Novartis Oncology Pipeline Update

June 15, 2020
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Our strategy in Oncology

Pipeline updates across our therapeutic modalities
- Targeted Therapies: Kisqali®, Piqray®, Tabrecta™, Tafinlar®+Mekinist®, LXH254, TNO155, Asciminib
- Immunotherapies: Canakinumab, MBG543, Spartalizumab
- Radioligand: Lutathera®, 177Lu-PSMA-617
- Cell & Gene: Kymriah®, YTB323

Q&A
Strong track record of pioneering innovation in Oncology

Novartis Oncology sales
USD billion, % CAGR

Novartis Oncology Pipeline Update | June 15, 2020
## Four therapeutic modalities to drive future growth

### Targeted Therapies

Select pipeline assets and opportunities

- **Kisqali®** in adjuvant BC
- **Alpelisib** in
  - HER2+ advanced BC
  - TNBC
  - Head & neck
  - Ovarian cancer
  - PROS
- **Adakvelo®** in sickle cell disease
- **Tabrecta™** in NSCLC, single agent and combinations
- **Jakavi®** in GvHD, and combinations (platform) in MF
- **Asciminib** in CML
- **LXH254** in RAS/RAF mutant melanomas and lung cancer
- **TNO155** in solid tumors

### Immunotherapies

- **Canakinumab** in
  - adjuvant NSCLC
  - 1st line NSCLC
  - 2nd line NSCLC
- **Spartalizumab+Tafinlar® and Mekinist®** in metastatic melanoma
- **Spartalizumab combinations** (platform) in metastatic melanoma
- **Spartalizumab+LAG525+carboplatin** in TNBC
- **Spartalizumab+Tabrecta™** in NSCLC
- **MBG453** in MDS and AML
- **VPM087** in CRC and RCC
- **NIS793** in solid tumors

### Radioligand

- **Lutathera®** in 1st line grade 2/3 advanced GEP-NET
- **177Lu-PSMA-617** in prostate cancer
- **177Lu-PSMA-R2** in prostate cancer
- **177Lu-NeoB** in multiple solid tumors
- **177Lu-FF58** in glioblastoma

### Cell & Gene

- **Kymriah®** in
  - r/r DLBCL after 1st relapse
  - r/r follicular lymphoma
  - r/r adult ALL
  - combinations (pembrolizumab; ibrutinib) in r/r DLBCL
  - pediatric NHL
  - 1st line high risk pediatric and young adult ALL
- **YTB323** in
  - r/r DLBCL
  - r/r CLL combination with ibrutinib
- **PHE885** in r/r MM

**Other targets:** BCMA&CD19, CD22&CD19, CD123, EGFRvIII
Ability to integrate drugs across modalities to increase depth and duration of response

SELECTED EXAMPLES

**TT + TT**
- Tabrecta™ + EGFR in NSCLC
- LXH254 (B/C-RAF) + LTT462 (ERK) in NSCLC, Melanoma
- LXH254 + Mekinist® in NSCLC, Melanoma
- TNO155 (SHP2) + Kisqali® in NSCLC, CRC

**TT + IO**
- Tafinlar® + Mekinist® + Spartalizumab in Melanoma
- Tabrecta™ + Spartalizumab in NSCLC
- TNO155 + Spartalizumab in NSCLC
- HDM201 + MBG453 (TIM3) in AML

**RLT + IO**
- Lutathera® + PD-1 in NET
- 177Lu-PSMA-617 + PD-1 in mCRPC

**CAR-T + IO**
- Kymriah® + PD-1 in DLBCL
- CAR-T EGFRvIII + Spartalizumab in Glioblastoma

**IO + IO**
- Canakinumab + PD-1 in NSCLC
- Spartalizumab + TGFβ in Multiple Solid Tumors

1. Investigator-initiated trials
Data from more than 170 abstracts¹ presented at ASCO, EHA and AACR

**ASCO 20 Virtual**

- KISQALI® ribociclib
  - OS data in patients with visceral mets

- Tafinlar® + Mekinist® (dabrafenib + trametinib)
  - COMBI-AD 5-year analysis

- ¹Lu-PSMA-617
  - TheraP IIT data

**EHA**

- MBG453
  - Phase 1 data in MDS and AML

- Asciminib
  - 3-year data in TKI-intolerant patients

**AACR**

- TABRECTA™ (capmatinib)
  - Brain mets data

- TNO155
  - New Drugs on the Horizon Symposium

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1. Including investigator-initiated trials / third party abstracts
Four therapeutic modalities to drive future growth

**Targeted Therapies**
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- 1st line NSCLC
- 2nd line NSCLC
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- PHE885 in r/r MM
- Other targets: BCMA&CD19, CD22&CD19, CD123, EGFRvIII

Select pipeline assets and opportunities

Novartis Oncology Pipeline Update | June 15, 2020
Kisqali®: Only CDK4/6 proven to extend the lives of patients in two Phase 3 trials

- Kisqali® was the fastest growing CDK4/6 inhibitor in Q1 2020, benefitting from two positive OS readouts (MONALEESA 3 & 7); third study (MONALEESA 2) expected to read out OS in 2021.

- Kisqali® has a differentiated profile vs. other CDK4/6 inhibitors, with preferential inhibition to CDK4 vs. CDK6, and a high concentration to inhibit the target.

- RWE evidence data shows that Kisqali® is well tolerated with lower incidence and severity of neutropenia\(^1\).

- NATALEE adjuvant study on track to complete enrollment in this year, with readout in 2022.

### Net sales
USD million, growth in % cc vs. PY period

<table>
<thead>
<tr>
<th>Year</th>
<th>Net Sales</th>
<th>Growth cc vs. PY</th>
</tr>
</thead>
<tbody>
<tr>
<td>FY 2017</td>
<td>76</td>
<td>0%</td>
</tr>
<tr>
<td>FY 2018</td>
<td>235</td>
<td>+82%</td>
</tr>
<tr>
<td>FY 2019</td>
<td>480</td>
<td></td>
</tr>
<tr>
<td>Q1 2020</td>
<td>161</td>
<td></td>
</tr>
</tbody>
</table>

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MONALEESA 3 & 7 data in visceral metastases, including liver, reinforce differentiated profile

- Presence of visceral metastases generally signifies a poor prognosis in HR+/HER2− metastatic breast cancer
- Approximately 60% of patients had visceral metastases in MONALEESA 3 & 7
- Similar to the overall population, there was a consistent OS and PFS benefit in patients with visceral metastases, including those with liver metastases, in both trials
- Safety profile was consistent with the overall patient population
Evidence suggests there are differences among CDK4/6 inhibitors

- CDK4 is a critical driver of HR+/HER2-advanced breast cancer, while CDK6 drives hematological toxicities.\(^1,2\)
- Kisqali\(^®\) inhibits CDK4 8x more than CDK6 in vitro.\(^3,4\)
- Higher unbound C\(_{avg}\) (average free drug concentration at steady state) means more drug is available to act on tumor cells.\(^4-7\)
- At clinically relevant doses and adjusting for differences in potency against CDK4/6 and protein binding, Kisqali\(^®\) should provide greater CDK4 inhibition in vivo than competitors

Select differences among CDK4/6 inhibitors\(^3-7\)

- CDK4 inhibition relative to CDK6 from a cellular assay
- Unbound C\(_{avg}\) relative to palbociclib

NATALEE: Pivotal Phase 3 study in adjuvant setting on track for readout in 2022

**NATALEE trial design**

- **HR+/HER2- EBC**
- **Pre- and post-menopausal**
- **Stage II & III**

- **R 1:1**
- **n = 4000**

**RIBO+ ET**
- Ribociclib 400 mg/d
- 3 weeks on/1 week off
- 36 months (~39 cycles)
- 60 months

**ET (NSAI 60 months)**
- (+Goserelin in premenopausal women and men)

**ET only**
- 60 months

**Unique aspects vs. other CDK4/6i adjuvant studies**

- Longer treatment duration: 3 years vs. 2 years
- Lower dose than in metastatic setting: 400mg vs. 600mg
- More homogeneous patient population: Intermediate and high-risk patients per AJCC defined prognostic factors

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1. Letrozole or anastrozole; treatment with NSAI may start up to 12 months before study treatment start date.
**Piqray®: Strong launch as first and only PI3Kα inhibitor, with significant expansion opportunities**

**Net sales**
USD million

<table>
<thead>
<tr>
<th>Quarter</th>
<th>Net Sales</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q2 2019</td>
<td>6</td>
</tr>
<tr>
<td>Q3 2019</td>
<td>43</td>
</tr>
<tr>
<td>Q4 2019</td>
<td>67</td>
</tr>
<tr>
<td>Q1 2020</td>
<td>74</td>
</tr>
</tbody>
</table>

- Continued uptake driven by expanded coverage and strong Rx momentum
- Continued uptake in PIK3CA testing, with goal to reach a rate of 40% by YE 2020
- Expanding geographical footprint with approvals in 13 markets
- Positive CHMP opinion received in May 2020

**EPIK expansion**

**Potential opportunity to serve an additional ~100k patients, more than tripling the number of patients in the current indication**

- TNBC trial enrolled first patient in June 2020; HER2+ aBC trial expected to start enrollment next

1. Refers to first filing year.  2. Filing in US based on RWE study.  PROS = PI3K Related Overgrowth Syndrome  aBC = advanced Breast Cancer

**PROS = PI3K Related Overgrowth Syndrome**

**aBC = advanced Breast Cancer**

**Additional indications beyond breast cancer**
- PROS (20201)  - Ovarian Cancer (20232)  - Head & Neck Cancer (20252)
BYLieve study reinforces efficacy of Piqray® use in post CDK4/6 setting with manageable side effects

Safety profile observed in BYLieve suggests that AE management strategies are effective:

- Fewer overall AE-related discontinuations (20.5% in BYLieve vs. 25% in SOLAR-1)
- Fewer discontinuations due to hyperglycemia (1.6% vs. 6.3%)

Overall approach to further mitigate AEs:

- Multiple safety studies ongoing (NVS and IIT) to optimize hyperglycemia management
- Continuing medication education

Primary endpoint for the prior CDKi + AI cohort was met (lower bound of 95% CI was > 30%), with 50.4% of patients alive without disease progression at 6 months

Secondary endpoint of median PFS was 7.3 months (95% CI, 5.6-8.3)
Oncogene dependency is a key therapeutic vulnerability in human cancers

Asciminib: First-in-class STAMP inhibitor

Asciminib is different from other TKIs as it is thought to specifically target the BCR-ABL1 myristoyl pocket (STAMP)

ATP = Adenosine Triphosphate; TKI = Tyrosine Kinase Inhibitor.

3-year follow-up of TKI intolerant patients in Phase 1 study

- Asciminib monotherapy was well tolerated and showed promising clinical activity in TKI intolerant patients
- 75% of patients were on treatment and in MMR after a median follow-up of over three years
- Median duration of treatment with asciminib was 32 months, vs. 3 months on previous therapy
- Pivotal Phase 3 study in 3rd line CML on track for readout in H2 2020, first submission in Q1 2021

Cumulative Molecular Response Rates

- Number at risk, n
  - MMR: 24, 12, 6, 5, 0, 0
  - MR4: 38, 26, 21, 19, 7, 3
  - MR4.5: 42, 38, 26, 24, 20, 9, 4
- Cumulative number of events, n
  - Patients with MMR: 0, 12, 15, 16, 16, 16
  - Patients with MR4: 0, 12, 14, 16, 18, 18
  - Patients with MR4.5: 0, 12, 14, 16, 18, 18

MR = BCR-ABL1 ≤ 0.1%; MR4 = BCR-ABL1 ≤ 0.01%.

a As of the cutoff date of August 30, 2019. Calculated based on the number of patients evaluable for response and without that response at baseline.
Targeting RTK/RAS/MAPK signaling in solid tumors

RTK/RAS/MAPK pathway

Metastatic lung adenocarcinoma

Dramatic clinical responses

- Roughly 1/3 to 1/2 of NSCLC patients have targetable genetic alterations
- To date, 7 molecular subsets of NSCLC can be targeted with standard of care therapies (EGFR, ALK, ROS1, RET, BRAF, TRK, MET)

Tabrecta™, approved by FDA in May, ready for omni-channel launch amid pandemic conditions

Current indication
- 3-4% of NSCLC patients have METex14 mutations, associated with poor prognosis and modest benefit from existing therapies
- Tabrecta™ is the first and only therapy approved by the FDA to specifically target METex14 mutated metastatic NSCLC
- Simultaneous FDA approval of METex14 CDx on FoundationOne®CDx tissue-based test; liquid test under development
- NCCN guidelines updated 9 days after approval, with Tabrecta™ as preferred option for MET mutant NSCLC, line agnostic
- Wave-based launch leveraging robust digital capabilities to accelerate patient access amid pandemic conditions
- Japan approval expected H1 2020

Maximizing potential
- Additional studies planned as monotherapy: Phase 3, brain metastases, tumor agnostic
- Moving into combinations:
  - PD-L1 high expressers regardless of MET status, in combination with pembrolizumab
  - METex14 skipping regardless of PD-L1 status, in combination with spartalizumab
  - Post-EGFR, in combination with EGFR inhibitor
Differentiated profile with clinical activity in METex14 mutated and MET amplified NSCLC

Results from cohorts 4 and 5b of GEOMETRY mono-1

- Capmatinib is highly active in previously treated and treatment-naïve METex14 NSCLC patients; in the 1L setting, ORR 67.9%, DCR 96.4%, mPFS 12.4 mos
- Among 13 patients with brain mets at baseline, intracranial responses were achieved in 54%, including 31% with CR; intracranial disease control achieved in 92% (AACR 2020)
- Among patients with high-level MET amplification (GCN ≥ 10), capmatinib also showed activity, with ORR 29% and 40% in previously treated and treatment-naïve patients, respectively (cohorts 1a and 5a)

Results from cohort 6 of GEOMETRY mono-1

- Capmatinib achieved meaningful efficacy in 2L patients with METex14 (ORR 48.4%, DCR 90.3%), confirming previously reported results
- Although no responses were observed in the 3 patients with MET GCN ≥ 10, all 3 had tumor regression and SD by RECIST
- Patients received capmatinib without fasting restrictions, supporting administration with and w/o food (as per USPI)
Expanding Tabrecta™ into first-line combinations with PD-1 agents in NSCLC

- MET also plays a role in immunomodulation in the following populations of the tumor microenvironment:
  - Neutrophils
  - Dendritic cells
  - T cells
- Combination of capmatinib (INC280) with anti-PD-1 enhances antitumor immunity irrespective of MET status

INC280I12201

**Study design**
A randomized, open label, multicenter Phase 2 study evaluating the efficacy and safety of INC280 plus pembrolizumab versus pembrolizumab alone as first-line treatment for locally advanced or metastatic non-small cell lung cancer with PD-L1 ≥ 50%

**Objective**
To assess efficacy of INC280+pembrolizumab combination vs. pembrolizumab monotherapy

**Status**
Enrolling, FPFV in Jan 2020

INC280J12201

**Study design**
A Phase 2, double-blind, placebo-controlled study consisting of a run-in part of INC280 plus spartalizumab, followed by a randomized part of INC280+spartalizumab vs. INC280+spartalizumab matching placebo

**Objective**
By adding spartalizumab to INC280, improve PFS and OS with maintained ORR in 1L NSCLC patients with METex14 skipping mutations compared to INC280 alone

**Status**
FPFV expected in July 2020
Tafinlar®+Mekinist®: 5-year analysis shows long-term benefit of adjuvant treatment in BRAF+ melanoma

**More than half of BRAF+ patients treated with adjuvant Tafinlar®+Mekinist® were relapse-free at 5 years, with curve trending towards plateau**

**Longest follow-up to-date from a Phase 3 study of any contemporary adjuvant therapy**

**COMBI-AD 5-year analysis**

<table>
<thead>
<tr>
<th>Months since randomization</th>
<th>Proportion Alive and Relapse Free</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>0.51 (95% CI: 0.42–0.61)</td>
</tr>
<tr>
<td>24</td>
<td>0.38 (95% CI: 0.34–0.43)</td>
</tr>
<tr>
<td>36</td>
<td>0.36 (95% CI: 0.32–0.41)</td>
</tr>
<tr>
<td>48</td>
<td>0.30 (95% CI: 0.26–0.34)</td>
</tr>
<tr>
<td>60</td>
<td>0.23 (95% CI: 0.19–0.27)</td>
</tr>
<tr>
<td>72</td>
<td>0.17 (95% CI: 0.13–0.21)</td>
</tr>
<tr>
<td>80</td>
<td>0.12 (95% CI: 0.08–0.17)</td>
</tr>
<tr>
<td>90</td>
<td>0.07 (95% CI: 0.04–0.12)</td>
</tr>
</tbody>
</table>

**Hazard ratio**

- **HR: 0.51**
- **95% CI: 0.42–0.61**
- **59% (95% CI: 55%–64%)**
- **55% (95% CI: 50%–60%)**
- **52% (95% CI: 48%–58%)**

**Net sales**

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<td>672</td>
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<tr>
<td>FY 2017</td>
<td>873</td>
</tr>
<tr>
<td>FY 2018</td>
<td>1,155</td>
</tr>
<tr>
<td>FY 2019</td>
<td>1,338</td>
</tr>
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<td>+26% cc</td>
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**Novartis Oncology Pipeline Update | June 15, 2020**
Additional data from COMBI-i parts 1 and 2 show durable anti-tumor activity of triplet therapy

Rationale for combining Tafinlar®+Mekinist® with anti-PD-1

MAPK inhibition may favorably alter the tumor microenvironment for an augmented and potentially synergistic immune response

Data from Phase 3 COMBI-i study safety run-in / biomarker cohort

Increased response rates vs. previously reported:

Triplet (spartalizumab+dabrafenib+trametinib, or S+D+T) treatment exhibited an ORR of 78%, including a promising CR rate of 44% in unresectable or metastatic BRAF-mutant melanoma

S+D+T may be associated with a high frequency of durable responses, with 24-month PFS and OS rates of 41% and 74%, respectively

No new safety signals were observed; AEs were consistent with the inclusion of each study drug

CR, complete response; LDH, lactate dehydrogenase; PR, partial response; SD, stable disease; ULN upper limit of normal.

a One patient with SD had a best percent change of 0% in the target lesion, while best percent change could not be calculated for 1 patient because best overall response was unknown.

b Best percent change in the target lesion was not available for 1 patient with progressive disease.

McArthur GA & Ribas A,
J Clin Oncol 2013;31:499–506
LXH254: Potentially best-in-class B/C-RAF inhibitor in RAS/RAF mutant melanomas and lung cancers

Highly potent and selective

- LXH254 inhibits both dimeric and monomeric B- and CRAF kinases
- B/CRAF inhibition targets RAS-mutant tumors and BRAF mutants both V600E and nonV600E

Tumor growth inhibition as single agent or in combination

- Antitumor activity of LXH254 single agent observed in patients with KRAS-mut and BRAF-mut cancers
- Preclinical data show robust activity in vertical combinations with MEK, ERK, and CDK4/6 inhibitors
- Favorable tolerability profile of LXH254 enables combinations, with potential benefit for BRAF-mut NSCLC patients (~4% of NSCLC), and BRAF-mut or NRAS-mut melanomas (~50% BRAF-mut, ~20% NRAS-mut)
- Clinical studies evaluating LXH254 in combination with LTT462 (ERKi), Mekinist® (MEKi), Kisqali® (CDK4/6i) and spartalizumab (anti-PD-1) in RAS/RAF mutant NSCLC and melanoma ongoing
Almost all patients develop resistance to targeted therapies: Role of SHP2 phosphatase

Multiple and diverse resistance mechanisms can develop in patients treated with targeted therapies, leading to clinical relapse.

For highly selective, next-generation targeted agents, resistance is often mediated by off-target mechanisms that lead to MAPK re-activation.

Combination strategies that target both the oncogenic driver and downstream signaling pathways are urgently needed.

TNO155: A first-in-class inhibitor of SHP2

**Required for RTK signaling**

RTK-SHP2-RAS-MAPK pathway activation has been implicated across the majority of human cancers

**Downstream transducer of PD-1**

SHP2 is a downstream transducer of PD-1 signaling, a critical immune checkpoint in human malignancies

**First SHP2i to enter the clinic**

Ideal drug-like properties (e.g. high permeability, solubility, no CYP450 inhibition, ideal preclinical PK profile)
TNO155: Broad combination strategy to blanket the MAPK pathway

**TNO155X2101**

**HCC827 (EGFRmut) tolerant cells**

Study design
An open-label, multi-center, Phase 1, dose finding study of oral TNO155 in adult patients with advanced solid tumors

Objective
To characterize the safety and tolerability of TNO155 as a single agent and in combination with nazartinib (EGF816) in solid tumors, and to identify recommended regimen(s) and dose(s) for future studies

Status
Enrolling, FPFV in May 2017

**TNO155B12101**

**MC38 syngeneic mouse model**

Study design
A Phase 1b, open-label, multi-center study of TNO155 in combination with spartalizumab or Kisqali® (ribociclib) in selected malignancies

Objective
To characterize the safety, tolerability, PK, and efficacy of TNO155 combined with spartalizumab or ribociclib, and to identify the MTD and/or RDE for each combination

Status
Enrolling, FPFV in July 2019

**TNO155C1**

**MIA PaCa-2 (PDAC, KRAS\textsuperscript{G12C/G12C}) with G12Ci**

Study design
A Phase 1/2 trial of MRTX849 in combination with TNO155 in patients with advanced solid tumors with KRASG12C mutation

Objective
To characterize the safety, tolerability, PK, and efficacy of MRTX849 combined with TNO155 in patients having advanced solid tumors with KRASG12C mutation

Status
Enrolling, FPFV in April 2020

*Study sponsored by Mirati
Four therapeutic modalities to drive future growth

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  - r/r CLL combination with ibrutinib
- PHE885 in r/r MM

Other targets: BCMA&CD19, CD22&CD19, CD123, EGFRvIII
IL-1β plays a key role in pro-tumor inflammation, a driver of tumor survival, growth and progression\textsuperscript{1,2}

Novartis is leading research on the role of pro-tumor inflammation (PTI) as a driver of cancer

Processes occur creating a tumor microenvironment conducive to PTI\textsuperscript{3,4}

There is preliminary evidence that IL-1β facilitates PTI by activating tumor processes and recruiting immunosuppressive cells\textsuperscript{2,5}

CANTOS: IL-1β antibody demonstrates reduction of lung cancer incidence and mortality

Lung cancer incidence

Dose-dependent effect, 67% relative risk reduction, P<0.0001 (canakinumab 300mg)

Lung cancer mortality

Dose-dependent effect, 77% relative risk reduction, P=0.0002 (canakinumab 300mg)

Adapted from Ridker et al, Lancet, 2017
# CANOPY: Three Phase 3 studies ongoing with canakinumab in NSCLC, first to read out in Q4 2020

## CANakinumab Outcomes in Patients with NSCLC StudY

<table>
<thead>
<tr>
<th>Indication</th>
<th>Patient population</th>
<th>Trial design</th>
<th>Status as of Jun 2020</th>
<th>Planned filing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adjuvant NSCLC (CANOPY-A)</td>
<td>High-risk Stage II-III</td>
<td>Canakinumab vs. placebo (n=1500 with 1:1 randomization) after post-resection chemotherapy</td>
<td>~40% of patients enrolled</td>
<td>2023</td>
</tr>
<tr>
<td>1&lt;sup&gt;st&lt;/sup&gt; line NSCLC (CANOPY-1)</td>
<td>Non-mutated, no prior treatment for metastatic disease or Stage III unresectable</td>
<td>Platinum doublet chemotherapy and pembrolizumab with or without canakinumab (n=600 with 1:1 randomization)</td>
<td>Enrollment completed; interim analysis expected in Q4 2020</td>
<td>2021</td>
</tr>
<tr>
<td>2&lt;sup&gt;nd&lt;/sup&gt; line NSCLC (CANOPY-2)</td>
<td>Non-mutated with no more than 2 prior lines of metastatic treatment (PD-1 ± chemo)</td>
<td>Docetaxel with or without canakinumab (n=226 with 1:1 randomization)</td>
<td>Enrollment completed; final analysis expected in 2021</td>
<td>2021</td>
</tr>
<tr>
<td>Neoadjuvant NSCLC (CANOPY-N; Phase 2)</td>
<td>Stage IB - IIIA</td>
<td>Canakinumab, canakinumab+pembrolizumab or pembrolizumab (n=110 with 2:2:1 randomization)</td>
<td>First patient enrolled in Q4 2019; ~20% of patients enrolled</td>
<td>Not registrational study</td>
</tr>
</tbody>
</table>

---

CANOPY: Three Phase 3 studies ongoing with canakinumab in NSCLC, first to read out in Q4 2020.
Phase 3 adjuvant study design presented at ASCO

CANOPY-A Study Design

Adjuvant setting:
Age ≥ 18 years
Stage IIA-IIIA and IIIB (T > 5cm, N2 disease only)
Any histology
Following complete surgical resection (R0)
Post-SOC adjuvant cisplatin-based chemotherapy (and SOC RT, if applicable)

R² (1:1)

Canakinumab
200mg SC Q3W

18 cycles

Placebo
SC Q3W

Safety follow-up:
Every 28 days for 130 days after end of treatment
Post-treatment Surveillance follow-up:
After end of treatment until disease recurrence
Survival follow-up:
Every 12 weeks

N = 1500
Next-generation inflammasome inhibitors are under development for cancer and other diseases

- Ongoing and planned clinical trials to assess in MDS, MPN, CRC and TNBC
- 6 novel antibodies and LMWs are currently being clinically developed and are potentially available for hematology indications
- Interest in expanding to chemoprevention in high-risk populations
**MBG453: Targeting TIM-3 in hematology**

**MBG453 mechanism**

- In vitro data shows that targeting TIM-3 with inhibitory antibody MBG453:\(^1\)\(^-\)\(^3\):  
  - Re-awakens immunity to restore an anti-leukemic immune response  
  - Selectively targets the LSC and blasts

- Broad ‘STIMULUS’ trial program initiated in myeloid malignancies

**Ongoing Phase 1 trial in HR-MDS and AML**

- **Up to 207 Adult Patients**
  - Unfit, newly diagnosed AML, ineligible for standard chemotherapy
  - R/R AML, ineligible for standard chemotherapy
  - IPSS-R high- or very high-risk MDS (HR-MDS)

- **Decitabine**
  - Days 1-5: 20 mg/m^2^

- **Azacitidine**
  - Days 1-7: 75 mg/m^2^

- **Additional study arms**
  - MBG453 ± spartalizumab
  - Spartalizumab + decitabine
  - Spartalizumab + decitabine + MBG453

- **Primary Endpoints:**
  - Maximum tolerated dose/recommended dose; safety and tolerability

- **Secondary Endpoints:**
  - Preliminary efficacy, pharmacokinetics

---

MBG453+HMA provides promising and durable response rates in ongoing Phase 1 trial

High CR/mCR rate with good safety profile and emerging durability in HR-MDS

1. Denominator is 14 (vs. N=16 in category label) due to 2 patients not yet reaching the time-point for their first scan.
## Building MBG453 backbone across myeloid diseases

### STIMULUS program

<table>
<thead>
<tr>
<th><strong>HR-MDS</strong></th>
<th><strong>Unfit AML</strong></th>
<th><strong>Novel combinations</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>STIMULUS-MDS-1</strong></td>
<td><strong>STIMULUS-AML-1</strong></td>
<td><strong>MDS/AML</strong></td>
</tr>
<tr>
<td>Phase 2 ongoing, enrollment expected to complete in 2020</td>
<td>Phase 2 combo HMA + venetoclax, enrollment expected to start H2 2020</td>
<td>Phase 1 combo with HDM201&lt;sup&gt;1&lt;/sup&gt; ongoing</td>
</tr>
<tr>
<td><strong>STIMULUS-MDS-2</strong></td>
<td></td>
<td><strong>Myelofibrosis</strong></td>
</tr>
<tr>
<td>Phase 3 ongoing, enrollment started in June 2020</td>
<td></td>
<td>Phase 1b/2 combo with Jakavi&lt;sup&gt;®&lt;/sup&gt; ongoing</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Phase 1 combo without Jakavi&lt;sup&gt;®&lt;/sup&gt; in post-JAKi patients</td>
</tr>
</tbody>
</table>

1. HDM201: MDM2 inhibitor
Four therapeutic modalities to drive future growth

Select pipeline assets and opportunities

**Targeted Therapies**
- Kisqali® in adjuvant BC
- Alpelisib in
  - HER2+ advanced BC
  - TNBC
- Canakinumab in
  - adjuvant NSCLC
  - 1st line NSCLC
  - 2nd line NSCLC
- Spartalizumab+Tafinlar®+Mekinist® in metastatic melanoma
- Spartalizumab combinations (platform) in metastatic melanoma
- Spartalizumab+LAG525+carboplatin in TNBC
- Spartalizumab+Tabrecta™ in NSCLC
- MBG453 in MDS and AML
- VPM087 in CRC and RCC
- NIS793 in solid tumors

**Immunotherapies**
- Lutathera® in 1st line grade 2/3 advanced GEP-NET
- 177Lu-PSMA-617 in prostate cancer
- 177Lu-PSMA-R2 in prostate cancer
- 177Lu-NeoB in multiple solid tumors
- 177Lu-FF58 in glioblastoma

**Radioligand**
- 177Lu-PSMA-617 in prostate cancer
- 177Lu-PSMA-R2 in prostate cancer
- 177Lu-NeoB in multiple solid tumors
- 177Lu-FF58 in glioblastoma

**Cell & Gene**
- Kymriah® in
  - r/r DLBCL after 1st relapse
  - r/r follicular lymphoma
  - r/r adult ALL
- combinations (pembrolizumab; ibrutinib) in r/r DLBCL
- pediatric NHL
- 1st line high risk pediatric and young adult ALL
- YTB323 in
  - r/r DLBCL
  - r/r CLL combination with ibrutinib
- PHE885 in r/r MM
- Other targets: BCMA&CD19, CD22&CD19, CD123, EGFRvIII
Maximizing Kymriah® to deliver CAR-T to more patients

Driving Kymriah® in market

$93m Q1 sales
+109% cc vs. PY

25 countries where Kymriah® is available and reimbursed

90% final products made available to patients globally, including OOS

Expanding manufacturing

7 global sites
Stein, Les Ulis, Morris Plains, FBRI, Fraunhofer, Cell Therapies & CBMG

7 clinical trials
DLBCL in 1st relapse, r/r FL, adult r/r ALL, r/r DLBCL combo with pembrolizumab, r/r DLBCL combo with ibrutinib, pediatric NHL, 1L high risk pediatric & young adult ALL

125% capacity increase
Q1 2020 vs. Q1 2019

2800+ therapies delivered for patients cumulatively

Moving into new indications

FDA designation
Regenerative Medicines Advanced Therapy (RMAT) designation received for r/r FL

RWE
demonstrated comparable efficacy and improved safety versus pivotal trials

240+ qualified treatment centers worldwide
Platform priorities

**Kymriah®**: Seven trials to research new or expanded indications focused on B cell malignancies

**Activated Rapid Manufacturing (ARM)**: Advancing a next-generation process to improve manufacturing reliability/simplicity, turnaround time, and possibly safety/efficacy

**YTB323**: First CAR-T using ARM platform, Phase 1 ongoing

**Other targets**: Including BCMA for multiple myeloma, CD22 for ALL, and combinations

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**Cell therapy pipeline**

<table>
<thead>
<tr>
<th>Study</th>
<th>Indication</th>
<th>Phase I</th>
<th>Ph II/PI</th>
<th>Phase III</th>
<th>Submitted</th>
<th>Approved</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAR-T CD19</td>
<td>ELIANA CTL01982202 Pediatric &amp; young adult r/r ALL</td>
<td></td>
<td></td>
<td></td>
<td>US, EU, CH, CA, AU, JP</td>
<td></td>
</tr>
<tr>
<td>YTB323A12191</td>
<td>r/r DLBCL. r/r CLL combo with ibritinib</td>
<td>STARTED 2019</td>
<td></td>
<td></td>
<td>STARTED 2019</td>
<td></td>
</tr>
<tr>
<td>CAR-T BCMA</td>
<td>PHEBES ADP101A12101 r/r MM</td>
<td></td>
<td></td>
<td></td>
<td>STARTED 2019</td>
<td></td>
</tr>
<tr>
<td>Other targets</td>
<td>CD19, BCMA, CD22, CD123, EGFRvIII</td>
<td></td>
<td></td>
<td></td>
<td>STARTED 2019</td>
<td></td>
</tr>
</tbody>
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## Four therapeutic modalities to drive future growth

<table>
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<th>Targeted Therapies</th>
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<td>Lutathera® in 1st line grade 2/3 advanced GEP-NET&lt;br&gt;177Lu-PSMA-617 in prostate cancer&lt;br&gt;177Lu-PSMA-R2 in prostate cancer&lt;br&gt;177Lu-NeoB in multiple solid tumors&lt;br&gt;177Lu-FF58 in glioblastoma</td>
<td>Kymriah&lt;sup&gt;®&lt;/sup&gt; in&lt;br&gt;• r/r DLBCL after 1st relapse&lt;br&gt;• r/r follicular lymphoma&lt;br&gt;• r/r adult ALL&lt;br&gt;• combinations (pembrolizumab; ibrutinib) in r/r DLBCL&lt;br&gt;• pediatric NHL&lt;br&gt;• 1st line high risk pediatric and young adult ALL&lt;br&gt;YTB323 in&lt;br&gt;• r/r DLBCL&lt;br&gt;• r/r CLL combination with ibrutinib&lt;br&gt;PHE885 in r/r MM&lt;br&gt;Other targets: BCMA&amp;CD19, CD22&amp;CD19, CD123, EGFRvIII</td>
</tr>
<tr>
<td>Alpelisib in&lt;br&gt;• HER2+ advanced BC&lt;br&gt;• TNBC&lt;br&gt;• Head &amp; neck&lt;br&gt;• Ovarian cancer&lt;br&gt;• PROS&lt;br&gt;Adakveo&lt;sup&gt;®&lt;/sup&gt; in sickle cell disease&lt;br&gt;Tabrecta™ in NSCLC, single agent and combinations&lt;br&gt;Jakavi&lt;sup&gt;®&lt;/sup&gt; in GvHD, and combinations (platform) in MF&lt;br&gt;Asciminib in CML&lt;br&gt;LXH254 in RAS/RAF mutant melanomas and lung cancer</td>
<td></td>
<td></td>
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</tbody>
</table>
Lutathera®: On track for blockbuster status in NET; real-world safety data featured at ASCO

- Real-world safety data from US expanded access program showed that Lutathera® is well-tolerated in patients with advanced NETs.
- Treatment-related adverse events (TRAEs) were generally mild or moderate and mostly gastrointestinal.
- Few patients experienced grade 3/4 TRAEs.
- The safety profile was consistent with the results of the Phase 3 NETTER-1 trial and other previous studies.

**Net sales**

USD million, growth in % cc vs. PY period

<table>
<thead>
<tr>
<th>Year</th>
<th>Sales</th>
<th>Growth</th>
</tr>
</thead>
<tbody>
<tr>
<td>FY 2018</td>
<td>167</td>
<td></td>
</tr>
<tr>
<td>FY 2019</td>
<td>441</td>
<td>+6% cc</td>
</tr>
<tr>
<td>Q1 2020</td>
<td>112</td>
<td></td>
</tr>
</tbody>
</table>

Blockbuster potential in current indication

Ongoing NETTER-2 study for 1st line use in advanced GEP-NET patients with high proliferation rate tumors (G2/3 segment) represents an incremental opportunity

Next wave of innovation in RLT includes $^{177}$Lu-PSMA-617 for mCRPC, including earlier lines, along with moving to alpha emitters and new targets.
TheraP: First randomized trial with $^{177}$Lu-PSMA-617, initiated and sponsored by ANZUP, presented at ASCO

**TheraP study design**

**Aim**
To determine the activity and safety of Lu-PSMA vs. cabazitaxel

**Key eligibility**
- mCRPC post docetaxel suitable for cabazitaxel
- Progressive disease with rising PSA and PSA ≥ 20 ng/mL
- Adequate renal, hematologic and liver function
- ECOG performance status 0-2
- $^{68}$Ga-PSMA + $^{18}$F-FDG PET/CT
  - PSMA SUVmax > 20 at any site
  - Measurable sites SUVmax > 10
  - No FDG positive/PSMA negative sites of disease
  - Centrally reviewed

**Randomization**
- 200 men 1:1 randomization
- 11 sites in Australia
- Stratified by:
  - Disease burden (>20 sites vs. ≤ 20 sites)
  - Prior enzalutamide or abiraterone
  - Study site

**Treatment**
- **$^{177}$Lu-PSMA-617**
  - 8.5 GBq IV q6 weekly
  - ↓ 0.5GBq each cycle
  - Up to 6 cycles
  - SPECT/CT @ 24 hours
    - Suspend Rx if exceptional response; recommence upon progression

- **CABAZITAXEL**
  - 20mg/m² IV q3 weekly
  - Up to 10 cycles

**Statistical power**
- 80% power to detect a true absolute difference of 20% in the PSA response rate (from 40% to 60%), with a 2-sided type 1 error of 5% and allowance of 3% for missing data.

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THERA-P is an independent investigator-initiated trial (IIT) sponsored by ANZUP: Australian & New Zealand Urogenital and Prostate (ANZUP) Cancer Trials Group. All data are taken from the ANZUP presentation at the 2020 ASCO Annual Meeting by Michael Hofman, MBBS. THERA-P is different from VISION; Novartis awaits the VISION study readout in H2 2020.
TheraP IIT showed higher PSA activity and less toxicity vs. an active comparator

Primary endpoint: PSA ≥ 50% response (PSA50-RR)

Lu-PSMA had 29% absolute (95% CI 16%-42%; p<0.0001) greater PSA ≥ 50% response rate compared to cabazitaxel

Relatively fewer Grade 3-4 AEs for 177Lu-PSMA-617 vs. cabazitaxel

Promising PSA response rate, awaiting radiographic endpoint
Results highlight potential clinical activity of 177Lu-PSMA-617
Pivotal Phase 3 VISION study of $^{177}$Lu-PSMA-617 on track to read out in H2 2020

VISION study design

1. Best standard of care / best supportive care: broad range of active treatment options, excluding investigational agents and chemotherapy.
2. NAAD = Novel Androgen Axis Drug (abiraterone or enzalutamide).

<table>
<thead>
<tr>
<th>Patient inclusion</th>
<th>$^{177}$Lu-PSMA-617</th>
<th>831 patients enrolled</th>
</tr>
</thead>
<tbody>
<tr>
<td>mCRPC</td>
<td>Best standard of care / best supportive care</td>
<td>Primary endpoints: rPFS and OS</td>
</tr>
<tr>
<td>Bone and/or soft tissue disease</td>
<td></td>
<td>Key secondary endpoints: ORR, time to symptomatic skeletal events</td>
</tr>
<tr>
<td>PSMA-positive scan</td>
<td>2:1</td>
<td></td>
</tr>
<tr>
<td>≥1 prior taxane</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥1 prior NAAD$^2$</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Important differences vs. TheraP study</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Comparator</strong></td>
</tr>
<tr>
<td><strong>Patient population</strong></td>
</tr>
<tr>
<td><strong>Primary endpoints</strong></td>
</tr>
</tbody>
</table>

1. Best standard of care / best supportive care: broad range of active treatment options, excluding investigational agents and chemotherapy.  
2. NAAD = Novel Androgen Axis Drug (abiraterone or enzalutamide).
Plans to take $^{177}$Lu-PSMA-617 into earlier lines, where there is significant unmet need

**Priority focus**

- Pre-taxane setting for metastatic Castration-Resistant Prostate Cancer (mCRPC)
- Metastatic Hormone-Sensitive Prostate Cancer (mHSPC)
