to HER2 amplifications

- **Preclinical evidence of oncogenic activity:**
  - constitutive activation of intracellular kinase and downstream signaling pathways
  - increased cell proliferation and tumor growth
  - 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)

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HR-positive HER2 Mutated Breast

Publications from SUMMIT trial HER2 mutant breast cohorts

- All (HR+/HR-) breast cancer → Neratinib monotherapy
- All (HR+/HR-) breast cancer → Neratinib monotherapy
- HR-positive breast cancer → Neratinib + fulvestrant
- HR-positive breast cancer → Neratinib + trastuzumab fulvestrant

Other case reports or secondary publications:

Efficacy comparison across HER2 mutant HR+ breast cancer cohorts

- 17% ORR; 3.6 mo mPFS
  - Neratinib Monotherapy (n=18)
- 30% ORR; 5.4 mo mPFS
  - Neratinib + Fulvestrant (n=39)
- 53% ORR; 9.8 mo mPFS
  - Neratinib + Trastuzumab + Fulvestrant (n=17)

Best percentage change in tumor from baseline is based on investigator-assessments per RECIST v1.1 criteria
HR-positive HER2 Mutated Breast

Progression-free survival (PFS): 
*HER2*-mutant HR+ breast cancer cohorts

![Graph showing progression-free survival (PFS) for different treatment regimens.

- **Neratinib monotherapy** (n=22): Median PFS (95% CI) 3.6 months (1.8–5.4)
- **Neratinib + fulvestrant** (n=45): Median PFS (95% CI) 5.7 months (3.8–10.3)
- **Neratinib + trastuzumab + fulvestrant** (n=20): Median PFS (95% CI) 9.8 months (4.2–NE)

<table>
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<tr>
<th>No. at risk</th>
<th>Time (months)</th>
<th>N alone</th>
<th>N + F</th>
<th>N + T + F</th>
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</table>
Amendment to Breast Cancer Cohort in SUMMIT for HR-positive/HER2-negative, HER2mut MBC Cohort to Support Accelerated Approval

Randomized 1:1:1

- fulvestrant
- fulvestrant + trastuzumab
- fulvestrant + trastuzumab + Neratinib

**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 Q1 2021-Q2 2021)
SUMMIT
Cervical Cancer Cohort
Characteristics of *HER2* Mutant Cervical Cancer

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

**Histology**
- Enriched in adenocarcinomas
- High occurrence in HPV+ tumors

**Genomics**
- Most common HER2\textsuperscript{mut} 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
SUMMIT (PUMA-NER-5201) Basket Trial

*EGFR* exon 18 lung cancer cohort update
EGFR exon 18 mutations are highly sensitive to neratinib (irreversible pan-HER TKIs) in vitro studies

Comparative TKI affects in EGFR exon 18+ cells

Western blot analyses of transfected HEK293 cells

EGFR exon 18 mutations are highly sensitive to neratinib in NSCLC patients from POC trial

Phase 2 trial of neratinib in lung cancer

4 of 167 (2%) patients had EGFR exon 18 mutations (G719X)
- One patient did not have measurable disease by central review
- All patients with G719 mutations (n=4) had clinical benefit
  - 3 PRs
  - mPFS 52.7 weeks, [90% CI 25.6 - 57.0 weeks]
  - 1 SD lasting >40 weeks

### Patient characteristics

<table>
<thead>
<tr>
<th>Median (range), years</th>
<th>Safety/Efficacy evaluable patients (n=11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;65 years, n (%)</td>
<td>67 (56-83)</td>
</tr>
<tr>
<td>≥65 years, n (%)</td>
<td>4 (36)</td>
</tr>
<tr>
<td></td>
<td>7 (64)</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Gender, n (%)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>5 (45)</td>
</tr>
<tr>
<td>Male</td>
<td>6 (55)</td>
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<th>ECOG performance status, n (%)</th>
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<td>5 (45)</td>
</tr>
<tr>
<td>1</td>
<td>6 (55)</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Race, n (%)</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Black or African American</td>
<td>1 (9)</td>
</tr>
<tr>
<td>White</td>
<td>10 (91)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Median number of prior therapies in metastatic/locally advanced setting (range)</th>
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<tbody>
<tr>
<td>2 (1 – 3)</td>
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</table>

<table>
<thead>
<tr>
<th>Prior checkpoint inhibitor, n (%)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior chemotherapy, n (%)</td>
<td>3 (27)</td>
</tr>
<tr>
<td>Prior tyrosine kinase inhibitor, n (%)</td>
<td>6 (55)</td>
</tr>
<tr>
<td>gelitinib/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: Baseline demographics and patient characteristics

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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>
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</thead>
<tbody>
<tr>
<td>Objective response (confirmed), a n</td>
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<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>36 (11–69)</td>
<td>40 (12–74)</td>
</tr>
<tr>
<td>Best overall response, n</td>
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</tr>
<tr>
<td>CR</td>
<td>6</td>
<td>6</td>
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<tr>
<td>PR</td>
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<td>0</td>
</tr>
<tr>
<td>Best overall response rate, % (95% CI)</td>
<td>54 (23–83)</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></td>
<td>(1.9*, 4.0, 7.5, 9.2*)</td>
<td>(1.9*, 4.0, 7.5, 9.2*)</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>6.9 b (2.1–NA)</td>
<td>9.1 (3.7–NA)</td>
</tr>
</tbody>
</table>

a 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

b Kaplan-Meier analysis in safety population. c Clinical benefit rate (CBR) is defined as confirmed CR or PR or stable disease (SD) for ≥16 weeks (within +/- 7-day visit window) DOIC, 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
EGFR exon 18 mutant lung cancer cohort receiving neratinib monotherapy: Most common treatment emergent adverse events >10%

<table>
<thead>
<tr>
<th>TEAE</th>
<th>Safety evaluable patients (n=11)</th>
<th>Any grade</th>
<th>Grade ≥ 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea</td>
<td></td>
<td>5 (45.5)</td>
<td>0</td>
</tr>
<tr>
<td>Vomiting</td>
<td></td>
<td>4 (36.4)</td>
<td>0</td>
</tr>
<tr>
<td>Constipation</td>
<td></td>
<td>3 (27.3)</td>
<td>0</td>
</tr>
<tr>
<td>Nausea</td>
<td></td>
<td>3 (27.3)</td>
<td>0</td>
</tr>
<tr>
<td>Decreased appetite</td>
<td></td>
<td>3 (27.3)</td>
<td>1 (9.1)</td>
</tr>
<tr>
<td>Dizziness</td>
<td></td>
<td>2 (18.2)</td>
<td>0</td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td>2 (18.2)</td>
<td>0</td>
</tr>
<tr>
<td>Dry mouth</td>
<td></td>
<td>2 (18.2)</td>
<td>0</td>
</tr>
<tr>
<td>Fatigue</td>
<td></td>
<td>2 (18.2)</td>
<td>0</td>
</tr>
</tbody>
</table>

Data cut-off: 21-Aug-2020
# EGFR exon 18 mutant lung cancer cohort receiving neratinib monotherapy: Characteristics of treatment emergent diarrhea

<table>
<thead>
<tr>
<th>Lung EGFR (N) (N = 11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>**Incidence of diarrhea, n (%)**a</td>
</tr>
<tr>
<td>Any grade</td>
</tr>
<tr>
<td>Grade 1</td>
</tr>
<tr>
<td>Grade 2</td>
</tr>
<tr>
<td>Grade 3</td>
</tr>
<tr>
<td><strong>Action taken with neratinib, n (%)</strong></td>
</tr>
<tr>
<td>Leading to temporary hold</td>
</tr>
<tr>
<td>Leading to dose reduction</td>
</tr>
<tr>
<td>Leading to permanent discontinuation</td>
</tr>
<tr>
<td><strong>Diarrhea leading to hospitalization, n (%)</strong></td>
</tr>
<tr>
<td><strong>Time to first diarrhea, median (range) in days</strong></td>
</tr>
<tr>
<td><strong>Time to first grade 2 diarrhea, median (range) in days</strong></td>
</tr>
<tr>
<td><strong>Duration of grade 2 diarrhea per episode, median (range) in days</strong></td>
</tr>
</tbody>
</table>

Data cut-off: 21-Aug-2020
Historical response rates of afatinib in NSCLC patients with \textit{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) |
| EGFR TKI-naïve patients | | | | | | | |
| Major uncommon mutation (n = 110) | | | | | | | |
| 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) |
| EGFR TKI-pre-treated patients | | | | | | | |
| Major uncommon mutation (n = 32) | | | | | | | |
| 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.

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 H1 2021

- 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 TKI in 2021
HER-Seq (PUMA-NER-9501): HER2 mutation screening protocol
HER-Seq: a convenient, minimally-invasive blood-based screening protocol to identify HER2 mutant patients for neratinib clinical trials

• Simple, non-invasive blood-based screening protocol for identifying HER2 mutations from plasma cfDNA

• HER-Seq NGS assay is analytically-validated, CE-marked, and ISO-certified

• Convenient for sites/institutions that lack access to routine/reimbursable molecular sequencing

• Allows for routine serial testing to identify acquired HER2 mutations through advancement of disease or therapy

• Patients identified with HER2 mutations can be readily tracked for protocol screening and seamless registration into SUMMIT or other neratinib clinical trials

Clinical trials.gov NCT: NCT03786107.
**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**
- Women and men who are ≥18 years old at signing 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

---

**Metastatic breast or cervical cancer patient**
**Patient consented**
**Blood sample collected**
**Sample shipped to central lab**
**HER2 mutation proprietary sequencing test performed**
**Test result reported to physician and sponsor within 2-4 weeks**

**HER2 mutation positive**
**Consider screening for neratinib treatment protocol**

**HER2 wild type**
**Retest in 3-6 months**
HER-Seq Trial

- Currently open at ~21 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
## IST Landscape – Other Cancers

### ISTs

<table>
<thead>
<tr>
<th>ISTs</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FC-7 (NSABP)</strong></td>
<td>Quad Wild-Type mCRC w/ prior cetuximab or panitumumab, dose finding for N + Cetuximab</td>
</tr>
<tr>
<td><strong>FC-11 (NSABP)</strong></td>
<td>Quad Wild-Type mCRC, HER2+ w/ prior EGFR ther or HER2-mutated: N+T, HER2+ w/o prior EGFR therapy: N+Cetuximab</td>
</tr>
<tr>
<td><strong>ACOMPLI (INSERM)</strong></td>
<td>HER2+ or HER2-mutated mCRC, N vs. SOC</td>
</tr>
<tr>
<td><strong>INSIGHt (DFCI)</strong></td>
<td>Tumors w/ unmethylated MGMT promoters, w/o IDH1 R132H mutation, SOC (temozolomide) vs. N vs. CC-115 vs. Abemaciclib</td>
</tr>
<tr>
<td><strong>NEREA (SOLTI)</strong></td>
<td>HR+/HER2-/HER2-enriched mBC, N + Ex/Ful/Tam</td>
</tr>
<tr>
<td>**201209135/MutHER (WU)</td>
<td>HER2-mutated mBC, ER-: N, ER+: N+Cetuximab</td>
</tr>
<tr>
<td><strong>PlasmaMATCH (ICR)</strong></td>
<td>HER2-mut mBC, line 2+, ER-: N, ER+: N+Ful</td>
</tr>
<tr>
<td><strong>2016-0537 (MDACC)</strong></td>
<td>iBC, HER2+: N+Pac+Per+T, HER2- /ER+: N+Pac</td>
</tr>
<tr>
<td><strong>2016-0430 (MDACC)</strong></td>
<td>Advanced/metastatic cancer with HER2/3/4 mutation or HER2/3+, N+Everolimus vs. N+Palbo vs. N+Trametinib</td>
</tr>
<tr>
<td><strong>POE 16-01 (MSKCC)</strong></td>
<td>Pediatric solid tumors and acute leukemias, N dose finding followed by N at RP2D</td>
</tr>
<tr>
<td><strong>MCC-17-13821 (VCU)</strong></td>
<td>P1 dose finding N + sodium valproate in advanced solid tumors, expansion in HER2+ BC and K-/N-RAS mutant cancers</td>
</tr>
</tbody>
</table>

### Cancer Types

- **Colorectal Cancer**
- **Glioblastoma**
- **Breast Cancer**
- **Multiple Tumor Types**
Puma - Expected Milestones

- Report Phase II data from HR positive breast cohort from the SUMMIT basket trial of neratinib in patients with HER2 mutations (Q4 20)

- Report additional data from Phase II CONTROL trial (Q4 20)

- Report Phase II data from cohort of patients in SUMMIT basket trial with bile duct cancer with HER2 mutations treated with neratinib monotherapy (Q1 21)

- 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 2021)
Puma - Expected Milestones

- Conduct pre-NDA meeting with the FDA to discuss accelerated approval of neratinib in HER2 mutated hormone receptor positive breast cancer and HER2 mutated cervical cancer (H1 21)

- Report Phase II TBCRC-022 trial of the combination of Kadcyla plus neratinib in patients with HER2 positive breast cancer with brain metastases who have previously been treated with Kadcyla (H1 2021)

- 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 (2021)
Intellectual Property

- Composition of matter patent issued (expires 2025)
  - Can be extended w/ 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)
- Additional use patents filed
Intellectual Property on EGFR T790M Mutations

- Issued claims in Europe, Asia, Australia (expires 2026)
  - Possibility to extend up to 5 years

- Pending claims in United States

- Patent claims upheld after European Opposition Hearing (February 2014)

- 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

Richard Bryce, MD
Chief Medical and Scientific Officer
  - Onyx, Roche, ICON Clinical Research

Jeff Ludwig
Chief Commercial Officer
  - Astellas, Amgen

Maximo F. Nougues
Chief Financial Officer
  - Getinge AB, Boston Scientific, The Clorox Company

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.*

Ann Miller, M.D.
Former VP, Marketing, Global Marketing, Sanofi S.A.; Eisai; Amgen; Merck

Michael Miller
Former *EVP U.S. Commercial, Jazz Pharmaceuticals; VP, Sales & Marketing, Genentech*

Jay Moyes
*Former CFO, Myriad Genetics*

Hugh O’Dowd
*President & CEO, Neon Therapeutics; Former Chief Commercial Officer, Novartis Oncology*

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*
Puma Biotechnology - Financial

- Currently trading on NASDAQ: PBYI
- Cash, cash equivalents and marketable securities at September 30, 2020: ~$109 million
- Cash earned in Q3 2020: ~$1.8 million
- Amended term loan agreement (June 2019)
  - New term loan of $100 million replaces loan of $155 million
  - $100 million drawn down
  - Oxford Finance
- Shares issued and outstanding: 39.8 million
Company Highlights

▪ NERLYNX® - First HER2 directed drug approved by FDA for extended adjuvant treatment of early stage HER2-positive breast cancer in patients who have received prior trastuzumab

▪ NERLYNX® - First HER2 directed tyrosine kinase inhibitor approved in both early stage and metastatic HER2-positive 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
Puma Biotechnology

Credit Suisse 29th Annual Virtual Healthcare Conference

November 2020
Puma Biotechnology

Credit Suisse 29th Annual Virtual Healthcare Conference

APPENDIX

November 2020
ExteNET Trial - HER2 Positive Extended Adjuvant Breast Cancer

- HER2 positive breast cancer
- Completed 1 year prior adjuvant treatment with trastuzumab prior to randomization
- Lymph node negative, positive or residual invasive disease after neoadjuvant treatment

Randomize 1:1

2840 patients total

Neratinib (1 year)

Placebo (1 year)

Primary endpoint: Invasive Disease Free Survival (IDFS)

Secondary endpoints: Disease Free Survival Including Ductal Carcinoma in Situ (DFS-DCIS), Time to Distant Recurrence, Incidence of CNS recurrence, Overall Survival

No loperamide prophylaxis used to prevent neratinib related diarrhea
Kaplan-Meier Estimates of Disease Free Survival
ITT Population

P-value = 0.009
HR (95% CI) = 0.67 (0.50–0.91)

No. at risk
Neratinib  1420  1291  1260  1229  1189  1150  1108  1033  662
Placebo  1420  1367  1324  1292  1243  1209  1163  1090  704
Kaplan-Meier Estimates of DFS
Hormone Receptor Positive Patients ITT Population

Disease-free survival (%)

P-value = 0.001
HR (95% CI) = 0.51 (0.33–0.77)

No. at risk
Neratinib 816 737 721 698 677 653 629 591 380
Placebo 815 784 761 741 716 699 669 622 401
Rationale for efficacy in HR+ subgroup

HER2 signalling decreases ER-regulated gene transcription

HER2 inhibition upregulates ER-regulated gene transcription

Inhibition of HER2 and ER is required for effective blockage in HER2+/HR+ tumors

Adapted from: Paplomata et al. Cancer 2015
5-year Analysis Shows Durable iDFS Benefit

ITT Population

Disease-free survival

HR (95% CI): 0.73 (0.57-0.92)
Two-sided P=0.008

At risk

Neratinib 1420 1316 1272 1225 1106 978 965 949 938 920 885
Placebo 1420 1354 1298 1248 1142 1029 1011 991 978 958 927

(Descriptive P value)
iDFS by Hormone Receptor Status
5-Year Analysis

Hormone receptor positive

HR (95% CI): 0.60 (0.43-0.83)  
Two-sided P=0.002

Hormone receptor negative

HR (95% CI): 0.95 (0.66-1.35)  
Two-sided P=0.762

At risk

Neratinib 816 757 731 705 642 571 565 558 554 544 523
Placebo 815 779 750 719 647 581 567 556 551 542 525

At risk

Neratinib 604 559 541 520 464 407 400 391 384 376 362
Placebo 605 575 548 529 495 448 444 435 427 416 402

(Descriptive P value)
iDFS for HR+ patients completing prior trastuzumab ≤1 year from randomization (2-year and 5-year Analyses) EC Approved Indication

51% relative reduction in risk of recurrence

42% relative reduction in risk of recurrence
DDFS for HR+ patients completing prior trastuzumab ≤1 year from randomization (2-year and 5-year Analyses)

EC Approved Indication

47% relative reduction in risk of recurrence

43% relative reduction in risk of recurrence

Gnant M, et al. SABCS 2018, poster #P2-13-01
iDFS for HR+ patients completing prior trastuzumab ≤1 year from randomization (2-year and 5-year Analyses) who had prior neoadjuvant therapy with no pCR

36% relative reduction in risk of recurrence

40% relative reduction in risk of recurrence