Novartis Investor Relations

# Novartis ASCO Event

**Investor Presentation**
**June 4, 2023**

NOVARTIS | Reimagining Medicine

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# Participants

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# Agenda

1 **Novartis at ASCO 2023**

2 *Kisqali* NATALEE trial in early breast cancer

3 *Kisqali*: Establishing the CDK4/6 of choice

4 Q&A

# Novartis oncology pipeline focused in areas of high unmet need where we have deep expertise

| | Solid Tumors | Hematology |
|---|---|---|
| **Disease areas** (Selected) | Breast Cancer<br>Prostate Cancer<br>Lung Cancer | Non-Hodgkin's Lymphoma<br>Myeloid Cancers<br>Non-Malignant Hematology |
| **Commercial assets** | KISQALI® ribociclib<br>PLUVICTO™<br>PIQRAY® (alpelisib) tablets<br>Tafinlar® (dabrafenib) + Mekinist® (trametinib)<br>Advanced Accelerator Applications LUTATHERA® | KYMRIAH® (tisagenlecleucel)<br>SCEMBLIX® (asciminib)<br>PROMACTA® (eltrombopag)<br>JAKAVI® ruxolitinib |
| **Pipeline assets and opportunities** | ***Kisqali*** Adjuvant HR+/HER2- BC<br>***Pluvicto*** Prostate cancer<br>**JDQ433** NSCLC<br>**NIS793** 1L mPDAC / 1L mCRC | **Iptacopan** PNH, aHUS<br>**Ianalumab** Multiple indications<br>**YTB323** Non-Hodgkin's Lymphoma<br>**PHE885** Multiple Myeloma |

**Leveraging advanced therapy platforms** such as radioligand therapy, cell therapy, and differentiated biologics

AML / MDS – Acute Myeloid Leukemia / Myelodysplastic Syndrome. HR+/HER2− – hormone receptor-positive / human epidermal growth factor receptor 2-negative. NSCLC – non-small cell lung cancer. mPDAC – metastatic pancreatic ductal adenocarcinoma. mCRC – metastatic colorectal cancer. PNH – paroxysmal nocturnal hemoglobinuria. aHUS – atypical hemolytic uremic syndrome.

# Key assets in solid tumors and hematology highlighted at ASCO

2023 ASCO ANNUAL MEETING

## 63 abstracts

5 oral presentations

3 poster discussions

36 posters

19 abstracts (publication only)

## Data highlights

*Kisqali* NATALEE Ph3 study in early breast cancer

New analyses from *Pluvicto* VISION trial in prostate cancer

JDQ443 KontRASt-01 trial in KRAS G12C-mutated lung cancer

PHE885 updated Ph1 data in r/r Multiple Myeloma

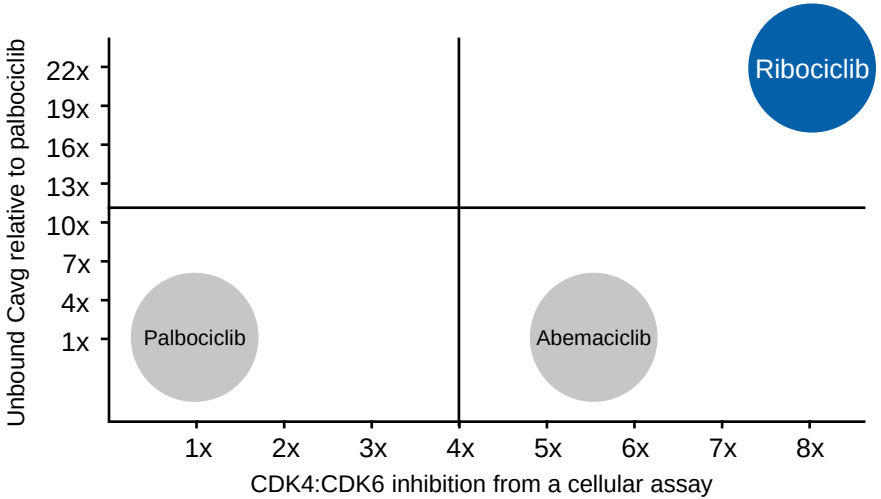
# *Kisqali*'s mechanism of action is unique in inhibiting CDK4 eight times more than CDK6[1-4]

At clinically relevant doses, **ribociclib provides greater CDK4 inhibition** in vivo than competitors

Higher unbound $C_{avg}$ means **more drug available** to act on tumor cells[1-4]

More time for on-target CDK4 inhibition enables **irreversible cell growth arrest (senescence)** of micro-metastases and immuno-modulation

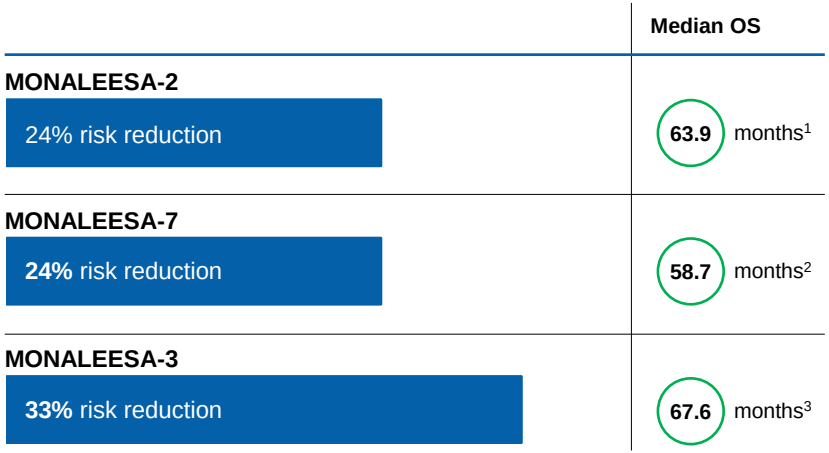
**Select differences among CDK4/6 inhibitors[1-4]**




1. Yu Q, Sicinska E, Geng Y, et al. Requirement for CDK4 kinase function in breast cancer. Cancer Cell. 2006;9(1):23-32. 2. An H-X, Beckmann MW, Reifenberger G, Bender HG, Niederacher D. Gene amplification and overexpression of CDK4 in sporadic breast carcinomas is associated with high tumor cell proliferation. Am JPathol. 1999;154(1):113-118. 3. Kim S, Tiedt R, Loo A, et al. The potent and selective cyclin-dependent kinases 4 and 6 inhibitor ribociclib (LEE011) is a versatile combination partner in preclinical cancer models. Oncotarget. 2018;9(81):35226-35240;(suppl). 4. Sammons SL, Topping DL, Blackwell KL. HR+, HER2-advanced breast cancer and CDK4/6 inhibitors: mode of action, clinical activity, and safety profiles. Curr Cancer Drug Targets. 2017;17(7):637-649.

# NATALEE study builds on a strong foundation in metastatic breast cancer (mBC), where *Kisqali* has a proven OS benefit

## *Kisqali* Ph3 OS results in 1L mBC




**Proven OS benefit across all three Phase 3 trials**: regardless of menopausal status, hormone therapy partner, or dose modifications[4]

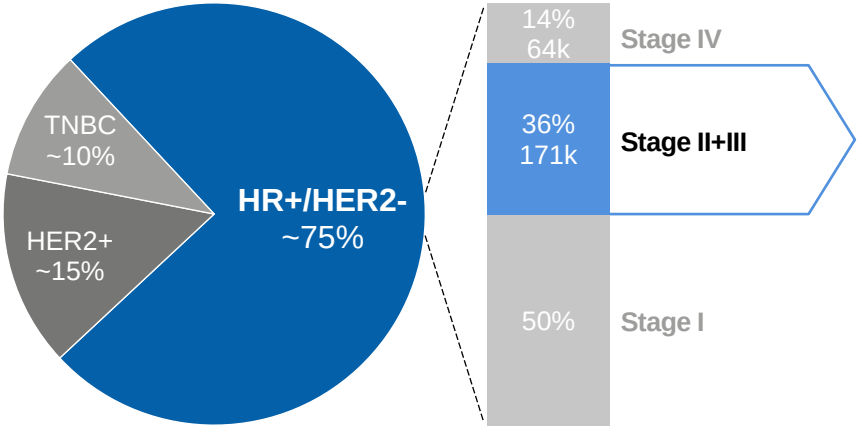
- ***Kisqali* is the only CDK4/6i with statistically significant OS benefit** proven across all three Ph3 trials, while maintaining or improving QoL
- **Kisqali set a new benchmark for survival, with unprecedented median OS of ~5 years** when combined with letrozole or fulvestrant in 1L mBC
- **NCCN guidelines** recommend *Kisqali* as the only Category 1 treatment for 1L mBC in combination with AI (~60% of 1L mBC patients)

1. In months vs. vs 51.4, P value: 0.008. Reference: Hortobagyi, GN et al., 2022. 2. vs 48.0. Reference: Lu, YS et al., 2022. 3. vs 51.8. Reference: Neven, P et al., 2022. 4. Based on an analysis of MONALEESA-2, -3 and -7.
OS – overall survival. 1L – first line. AI – aromatase inhibitor.

# Early Breast Cancer (eBC) remains an area of high unmet need

## Total breast cancer patient population

Annual incidence, US+EU5 ~620k




**Risk of recurrence**

Stage II and III eBC patients are at significant risk of recurrence[1]:

- **Between a third and a half will see their cancer recur** in their lifetime[1]
- Half of recurrences occur beyond 5 years[2]

**Quality of life (QoL)**

Improving patient outcomes without putting additional burden on the patient is essential[3]

The treatment goal in eBC is to prevent disease recurrence while maintaining QoL

Data Source: Kantar Health – US/ EU5 Patient Metrics 2023 1. Pan H, et al. N Engl J Med. 2017;377:1836-1846. 2. Gomis RR, et al. Mol Oncol. 2017; 11:62-78. 3. Cerner Enviza CancerMpact surveyed data as of Sep'22.

# Agenda

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# NATALEE study design

## NATALEE: Adult patients with HR+/HER2- eBC | Prior ET allowed up to 12 months

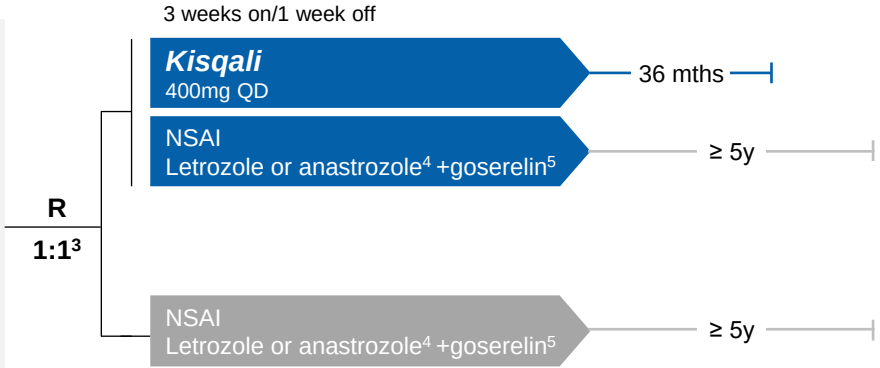
**Anatomic stage IIA[1]**

- N0 with:
  - Grade 2 and evidence of high risk: Ki-67 ≥ 20%; Oncotype DX Breast Recurrence Score ≥ 26; or high risk vs. genomic risk profiling
  - Grade 3
- N1

**Anatomic stage IIB[1] & III**

- Stage IIB: N0 or N1
- Stage III: N0, N1, N2 or N3

N=5101[2]




**Randomization stratification:**

- **Anatomic stage** II vs. III
- **Menopausal status** Premenopausal women & men vs. postmenopausal women
- **Receipt of prior (neo)adjuvant chemotherapy:** Yes/No
- **Geographic location:** North America/Western Europe/ Oceania vs. Rest of World

**Primary endpoint:**

- iDFS using STEEP criteria

**Secondary endpoints:**

- Recurrence-free survival
- Distant disease-free survival
- OS
- PROs
- Safety and tolerability
- PK

**Exploratory endpoints:**

- Loco-regional recurrence-free survival
- Gene expression and alterations in tumor ctDNA/ctRNA samples

1. Enrollment of patients with stage II disease was capped at 40%. 2. 5101 patients were randomized from 10 Jan 2019 to 20 April 2021. 3. Open-label design. 4. Per investigator choice. 5. In pre-menopausal women and in men.
ET – endocrine therapy. CT – chemotherapy. ctDNA/RNA – circulating tumor DNA/RNA. eBC – early breast cancer. iDFS – invasive disease-free survival. NSAI – nonsteroidal aromatase inhibitor. PAM50 – prediction analysis of microarray 50. PK – pharmacokinetics. PRO – patient reported outcome. R – randomized. STEEP – Standardized Definitions for Efficacy End Points in Adjuvant Breast Cancer Trials.

# NATALEE was uniquely designed to leverage *Kisqali*'s strengths and address significant unmet needs in eBC

| | Insights | | NATALEE trial design |
|---|---|---|---|
| **Population** | Stage II and III patients are at significant risk of recurrence | ▶ | Broad population of stage II and III eBC patients, including those with N0 disease |
| **Dose** | Tumor control achievable with lower drug concentration vs. mBC, given lower tumor burden | ▶ | Lower dose (400mg) to improve tolerability and adherence while maintaining efficacy |
| **Treatment period** | Longer on-target CDK4 inhibition may be critical to induce senescence to prevent both early and late recurrences | ▶ | 3-year treatment duration to address risk of recurrence |

N – node. N0 – no nodal involvement.

# NATALEE included a broad population of stage II and III patients at risk of recurrence, including those with no nodal involvement

| AJCC Anatomical Staging[1] | TN (M0) | NATALEE[2,3] |
|---|---|---|
| Stage IA | T1N0 | X |
| Stage IB | T0N1mi | X |
| | T1N1mi | X |
| Stage IIA | T0N1 | ✓ |
| | T1N1 | ✓ |
| | T2N0 | If G3; or G2 with Ki-67 ≥ 20%; or high genomic risk |
| Stage IIB | T2N1 | ✓ |
| | T3N0 | ✓ |
| Stage IIIA | T0N2 | ✓ |
| | T1N2 | ✓ |
| | T2N2 | ✓ |
| | T3N1 | ✓ |
| | T3N2 | ✓ |
| Stage IIIB | T4N0 | ✓ |
| | T4N1 | ✓ |
| | T4N2 | ✓ |
| Stage IIIC | Any TN3 | ✓ |

Patients at risk of recurrence, regardless of nodal status

1. Amin MB, et al, eds. AJCC Cancer Staging Manual. 8th ed. New York, NY: Springer; 2017:587-636. 2. Slamon DJ, et al. J Clin Oncol. 2019;37(suppl 15). Abstract TPS597. 3. Data on file. NATALEE CLEE011O12301C (TRIO033). Clinical study protocol. V4.0. Novartis Pharmaceuticals Corp; August 27, 2020.

# Baseline characteristics were balanced between treatment arms

| Parameter | | RIB + NSAI n = 2549 | NSAI alone n = 2552 | All patients N = 5101 |
|---|---|---|---|---|
| **Age, median (min-max), years** | | 52 (24-90) | 52 (24-89) | 52 (24-90) |
| **Menopausal status, n (%)** | Premenopausal women and men[1]<br>Postmenopausal women | 1126 (44)<br>1423 (56) | 1132 (44)<br>1420 (56) | 2258 (44)<br>2843 (56) |
| **Anatomic stage[2,3], n (%)** | Stage IIA<br>Stage IIB<br>Stage III | 479 (19)<br>532 (21)<br>1528 (60) | 521 (20)<br>513 (20)<br>1512 (59) | 1000 (20)<br>1045 (20)<br>3040 (60) |
| **Nodal status at diagnosis, n (%)** | NX<br>N0<br>N1<br>N2/N3 | 272 (11)<br>694 (27)<br>1050 (41)<br>483 (19) | 264 (10)<br>737 (29)<br>1049 (41)<br>467 (18) | 536 (11)<br>1431 (28)<br>2099 (41)<br>950 (19) |
| **Prior ET, n (%)[4]** | Yes | 1824 (72) | 1801 (71) | 3625 (71) |
| **Prior (neo)adjuvant CT, n (%)** | Yes | 2249 (88) | 2245 (88) | 4494 (88) |
| **ECOG PS, n (%)** | 0<br>1 | 2106 (83)<br>440 (17) | 2132 (84)<br>418 (16) | 4238 (83)<br>858 (17) |

1. In the RIB+NSAI arm there were 11 men (0.4%) and in the NSAI alone arm there were 9 men (0.4%). 2. A total of 14 patients with Stage I disease were included: 9 pts (0.4%) in the RIB + NSAI arm and 5 pts (0.2%) in the NSAI alone arm. 3. Stage is derived using TNM from surgery for patients having not received (neo)adjuvant treatment, or as worst stage derived using TNM at diagnosis and TNM from surgery for patients having received (neo)adjuvant treatment. 4. Prior OFS was received by 670 pts (26.3%) in the RIB + NSAI arm and 620 pts (24.3%) in the NSAI alone arm. RIB – ribociclib. CT – chemotherapy. N0 – no nodal involvement. N1 – 1-3 axillary lymph nodes. N2 – 4-9 axillary lymph nodes. N3 – 10 or more axillary lymph nodes or collarbone lymph nodes. NX – regional nodes were not assessed.

# At the interim analysis, median follow-up for iDFS was 27.7 months; 20% patients in the *Kisqali* arm had completed 3 years of treatment

**Median follow-up for iDFS at the IA:**
27.7 months[1]

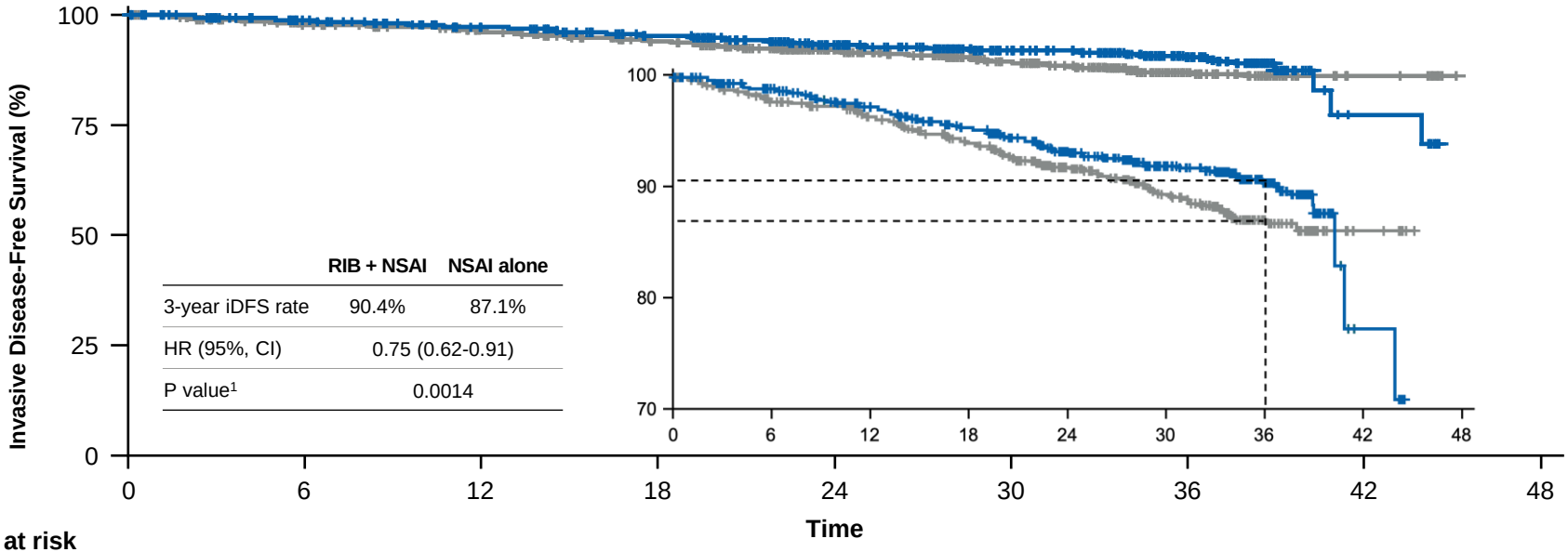
57% of patients in *Kisqali* arm had completed 2 years of treatment[2]

20% of patients in *Kisqali* arm had completed 3 years of treatment

| | ***Kisqali* + NSAI** | **NSAI Alone** |
|---|---|---|
| **ITT population** | N = 2549 | N = 2552 |
| **Received study treatment** | n = 2526 | n = 2442 |

1. Overall study median follow-up 34.0 months (minimum, 21 months); median follow-up for iDFS 27.7 months. 2. Includes patients who are still ongoing on treatment. IA – interim analysis.

# *Kisqali* showed a clinically meaningful and statistically significant improvement in iDFS, reducing the risk of recurrence by 25%



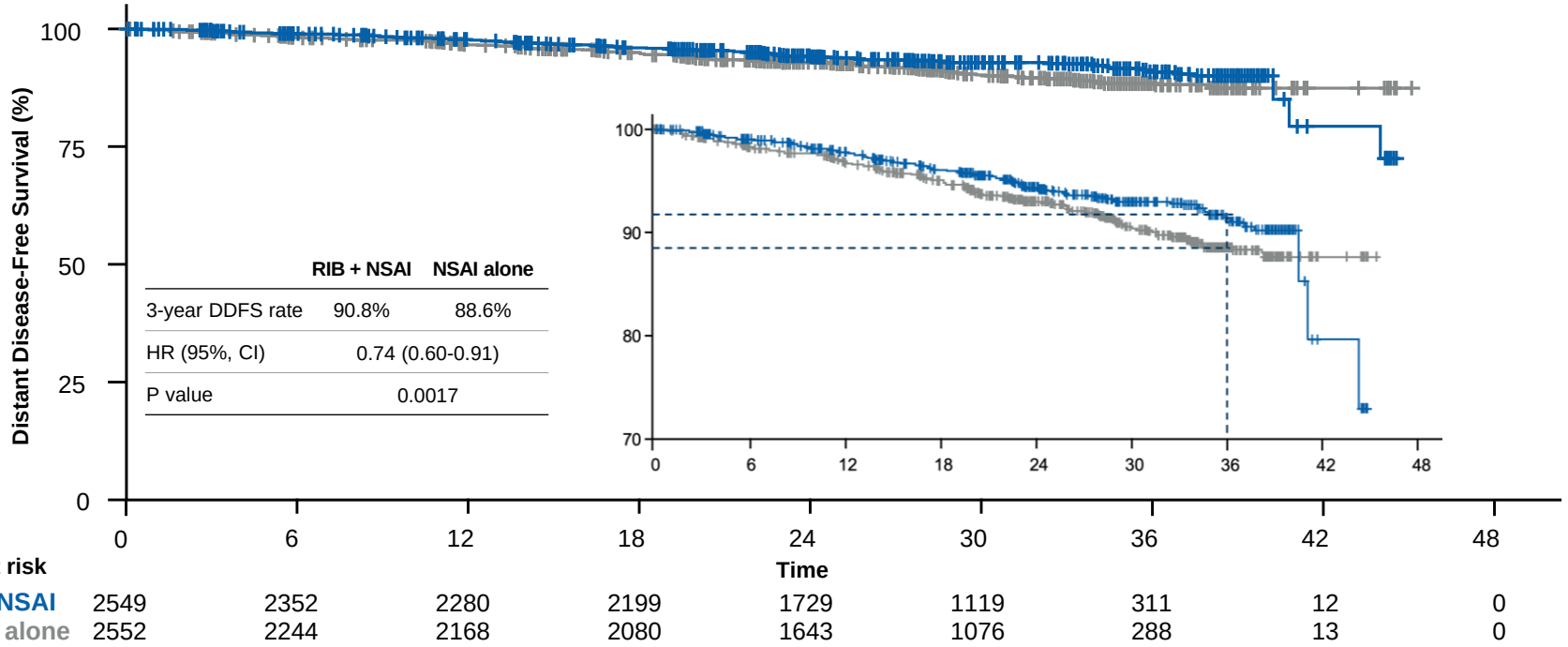

1. One-sided P value. iDFS – invasive disease-free survival.

# iDFS benefit was consistent across subgroups, including stage II and stage III, and node-negative and node-positive patients

| | | HR | (95% CI) |
|---|---|---|---|
| **Menopausal status** | ☑ Pre-menopausal women and men | 0.72 | (0.53, 0.98) |
| | ☑ Post-menopausal women | 0.78 | (0.61, 0.997) |
| **AJCC stage** | ☑ Stage II | 0.76 | (0.53, 1.10) |
| | ☑ Stage III | 0.74 | (0.59, 0.92) |
| **Prior CT** | ☑ Neoadjuvant | 0.78 | (0.61, 1.01) |
| | ☑ Adjuvant | 0.67 | (0.49, 0.93) |
| **Prior ET** | ☑ Yes | 0.76 | (0.60, 0.96) |
| | ☑ No | 0.77 | (0.56, 1.08) |
| **Region** | ☑ North America/Western Europe/Oceania | 0.76 | (0.59, 0.97) |
| | ☑ Rest of world | 0.76 | (0.56, 1.02) |
| **Histological grade at time of surgery** | ☑ Grade 1 | 0.78 | (0.33, 1.85) |
| | ☑ Grade 2 | 0.75 | (0.58, 0.97) |
| | ☑ Grade 3 | 0.78 | (0.55, 1.08) |
| **Ki-67 status[1]** | ☑ Ki-67 ≤20 | 0.80 | (0.59, 1.08) |
| | ☑ Ki-67 >20 | 0.75 | (0.56, 0.996) |
| **Nodal status[2,3]** | ☑ N0 | 0.63 | (0.34, 1.16) |
| | ☑ N1-N3 | 0.77 | (0.63, 0.94) |

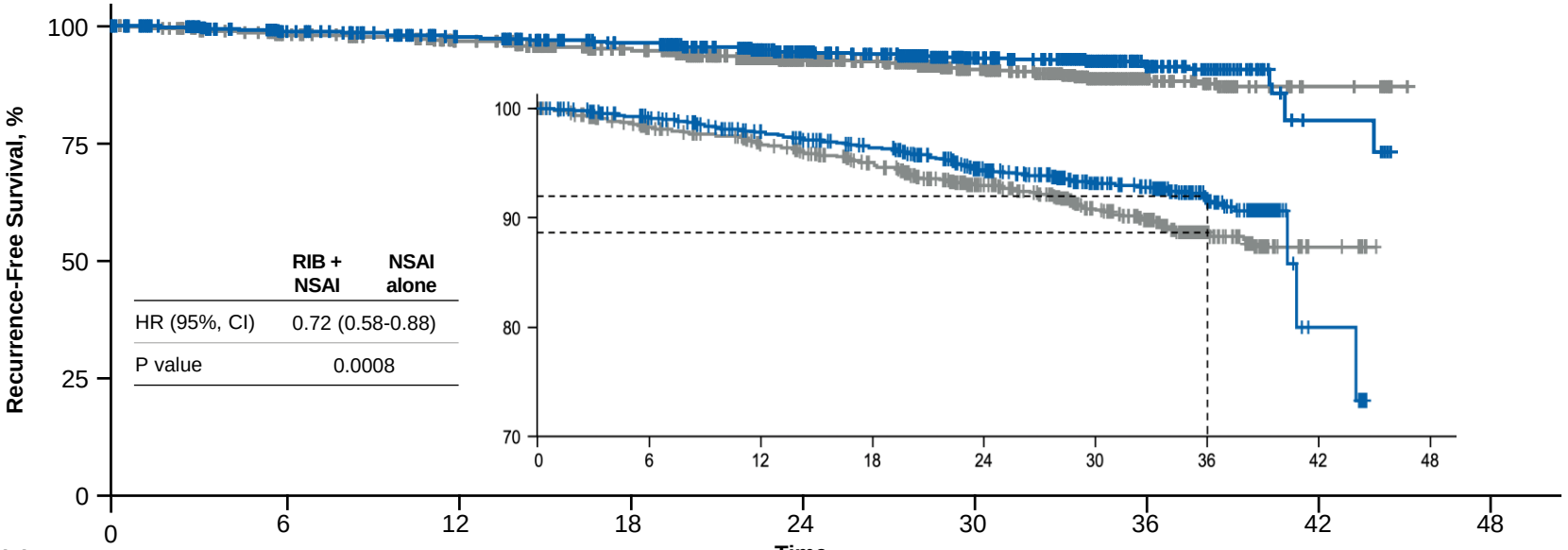
1. From archival tumor tissue. 2. Nodal status classification according to AJCC staging. 3. Nodal status is from the worse stage derived per surgical specimen or at diagnosis. AJCC – American Joint Committee on Cancer.

# *Kisqali* demonstrated a consistent benefit in distant disease-free survival, with a 26% risk reduction…




Distant disease-free survival (DDFS) defined as the time from date of randomization to date of first event of distant recurrence, death (any cause), or second primary non-breast invasive cancer.

# … and a 28% risk reduction with respect to recurrence-free survival




| No. at risk | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| RIB+NSAI | 2549 | 2358 | 2283 | 2210 | 1733 | 1124 | 314 | 12 | 0 |
| NSAI alone | 2552 | 2247 | 2174 | 2086 | 1646 | 1080 | 290 | 13 | 0 |

# *Kisqali* showed a trend for improved overall survival, reducing the risk of death by 24%

- While OS data remain immature in the ITT population, Kisqali + NSAI showed a trend for improved overall survival, **reducing the risk of death by 24%** compared to NSAI alone
- **Additional follow-up** for OS is planned

| | RIB + NSAI | NSAI alone |
|---|---|---|
| n/N (%) | 61/2549 (2.4) | 73/2552 (2.9) |
| HR (95%, CI) | 0.76 (0.54-1.07) | |
| P value | 0.0563 | |

ITT – intent to treat

# *Kisqali* at the 400mg dose was safe and well tolerated, with low rates of symptomatic AEs…

| | | RIB + NSAI n = 2524 | | NSAI Alone n = 2444 | |
|---|---|---|---|---|---|
| | | Any Grade | Grade ≥ 3 | Any Grade | Grade ≥ 3 |
| **AESIs, %** | Neutropenia[1] | 62.1 | **43.8** | 4.5 | **0.8** |
| | Febrile neutropenia | 0.3 | **0.3** | 0 | **0** |
| | Liver-related AEs[2] | 25.4 | **8.3** | 10.6 | **1.5** |
| | QT interval prolongation | 5.2 | **1.0** | 1.2 | **0.5** |
| | ECG QT prolonged | 4.2 | **0.2** | 0.7 | **0** |
| | ILD pneumonitis[3] | 1.5 | **0** | 0.8 | **0.1** |
| **Other clinically relevant AEs,%** | Arthralgia | 36.5 | **1.0** | 42.5 | **1.3** |
| | Nausea | 23.0 | **0.2** | 7.5 | **<0.1** |
| | Headache | 22.0 | **0.4** | 16.5 | **0.2** |
| | Fatigue | 21.9 | **0.7** | 12.7 | **0.2** |
| | Diarrhea | 14.2 | **0.6** | 5.4 | **0.1** |
| | VTE | 1.4 | **0.6** | 0.6 | **0.2** |

1. This is a grouped term that combines neutropenia and neutrophil count decreased. 2. This is a grouped term that includes all preferred terms identified by Standardized MedDRA Queries for drug-related hepatic disorders and included ALT and AST increased, γ-glutamyltransferase increased, blood alkaline phosphatase increased, and blood bilirubin increased. 3. This is a grouped term that includes all preferred terms identified by Standardized MedDRA Queries for interstitial lung disease. AE – adverse event. ALT – alanine aminotransferase. AST – aspartate aminotransferase. ILD – interstitial lung disease.

# … which contributed to limited treatment modifications when administered up to three years

Overall incidence, types and severity of AEs, as well as discontinuation rates due to AEs, were **predictable and manageable**, with no new safety signals identified with longer follow-up

19% of patients discontinued due to AEs, about half **protocol-mandated due to asymptomatic liver-related AEs**, e.g. ALT/AST increases (in which case patients can continue ET)

Most discontinuations **occurred early in treatment**; median time to onset within first 4 months

**Symptomatic AEs were low** and not key drivers of dose reductions or discontinuations

**Only 22% of patients on *Kisqali* reduced the dose**

# NATALEE results support *Kisqali* + ET as treatment of choice in a broad population of stage II and III patients at risk of recurrence

1

**_Kisqali_ demonstrated robust efficacy...**

- ☑ Statistically significant improvement in iDFS
- ☑ Consistent benefit across subgroups
- ☑ Trend for improved overall survival
- ☑ RFS and DDFS consistent with primary endpoints

2

**... with a favorable safety profile**

- ☑ No new safety signals
- ☑ 400mg dose well tolerated, with limited need for dose reductions
- ☑ Symptomatic AEs were low and not key drivers of discontinuation

Global regulatory filings including US and EU expected in H2 2023

# Agenda

1 Novartis at ASCO 2023

2 *Kisqali* NATALEE trial in early breast cancer

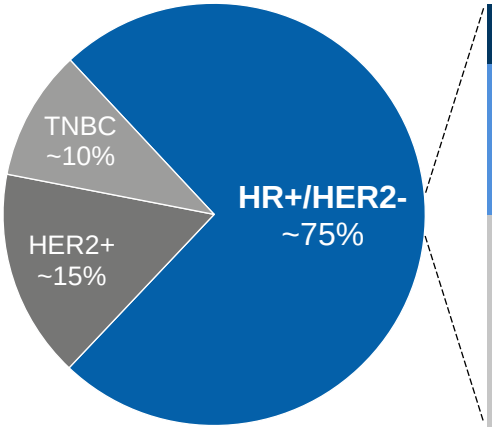
3 ***Kisqali*: Establishing the CDK4/6 of choice**

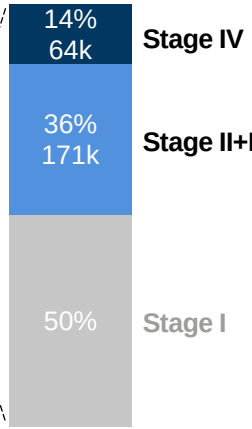
4 Q&A

# Of all CDK4/6 inhibitors, *Kisqali* has the potential to address the unmet needs of the broadest range of HR+/HER2- BC patients

## Total breast cancer patient population

Annual incidence, US+EU5 ~620k




**Stage IV**

**Stage II+III**

**Stage I**

**Metastatic Breast Cancer (mBC)**

- *Kisqali* is the only CDK4/6 inhibitor with proven OS benefit across 3 Ph3 trials
- Consistent OS benefit **regardless of combination partner, line of therapy, menopausal status, or site and number of metastases**
- Incident population: 32k US, 32k EU5
- Treatment rate (CDK4/6i): 50-60%[1]

**Early Breast Cancer (eBC)**

- *Kisqali* demonstrated efficacy in the at-risk stage II and III patient population, **regardless of nodal involvement**
- Consistent benefit across subgroups
- Incident population (stage II and III): 81k US, 90k EU5
- Treatment rate (ET; stage II and III): 70-80%[1]

Data Source: Kantar Health – US/ EU5 Patient Metrics 2023 1. Cerner Enviza CancerMpact surveyed data as of Sep'22.

# NATALEE would significantly expand our reach, compared to metastatic and compared to competition

## NATALEE population

**More than double the patient opportunity** compared to the mBC setting, and compared to monarchE in eBC[1]

## Incident population (estimated)[2]

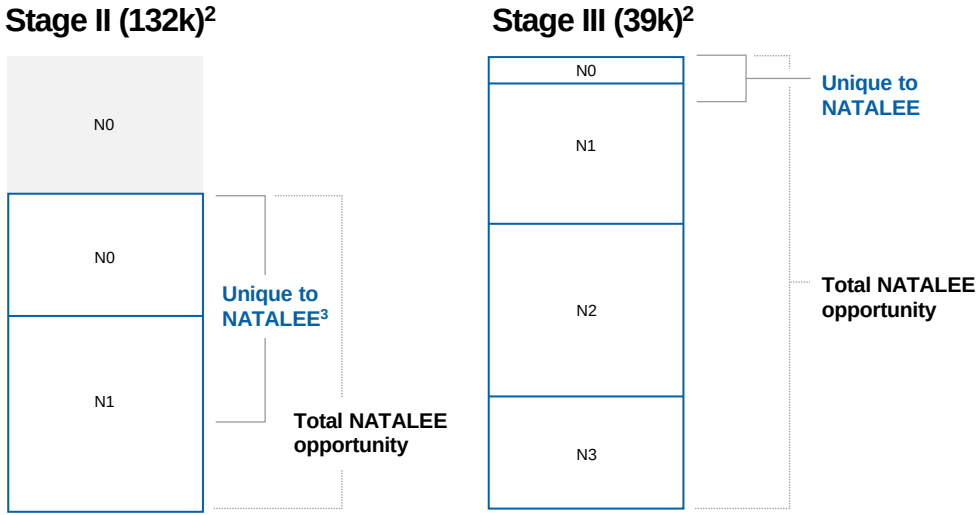
| | US | EU5 |
|---|---|---|
| Stage II (eBC) | 66k | 66k |
| Stage III (eBC) | 15k | 24k |
| Stage IV (mBC) | 32k | 32k |

## *Kisqali* opportunity[4]

eBC multibillion USD

mBC multibillion USD

## NATALEE covers broad population in HR+/HER2- eBC

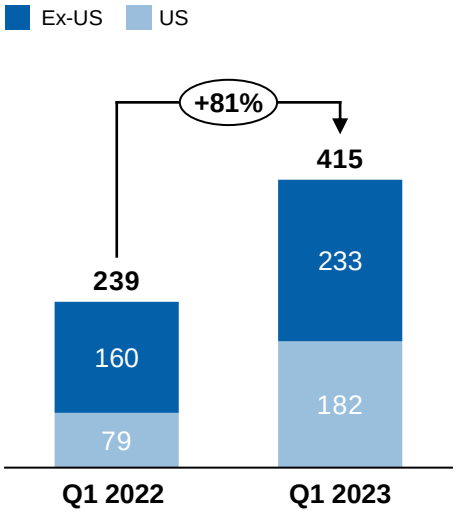



1. Data on file, Novartis. 2. Estimated incidence data sources: DRG (US) and Kantar (EU5). TNM and grade information based on SEER AJCC 8th Incidence Report. 3. Under stage II: N0, T0N1 is excluded; T2N0 only if G3, or G2 with Ki67≥20% or high risk on Oncotype DX / Prosigna / MammaPrint / EndoPredict. 4. Unprobabilized peak sales.

# Continuing momentum in mBC expected to lay the foundation for a successful launch in eBC

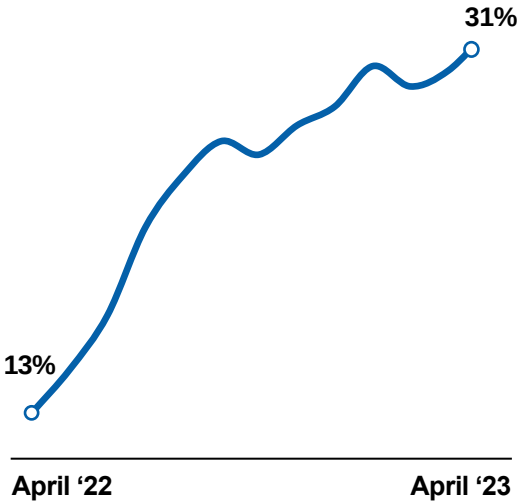
## Sales evolution

USD m, % cc



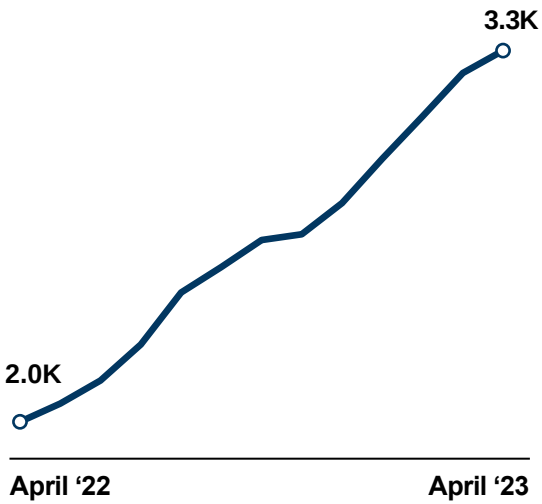

## US mBC NBRx share[1]

R3M, %




## US mBC Total Writers[2]

R3M




NBRx – new to brand prescription. R3M – rolling 3 months. 1. Of CDK4/6 mBC market, US Q1 R3M.

# Improvement in US coverage has contributed to recent performance

**Over 50% more lives covered to label vs. PY**

- Reflects increasing recognition among payers that a step through Ibrance is unethical in light of *Kisqali*'s proven OS benefit

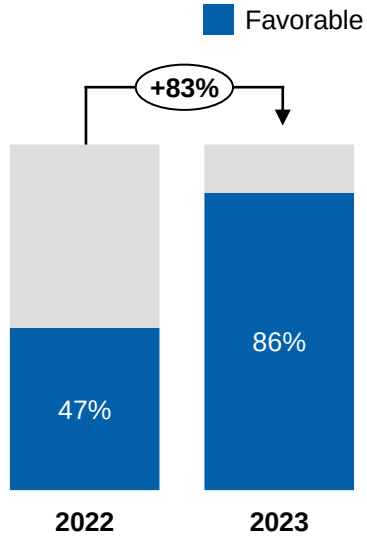
**Recent access wins expected to support continued growth**

- Commercial: Express Scripts (22m lives), Cigna (9.1m), HCSC (6.5m)
- Medicare: CVS/Aetna (8.7m), Humana (8.1m), Wellcare (5.6m)

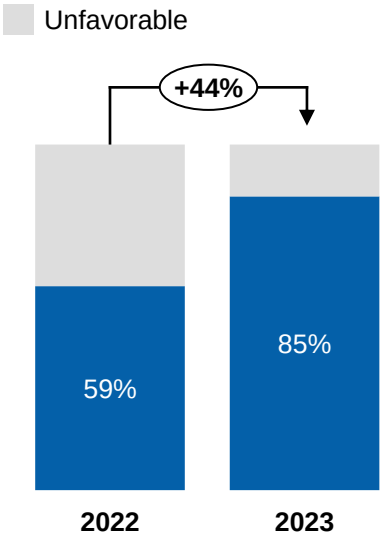
**Strong coverage in both Medicare and Commercial critical for long-term success**

- Commercial increasingly important for eBC, given younger patient population

**Medicare unrestricted coverage at 86%**




**Commercial unrestricted coverage at 85%**



# Physicians treating eBC and mBC have significant overlap and experience with *Kisqali*

**High overlap in HCPs that treat eBC and mBC in the US**

- 6k HCPs contribute 90% of prescriptions in both indications

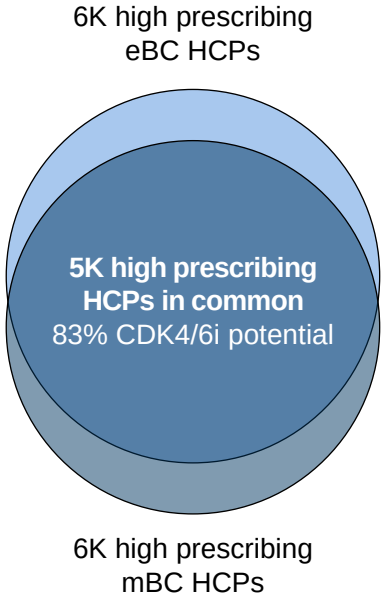
**For every 1 patient they see with mBC, they see 10+ with eBC (stages I-III)**

**Majority of high CDK4/6i eBC writers have *Kisqali* experience**

- 4.5K HCPs with *Kisqali* experience in the last 12 months (in academic and community settings) in mBC have 70% of eBC CDK4/6i prescribing potential
- They know the profile of the medicine and adoption is increasing

**Most patients are in the community setting, where we already have coverage with *Kisqali***

- 77% of eBC patients (all stages) are treated in the community setting




Source: IQVIA Xponent and Claims Data, ending March 2023. HCP – healthcare practitioner.

# With *Kisqali*, we can potentially offer at-risk eBC patients protection from cancer recurrence with favorable tolerability

**Stage II and III HR+/HER2- eBC patients are at significant risk of cancer recurrence**, and there's a need for improved treatment options to keep these patients cancer-free

*Kisqali* is the first and only CDK4/6 inhibitor to demonstrate a **consistent, clinically meaningful benefit across a broad population** of patients with HR+/HER2- eBC, regardless of disease stage, menopausal or nodal status

Results were **consistent across all secondary endpoints**, including distant disease-free survival and recurrence-free survival, with a trend for improved overall survival

The **safety profile of *Kisqali* was favorable** at 400mg with low rates of symptomatic AEs and limited treatment modifications when administered up to 3 years

Collectively, NATALEE results have the potential to **more than double** the number of patients who could benefit from treatment with a CDK4/6 inhibitor in the eBC setting

# Agenda

1 Novartis at ASCO 2023

2 *Kisqali* NATALEE trial in early breast cancer

3 *Kisqali*: Establishing the CDK4/6 of choice

4 **Q&A**

# NATALEE results support *Kisqali* + ET as treatment of choice in a broad population of stage II and III patients at risk of recurrence

| Robust efficacy | HR | 95% CI |
|---|---|---|
| ☑ iDFS – total population | **0.75** | (0.62, 0.91) |
| ☑ iDFS – stage II | **0.76** | (0.53, 1.10) |
| ☑ iDFS – stage III | **0.74** | (0.59, 0.92) |
| ☑ iDFS – node negative | **0.63** | (0.34, 1.16) |
| ☑ iDFS – node positive | **0.77** | (0.63, 0.94) |
| ☑ RFS | **0.72** | (0.58, 0.88) |
| ☑ DDFS | **0.74** | (0.60, 0.91) |
| ☑ OS | **0.76** | (0.54, 1.07) |

**Favorable safety**

- ☑ No new safety signals
- ☑ 400mg dose well tolerated, with limited need for dose reductions (22%)
- ☑ AE-related discontinuations (19%) were mostly protocol-mandated due asymptomatic lab findings
- ☑ Low rates (<1%) of symptomatic AEs such as Gr3 diarrhea and fatigue
- ☑ Gr3 VTE and ILD also low (<1%)

“These landmark results will fundamentally change how we treat patients with stage II and III HR+/HER2- eBC who are in need of new, well-tolerated options that prevent their cancer from coming back.

Addressing this unmet need across such a broad patient population could help streamline treatment decisions for healthcare providers and keep many more at-risk patients cancer-free without disrupting their daily lives.”

**DENNIS J. SLAMON**
M.D., Director of Clinical/Translational Research, University of California, Los Angeles Jonsson Comprehensive Cancer Center and Chairman and Executive Director of Translational Research In Oncology (TRIO) and NATALEE trial lead investigator

NOVARTIS | Reimagining Medicine

# Appendix

# Novartis oncology pipeline focused in areas of high unmet need where we have deep expertise

| | Solid Tumors | Hematology |
|---|---|---|
| **Disease areas** (Selected) | Breast Cancer<br>Prostate Cancer<br>Lung Cancer | Non-Hodgkin's Lymphoma<br>Myeloid Cancers<br>Non-Malignant Hematology |
| **Commercial assets** | Kisqali (ribociclib), Pluvicto, Piqray (alpelisib) tablets, Tafinlar (dabrafenib) + Mekinist (trametinib), Lutathera | Kymriah (tisagenlecleucel), Scemblix (asciminib), Promacta (eltrombopag), Jakavi (ruxolitinib) |
| **Pipeline assets and opportunities** | ***Kisqali*** Adjuvant HR+/HER2- BC<br>***Pluvicto*** Prostate cancer<br>**JDQ433** NSCLC<br>**NIS793** 1L mPDAC / 1L mCRC | **Iptacopan** PNH, aHUS<br>**Ianalumab** Multiple indications<br>**YTB323** Non-Hodgkin's Lymphoma<br>**PHE885** Multiple Myeloma |

**Leveraging advanced therapy platforms** such as radioligand therapy, cell therapy, and differentiated biologics

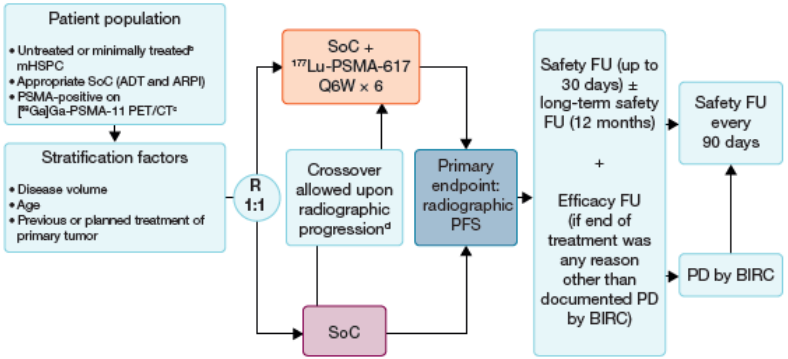
AML / MDS – Acute Myeloid Leukemia / Myelodysplastic Syndrome. HR+/HER2− – hormone receptor-positive / human epidermal growth factor receptor 2-negative. NSCLC – non-small cell lung cancer. mPDAC – metastatic pancreatic ductal adenocarcinoma. mCRC – metastatic colorectal cancer. PNH – paroxysmal nocturnal hemoglobinuria. aHUS – atypical hemolytic uremic syndrome.

# *Pluvicto*: Additional analyses of VISION data further support clinical adoption in mCRPC; Ph3 PSMAddition study underway in mHSPC

## New analyses of VISION data in mCRPC further support clinical adoption

- Updated results of a **VISION dosimetry sub-study** showed that in addition to the good safety profile and low radiotoxicity of *Pluvicto* in at-risk organs, tumor dosimetry results were consistent with previously published estimates
- Post-hoc multivariate analysis of VISION data identified more **predictive markers for long-term outcomes** (e.g. OS and rPFS) than in previous models, helping physicians identify appropriate patients for *Pluvicto*

## PSMAddition: Ph3 trial assessing *Pluvicto* + SOC vs. SOC alone in mHSPC patients




- N=~1126; primary analysis after ~418 rPFS events[1]
- Data readout and submission anticipated in 2024

1. As per blinded independent central review (BICR). PSMA – prostate-specific membrane antigen. RR – response rate. mHSPC – metastatic hormone sensitive prostate cancer. PFS – progression free survival. FU – follow-up. PD – progressive disease.

# JDQ443: Updated data from KontRASt-01 study show 55% ORR at recommended dose and favorable safety profile for combinations

Abstract data; final data to be presented on Tuesday

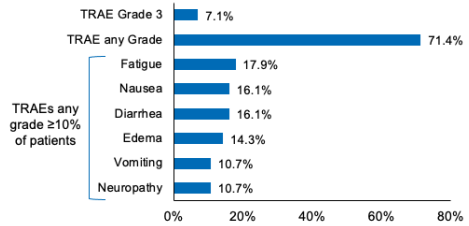
## JDQ443 is a structurally unique KRAS$^{G12C}$ inhibitor that exhibits antitumor activity in NSCLC

- 84 pts were treated with JDQ443 monotherapy, orally, continuously, across three cohorts (dose escalation, dose expansion and food effects)
- Median age was 61 years; median prior lines of therapy was 3
- Indications included NSCLC (n = 38), CRC (n = 42) and others (n = 4)
- Median duration of exposure was 14.6 weeks for all patients and 15.1 weeks for patients treated at RD of 200 mg BID

Among response evaluable patients with NSCLC, confirmed ORR was 54.5% (6/11 pts) at 200 mg BID and 41.7% (10/24 pts) across dose levels

## Safety and tolerability profile supports potential for combination strategies

**TRAEs among patients treated at RD 200mg BID (n=56)**




- TRAEs were low-frequency, low-grade events
- No Grade 4/5 TRAEs
- No nausea, vomiting, or diarrhea higher than Grade 2
- ALT/AST Grade 2/3 elevation events were rare & of limited duration

JDQ443 doublet combinations with tislelizumab (anti-PD-1) and TNO155 (SHP2i) in KontRASt-01 have completed dose escalation; now in Ph2 dose expansion

ORR – overall response rate. NSCLC – non-small cell lung cancer. TRAE – treatment related adverse events. ALT – alanine transaminase. AST – aspartate aminotransferase.

# PHE885: 100% ORR at active doses with no unexpected safety findings in Ph1; Ph2 study underway in r/r MM

## *T-Charge* platform – quick production with potential for outstanding clinical impact

**T-Charge™**

**Preserves T-cell stemness[1-3]**

maintaining the stem and central memory T-cells[3]

**Enhances in vivo expansion[2,3]**

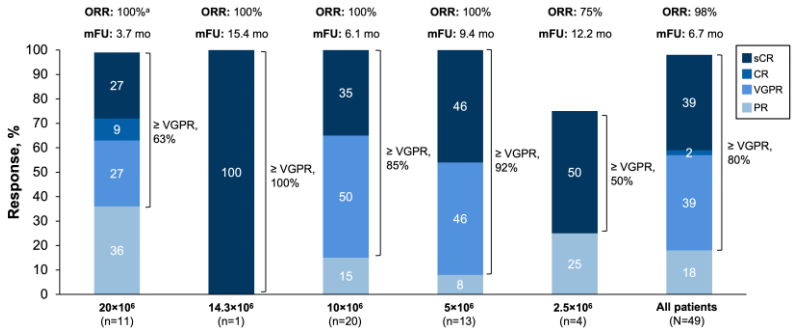
with potential to improve efficacy, and increase persistence and durability of response

**Has <2-day manufacturing time[2,3]**

and aim of <10-day door-to-door time in the United States

- *T-Charge* manufacturing preserves early memory phenotype in the PHE885 final product
- PHE885 was successfully produced for all patients with unprecedented short manufacturing times

## PHE885 achieved 100% ORR at active doses; clinical responses deepen over time




- No unexpected safety findings, including no reports of parkinsonism or delayed neurotoxicity
- PHE885 reliably expanded in vivo and showed prolonged persistence with preserved T-cell stemness

1. Engels B, et al. Blood. 2021;138(supp 1): Abstract 2949. 2. Barba P, et al. Blood. 2022;140(suppl 1):1056-1059. 3. Sperling AS, et al. European Hematology Association (EHA) 2022 Congress; June 9-12, 2022; Vienna, Austria. Poster P1446. ORR – overall response rate. MM – multiple myeloma. CRS – cytokine release syndrome.

# Novartis oncology key mid-term pipeline milestones on track

| 2023 | 2024 | 2025 |
|---|---|---|
| **Iptacopan**<br>PNH<br>FDA submission in **H1** | ***Pluvicto***<br>mHSPC<br>PSMAddition Ph3 readout | **Ianalumab**<br>1L and 2L ITP<br>VAYHIT1 and -2 Ph3 readouts |
| ***Pluvicto***<br>mCRPC (post-ARDT, pre-taxane)<br>PSMAfore FDA submission in **H2** | ***Scemblix***<br>1L CML-CP<br>ASC4FIRST Ph3 readout | **YTB323**<br>1L HR LBCL<br>Ph2 readout |
| **AAA603**<br>Breast cancer<br>Ph1 readout in **H2** | **Nisevokitug (NIS793)**<br>1L mPDAC<br>daNIS-2 Ph3 readout | |