



Novartis AG
Investor Relations

Novartis Oncology Pipeline Update

June 15, 2020

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Agenda

Our strategy in Oncology

Pipeline updates across our therapeutic modalities

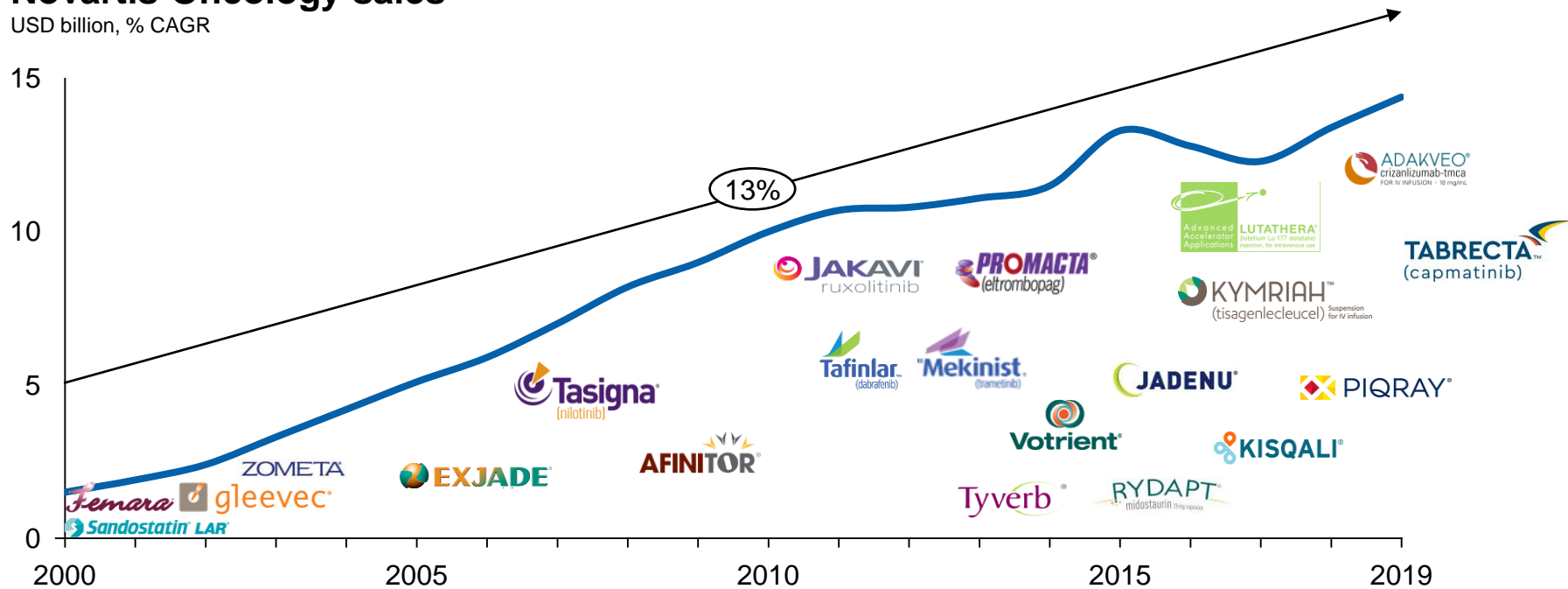
- Targeted Therapies: Kisqali[®], Piqray[®], Tavegyl[™], Tafinlar[®]+Mekinist[®], LXH254, TNO155, Asciminib
 - Immunotherapies: Canakinumab, MBG543, Spartalizumab
 - Radioligand: Lutathera[®], ¹⁷⁷Lu-PSMA-617
 - Cell & Gene: Kymriah[®], YTB323
-

Q&A

Strong track record of pioneering innovation in Oncology

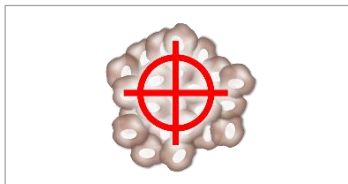
Novartis Oncology sales

USD billion, % CAGR



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

Adakveo® in sickle cell disease

Tabrecta™ in NSCLC, single agent and combinations

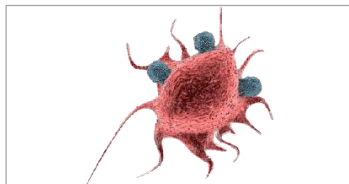
Jakavi® in GvHD, and combinations (platform) in MF

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®+

Mekinist® in metastatic melanoma

Spartalizumab combinations

(platform) in metastatic melanoma

Spartalizumab+LAG525+ carboplatin in TNBC

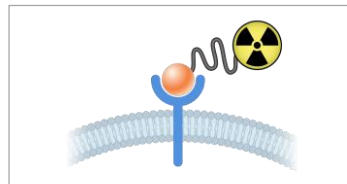
Spartalizumab+Tabrecta™ in NSCLC

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

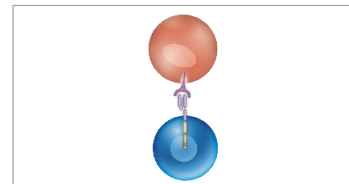
¹⁷⁷Lu-NeoB

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
 LXH254 + Kisqali® in 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 + IO¹

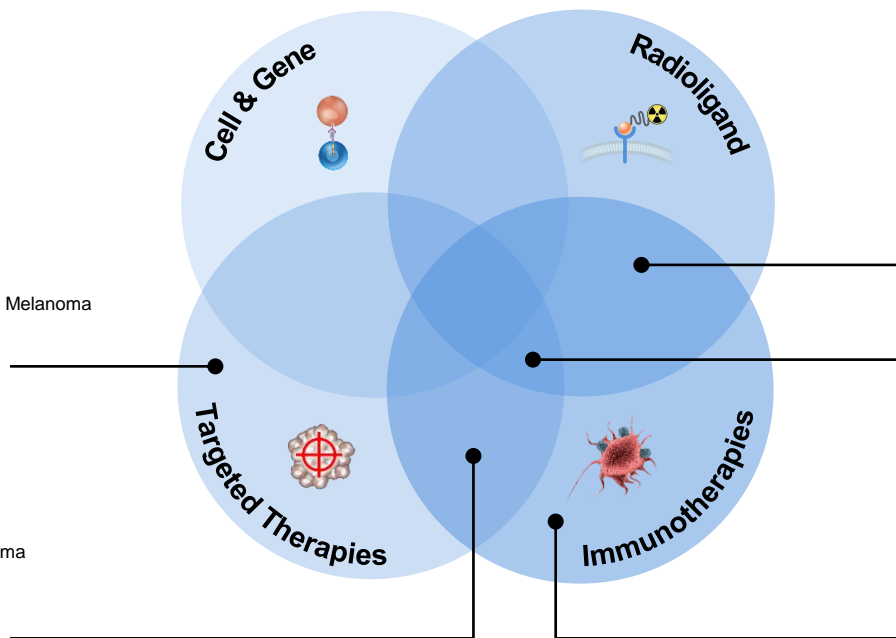
Lutathera® + PD-1 in NET
¹⁷⁷Lu-PSMA-617 + PD-1 in mCRPC

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



OS data in patients with visceral mets



COMBI-AD 5-year analysis

¹⁷⁷Lu-PSMA-617

TheraP IIT data



MBG453

Phase 1 data in MDS and AML

Asciminib

3-year data in TKI-intolerant patients

AACR American Association for Cancer Research[®]



Brain mets data

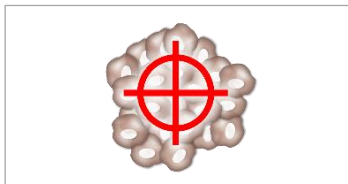
TNO155

New Drugs on the Horizon Symposium

1. Including investigator-initiated trials / third party abstracts

Four therapeutic modalities to drive future growth

Targeted Therapies



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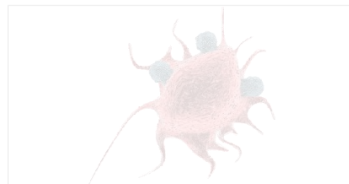
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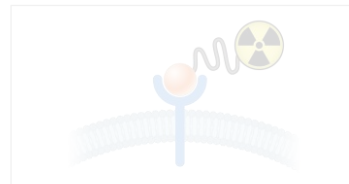
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PHE885 in r/r MM

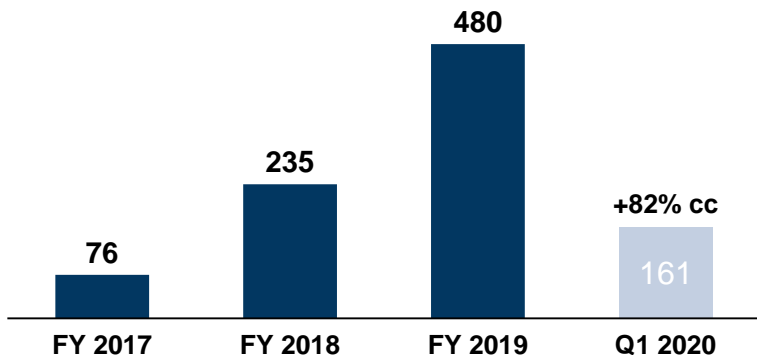
Other targets: BCMA&CD19, CD22&CD19, CD123, EGFRvIII



Kisqali®: Only CDK4/6 proven to extend the lives of patients in two Phase 3 trials

Net sales

USD million,
growth in % cc vs. PY period



- 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 vs. palbociclib¹
- NATALEE adjuvant study on track to complete enrollment in this year, with readout in 2022

1. Schwartzberg, L.S., Zarate, J.P., Chandiwana, D., et. al. Real-world incidence, duration, and severity of treatment-emergent (TE) neutropenia among patients (pts) with metastatic breast cancer (MBC) treated with ribociclib (RIB) or palbociclib (PAL). J of Clin Onc. 2020;38(15 suppl).

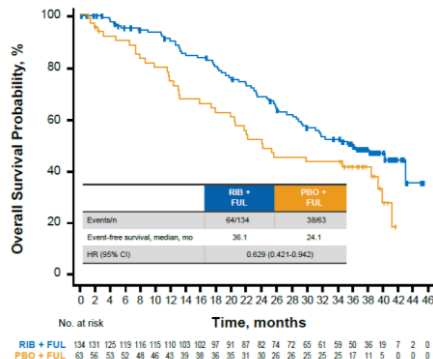


MONALEESA 3 & 7 data in visceral metastases, including liver, reinforce differentiated profile

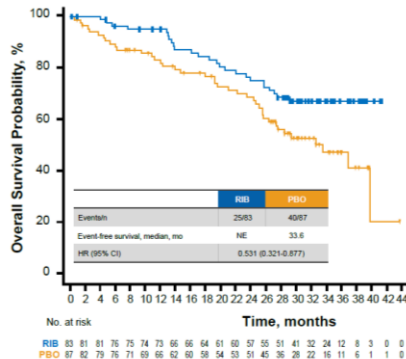
ASCO20 Virtual

OS in patients with liver metastases

A. ML-3



B. ML-7 NSAI Cohort

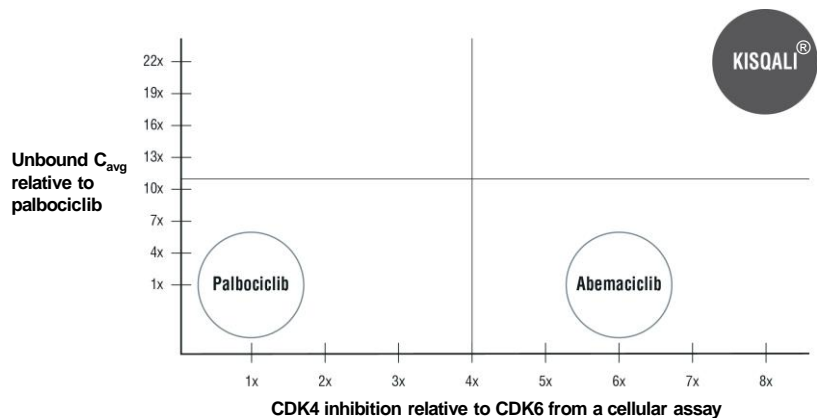


- Presence of visceral metastases generally signifies a poor prognosis in HR+/HER2- metastatic breast cancer
- Approximately 60% of patients had visceral metastases in MONALEESA 3 & 7
- Similar to the overall population, there was a consistent OS and PFS benefit in patients with visceral metastases, 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

Select differences among CDK4/6 inhibitors³⁻⁷



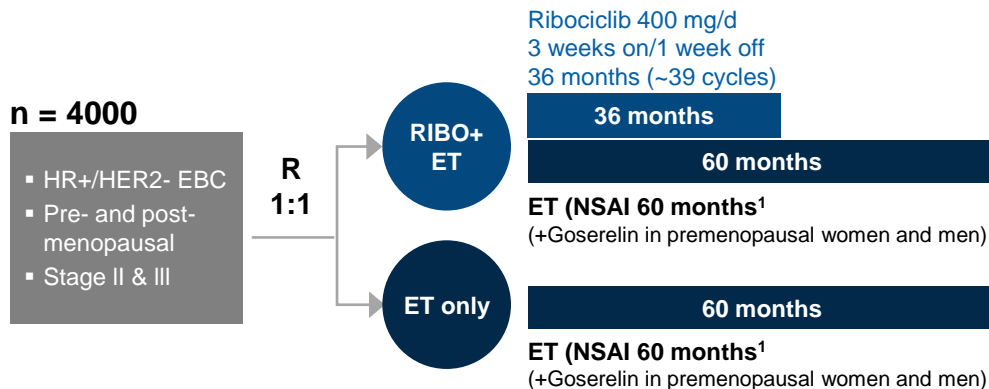
- CDK4 is a critical driver of HR+/HER2- advanced breast cancer, while CDK6 drives hematological toxicities^{1,2}
- Kisoqali® inhibits CDK4 8x more than CDK6 in vitro^{3,4}
- Higher unbound C_{avg} (average free drug concentration at steady state) means more drug is available to act on tumor cells⁴⁻⁷
- At clinically relevant doses and adjusting for differences in potency against CDK4/6 and protein binding, Kisoqali® should provide greater CDK4 inhibition in vivo than competitors

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, Reifemberger G, Bender HG, Niederacher D. Gene amplification and overexpression of CDK4 in sporadic breast carcinomas is associated with high tumor cell proliferation. *Am J Pathol*. 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. 4. Chen P, Lee NV, Hu W, et al. Spectrum and degree of CDK drug interactions predicts clinical performance. *Mol Cancer Ther*. 2016;15(10):2273-2281;(suppl tables). 5. Infante JR, Cassier PA, Gerecitano JF, et al. A phase I study of the cyclin-dependent kinase 4/6 inhibitor ribociclib (LEE011) in patients with advanced solid tumors and lymphomas. *Clin Cancer Res*. 2016;22(23):5696-5705. 6. Flaherty KT, LoRusso PM, DeMichele A, et al. Phase I, dose-escalation trial of the oral cyclin-dependent kinase 4/6 inhibitor PD 0332991, administered using a 21-day schedule in patients with advanced cancer. *Clin Cancer Res*. 2012;18(2):568-576. 7. Patnaik A, Rosen LS, Tolane SM, et al. Efficacy and safety of abemaciclib, an inhibitor of CDK4 and CDK6, for patients with breast cancer, non-small cell lung cancer, and other solid tumors. *Cancer Discov*. 2016;6(7):740-753.



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

NATALEE trial design



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

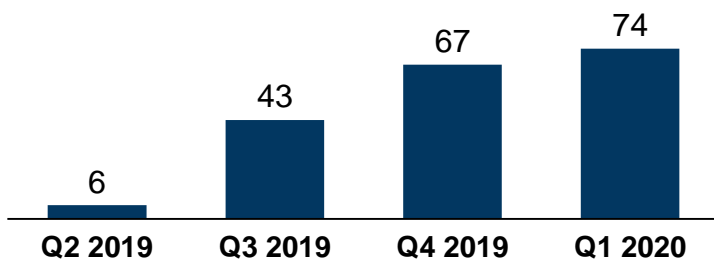
More homogeneous patient population: Intermediate and high-risk patients per AJCC defined prognostic factors

1. Letrozole or anastrozole; treatment with NSAI may start up to 12 months before study treatment start date.



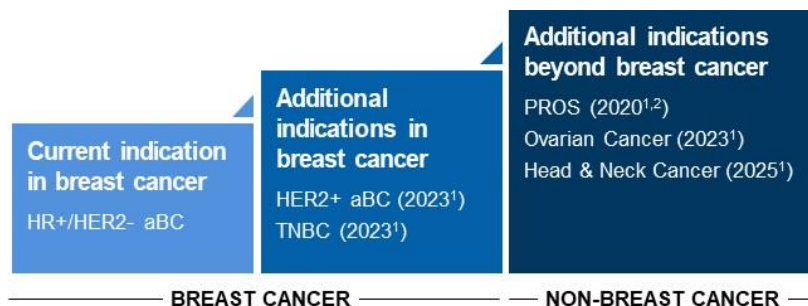
Piqray®: Strong launch as first and only PI3K α inhibitor, with significant expansion opportunities

Net sales USD million



- 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

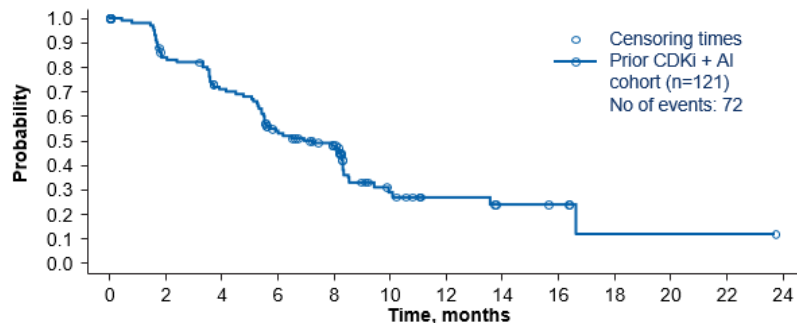
1. Refers to first filing year. 2. Filing in US based on RWE study. PROS = PI3K Related Overgrowth Syndrome aBC = advanced Breast Cancer



BYLieve study reinforces efficacy of Piqray[®] use in post CDK4/6 setting with manageable side effects

ASCO 20 Virtual

Efficacy data



No. of patients still at risk

Prior CDKi + AI	121	95	77	54	40	15	8	5	4	1	1	1	0
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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)

Safety profile

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%)

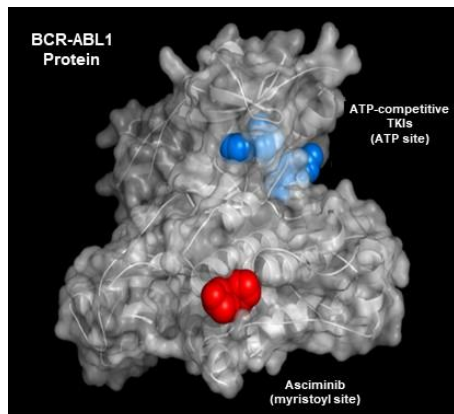
Overall approach to further mitigate AEs:

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

Oncogene dependency is a key therapeutic vulnerability in human cancers



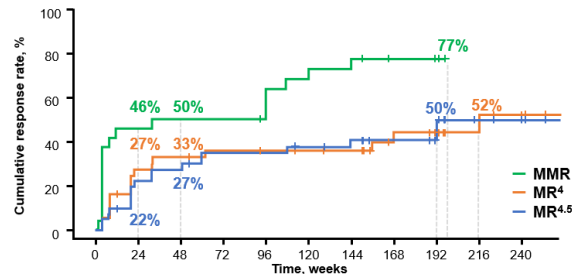
Asciminib: First-in-class STAMP inhibitor



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

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

Cumulative Molecular Response Rates^a



Number at risk, n^b

MiMR	24	12	8	5	0	0
MR ⁴	38	24	21	19	7	3
MR ^{4.5}	42	28	24	20	8	4

Cumulative number of events, n

Patients with MiMR	0	12	15	18	18	18
Patients with MR ⁴	0	12	13	13	15	16
Patients with MR ^{4.5}	0	12	14	16	18	18

MR⁴: BCR-ABL1^{IS} ≤ 0.01%; MR^{4.5}: BCR-ABL1^{IS} ≤ 0.0032%

^a As of the cutoff date of August 30, 2019; ^b Calculated based on the number of patients evaluable for response and without that response at baseline.

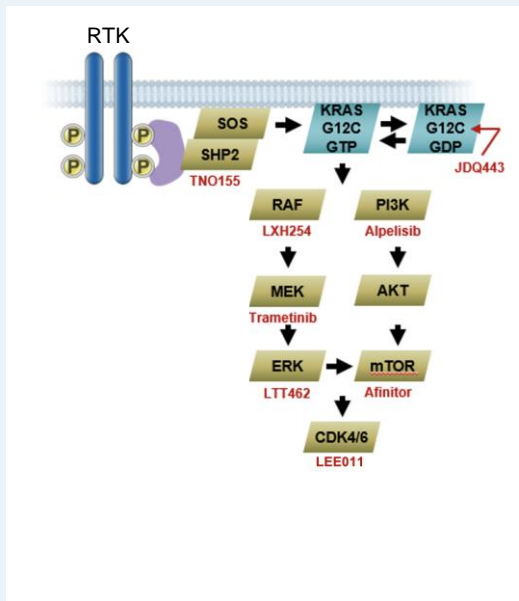
- Asciminib monotherapy was well tolerated and showed promising clinical activity in TKI intolerant patients
- 75% of patients were on treatment and in MMR after a median follow-up of over three years
- Median duration of treatment with asciminib was 32 months, vs. 3 months on previous therapy
- Pivotal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

ATP = Adenosine Triphosphate; TKI = Tyrosine Kinase Inhibitor.

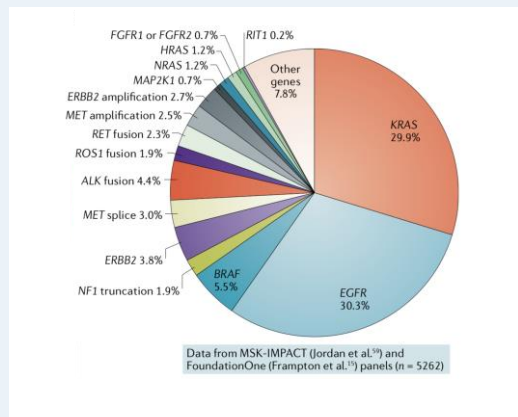


Targeting RTK/RAS/MAPK signaling in solid tumors

RTK/RAS/MAPK pathway

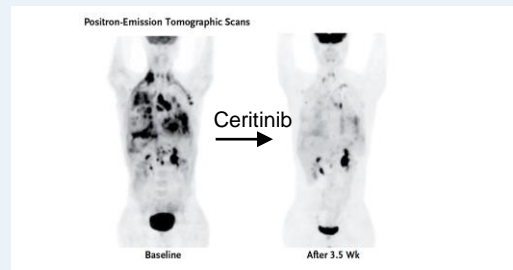


Metastatic lung adenocarcinoma¹

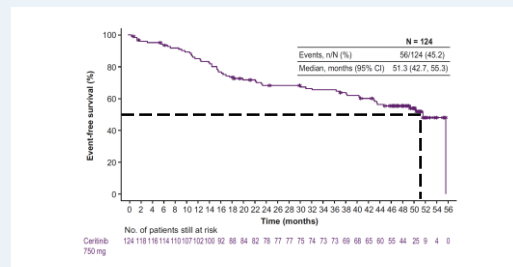


- Roughly 1/3 to 1/2 of NSCLC patients have targetable genetic alterations
- To date, 7 molecular subsets of NSCLC can be targeted with standard of care therapies (EGFR, ALK, ROS1, RET, BRAF, TRK, MET)

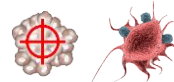
Dramatic clinical responses²



Prolonged overall survival³



1. Skoulidis and Heymach, Nat Rev CA, 2019. 2. Shaw NEJM Ph1 ceritinib 2014 (ASCEND 1). 3. Nishio JTO Ph2 ceritinib 2020 (ASCEND 3 study)



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

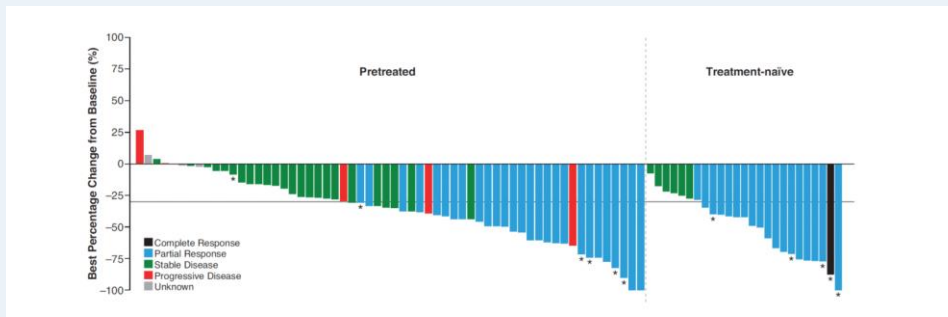
- Additional studies planned as monotherapy: Phase 3, brain metastases, tumor agnostic
- Moving into combinations:
 - PD-L1 high expressers regardless of MET status, in combination with pembrolizumab
 - METex14 skipping regardless of PD-L1 status, in combination with spartalizumab
 - Post-EGFR, in combination with EGFR inhibitor



Differentiated profile with clinical activity in METex14 mutated and MET amplified NSCLC

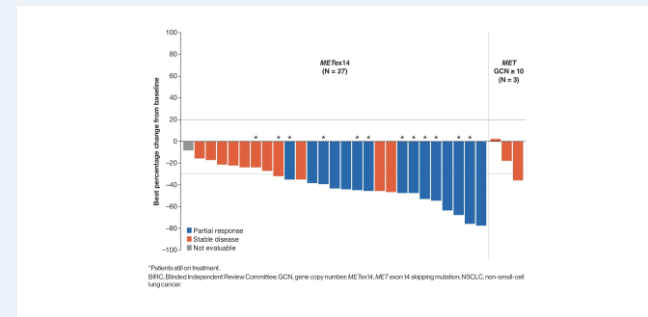
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Results from cohorts 4 and 5b of GEOMETRY mono-1

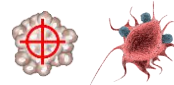


- Capmatinib is highly active in previously treated and treatment-naïve METex14 NSCLC patients; in the 1L setting, ORR 67.9%, DCR 96.4%, mPFS 12.4 mos
- Among 13 patients with brain mets at baseline, intracranial responses were achieved in 54%, including 31% with CR; intracranial disease control achieved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

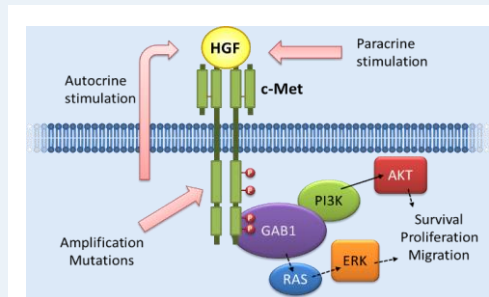
Results from cohort 6 of GEOMETRY mono-1



- 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 \geq 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 immuno-modulation 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 \geq 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

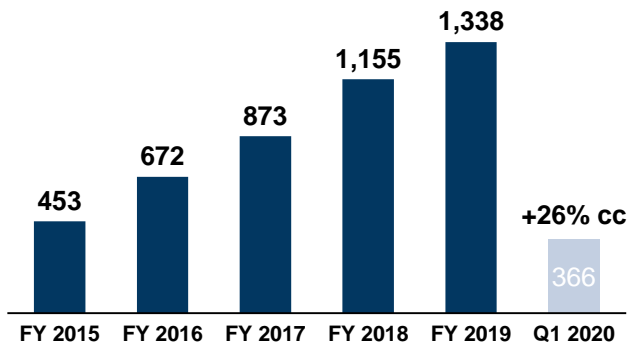


Tafinlar[®]+Mekinist[®]: 5-year analysis shows long-term benefit of adjuvant treatment in BRAF+ melanoma

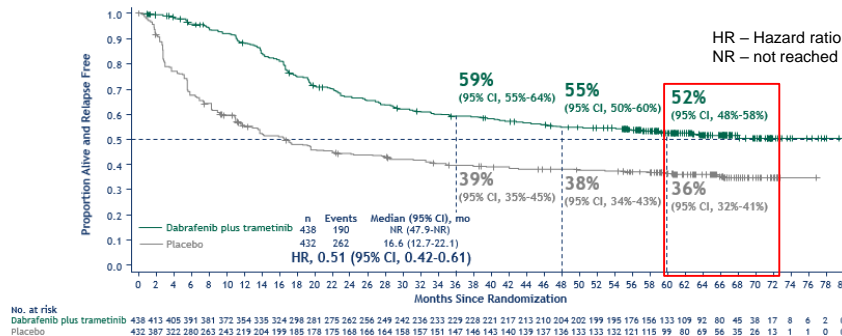
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Net sales

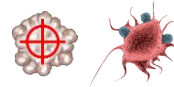
USD million
growth in % cc vs. PY period



COMBI-AD 5-year analysis



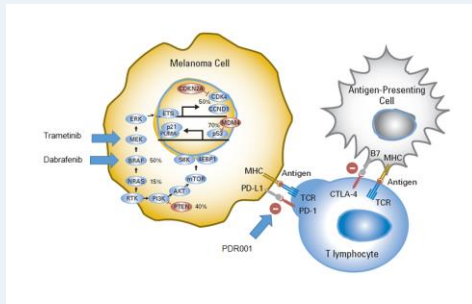
- More than half of BRAF+ patients treated with adjuvant Tafinlar[®]+Mekinist[®] were relapse-free at 5 years, with curve trending towards plateau
- Longest follow-up to-date from a Phase 3 study of any contemporary adjuvant therapy



Additional data from COMBI-i parts 1 and 2 show durable anti-tumor activity of triplet therapy

ASCO20 Virtual

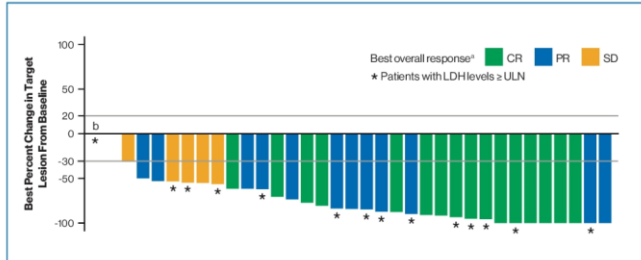
Rationale for combining Tafinlar®+Mekinist® with anti-PD-1



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

McArthur GA & Ribas A, *J Clin Oncol* 2013;31:499-506

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



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.

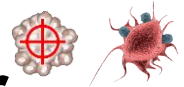
^b Best percent change in the target lesion was not available for 1 patient with progressive disease.

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

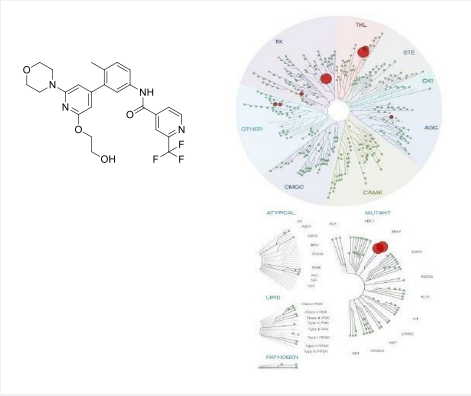
S+D+T may be associated with a high frequency of durable responses, with 24-month PFS and OS rates of 41% and 74%, respectively

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



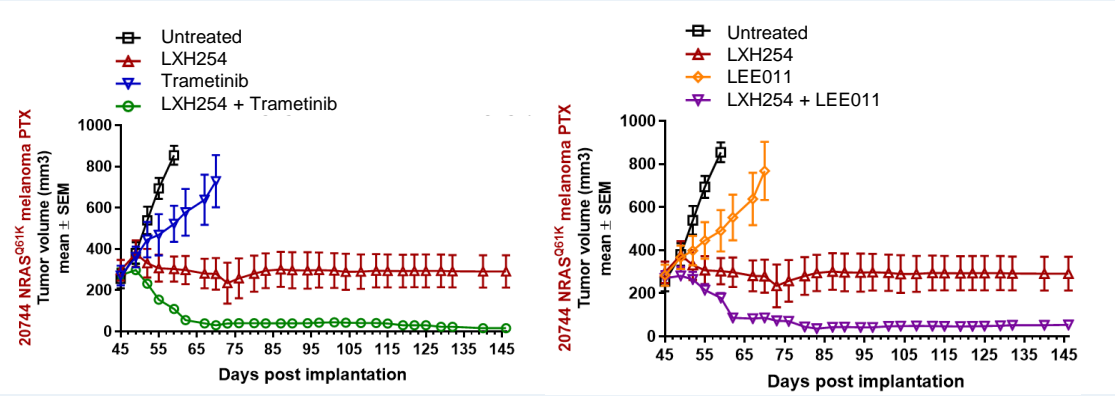
LXH254: Potentially best-in-class B/C-RAF inhibitor in RAS/RAF mutant melanomas and lung cancers

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

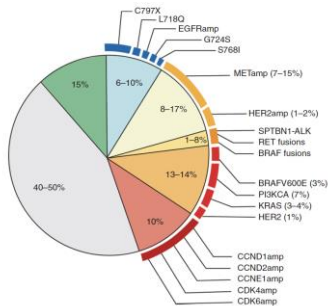


- Antitumor activity of LXH254 single agent observed in patients with KRAS-mut and BRAF-mut cancers
- Preclinical data show robust activity in vertical combinations with MEK, ERK, and CDK4/6 inhibitors
- Favorable tolerability profile of LXH254 enables combinations, with potential benefit for BRAF-mut 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

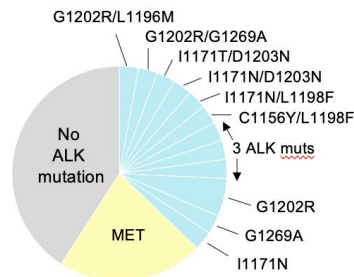


Almost all patients develop resistance to targeted therapies: Role of SHP2 phosphatase

1L Tagrisso® in EGFR¹



2L+ Lorbrena® in ALK²

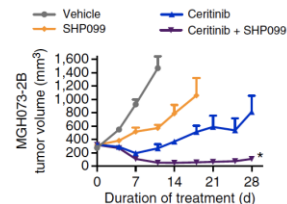
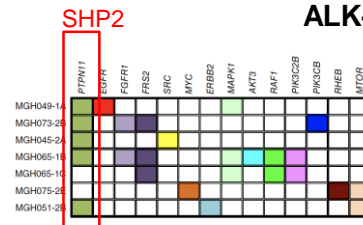


Multiple and diverse resistance mechanisms can develop in patients treated with targeted therapies, leading to clinical relapse

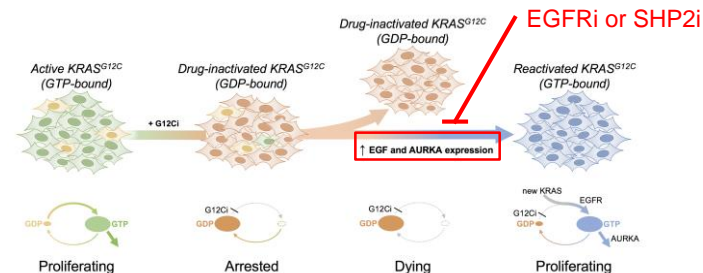
For highly selective, next-generation targeted agents, resistance is often mediated by off-target mechanisms that lead to MAPK re-activation

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

ALK+ NSCLC³



KRAS^{G12C} NSCLC⁴



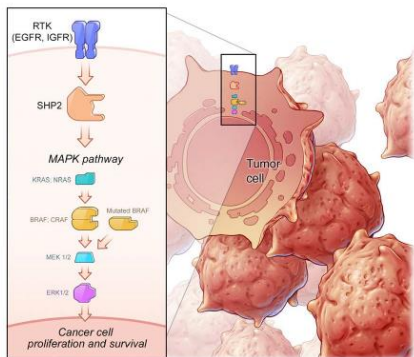
1. Leonetti Br J Cancer 2019. 2. Dagogo-Jack, Clin Canc Res, 2020. 3. Dardaei Nat Med 2018. 4. Based on Xue Nature 2020



TNO155: A first-in-class inhibitor of SHP2

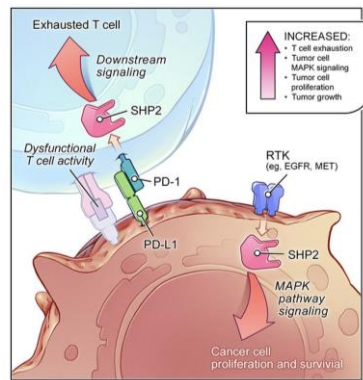
AACR American Association for Cancer Research

Required for RTK signaling



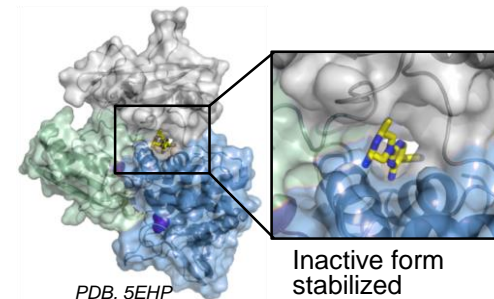
RTK-SHP2-RAS-MAPK pathway activation has been implicated across the majority of human cancers

Downstream transducer of PD-1

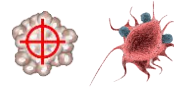


SHP2 is a downstream transducer of PD-1 signaling, a critical immune checkpoint in human malignancies

First SHP2i to enter the clinic



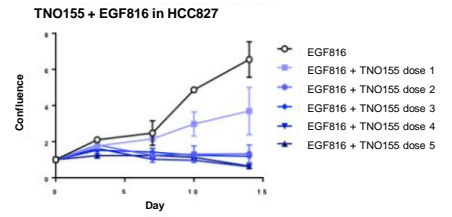
Ideal drug-like properties (e.g. high permeability, solubility, no CYP450 inhibition, ideal preclinical PK profile)



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

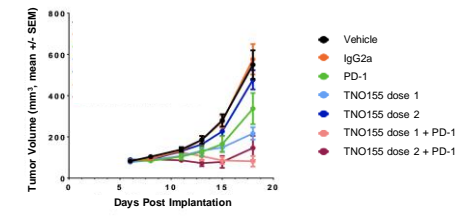
To characterize the safety and tolerability of TNO155 as a single agent and in combination with **nazartinib** (EGF816) in solid tumors, and to identify recommended regimen(s) and dose(s) for future studies

Status

Enrolling, PPFV 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

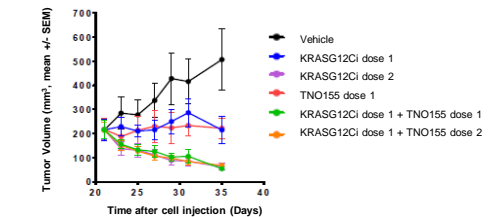
To characterize the safety, tolerability, and efficacy of TNO155 in combination with spartalizumab or ribociclib, and to identify the MTD and/or RDE for each combination

Status

Enrolling, PPFV in July 2019

TNO155C1*

MIA PaCa-2 (PDAC, KRAS^{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, PPFV in April 2020

*Study sponsored by Mirati

Four therapeutic modalities to drive future growth

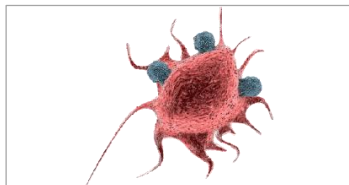
Select pipeline assets and opportunities

Targeted Therapies



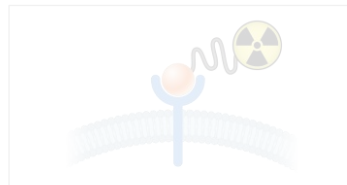
Kisqali® in adjuvant BC
Alpelisib in
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 ▪ TNBC
 ▪ Head & neck
 ▪ Ovarian cancer
 ▪ PROS
Adakveo® in sickle cell disease
Tabrecta™ in NSCLC, single agent and combinations
Jakavi® in GvHD, and combinations (platform) in MF
Asciminib in CML
LXH254 in RAS/RAF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

Immunotherapies



Canakinumab in
 ▪ adjuvant NSCLC
 ▪ 1st line NSCLC
 ▪ 2nd line NSCLC
Spartalizumab+Tafinlar®+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

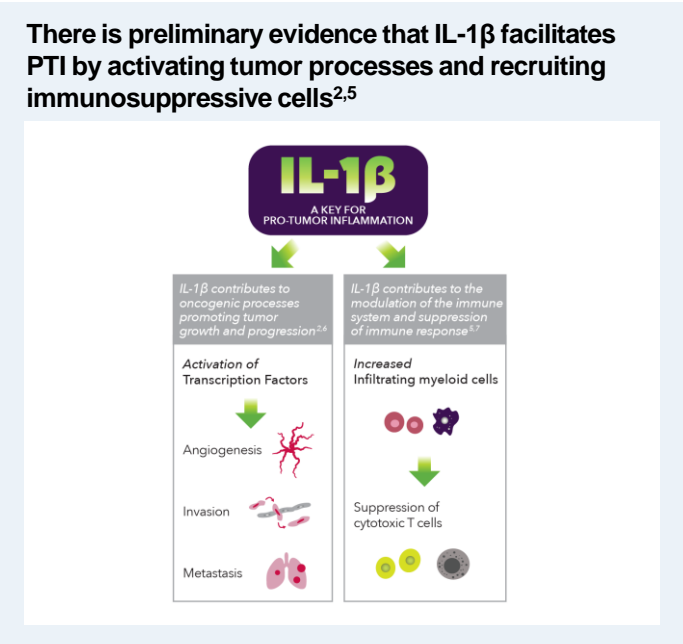
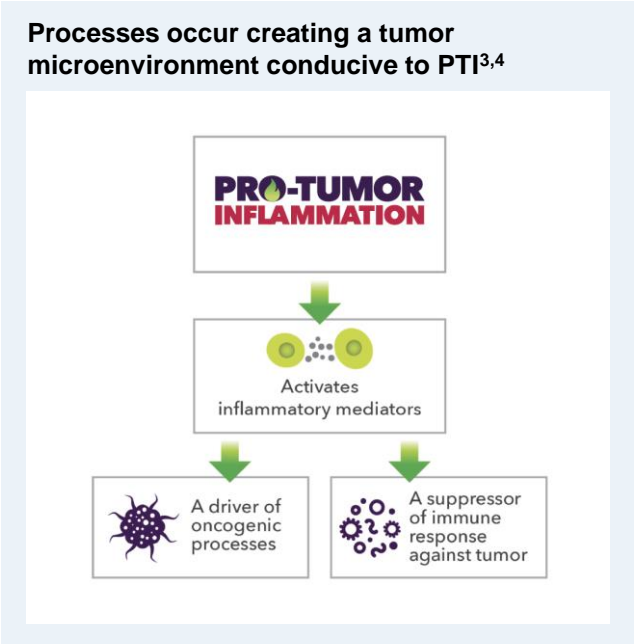


Kymriah® in
 ▪ r/r DLBCL after 1st relapse
 ▪ r/r follicular lymphoma
 ▪ r/r adult ALL
 ▪ combinations (pembrolizumab; ibrutinib) in r/r DLBCL
 ▪ pediatric NHL
 ▪ 1st line high risk pediatric and young adult ALL
YTB323 in
 ▪ r/r DLBCL
 ▪ r/r CLL combination with ibrutinib
PHE885 in r/r MM
Other targets: BCMA&CD19, CD22&CD19, CD123, EGFRvIII



IL-1 β plays a key role in pro-tumor inflammation, a driver of tumor survival, growth and progression^{1,2}

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



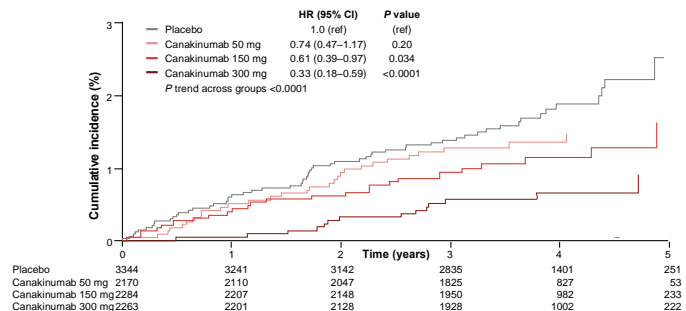
1. Carmi Y, et al. J Immunol. 2013;190(7):3500-3509. 2. Chaudhry SI, et al. Oncogene. 2013;32(6):747-758. 3. Grivennikov SI, et al. Cell. 2010;140(6):883-899. 4. Greten FR, Grivennikov SI. Immunity. 2019;51(1):27-41. 5. Bunt SK, et al. J Immunol. 2006;176(1):284-290. 6. Taniguchi K, et al. Nat Rev Immunol. 2018;18(5):309-325. 7. Chen L, et al. Cell Mol Life Sci. 2018;75(11):2045-2058.



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

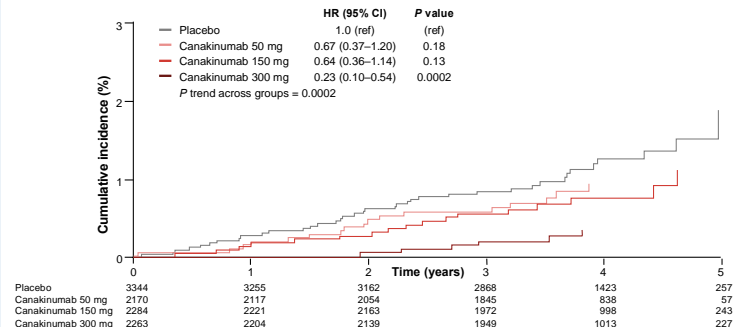
Lung cancer incidence

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

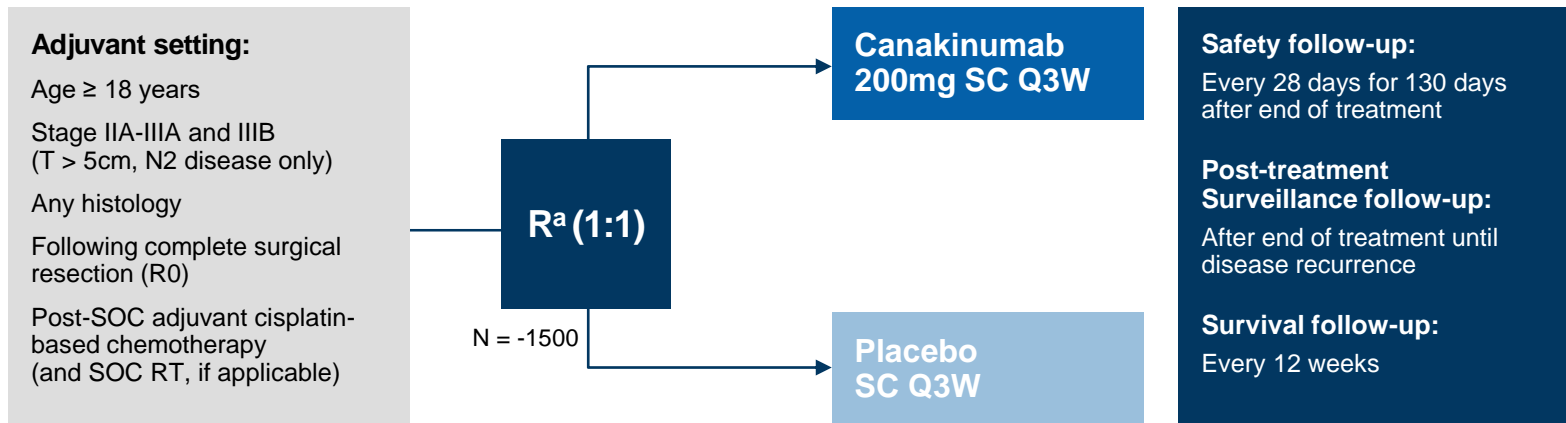
Indication	Patient population	Trial design	Status as of Jun 2020	Planned filing
Adjuvant NSCLC (CANOPY-A)	High-risk Stage II-III	Canakinumab vs. placebo (n=1500 with 1:1 randomization) after post-resection chemotherapy	~40% of patients enrolled	2023
1st line NSCLC (CANOPY-1)	Non-mutated, no prior treatment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

Phase 3 adjuvant study design presented at ASCO



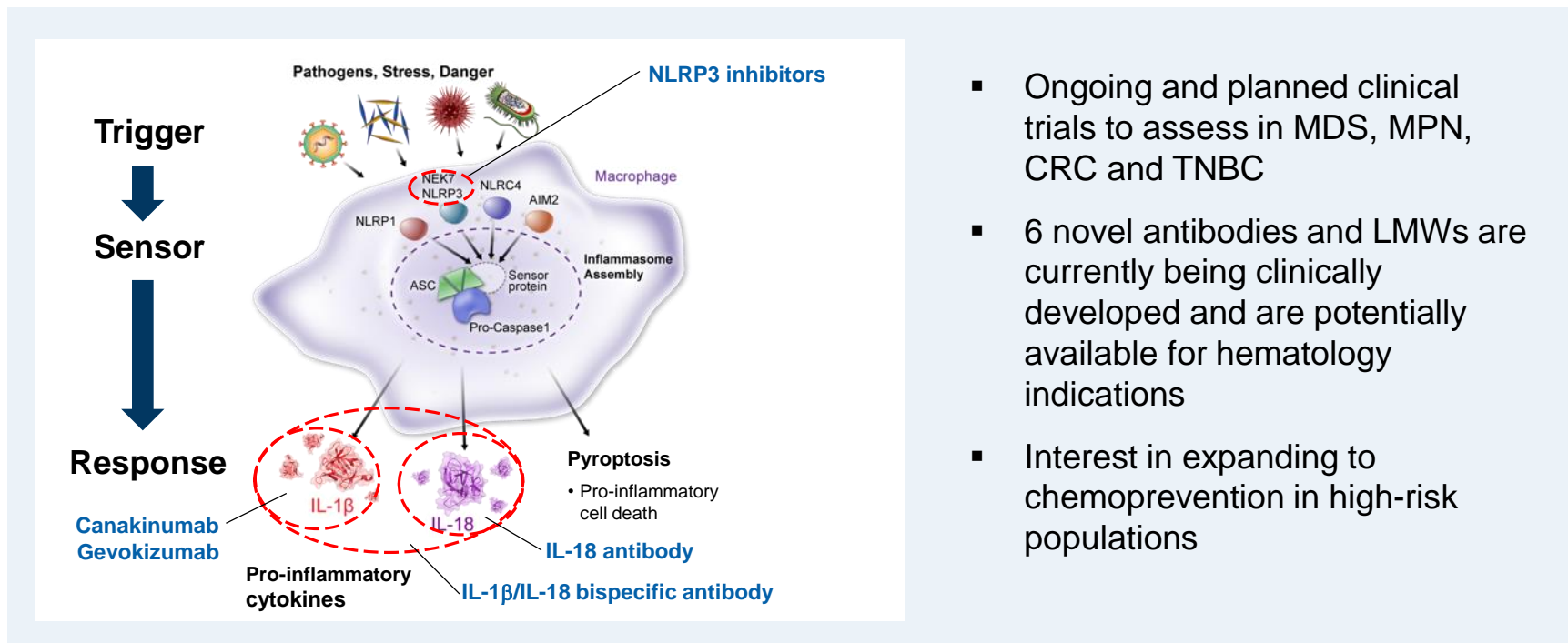
ASCO20 Virtual

CANOPY-A Study Design





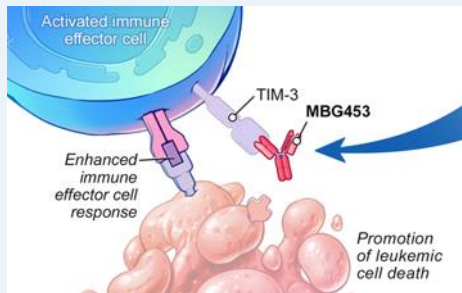
Next-generation inflammasome inhibitors are under development for cancer and other diseases





MBG453: Targeting TIM-3 in hematology

MBG453 mechanism

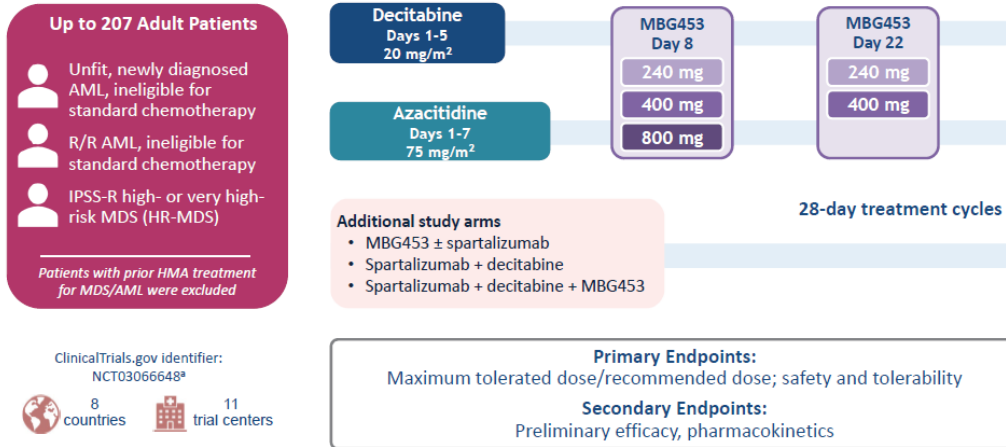


In vitro data shows that targeting TIM-3 with inhibitory antibody MBG453¹⁻³:

- 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



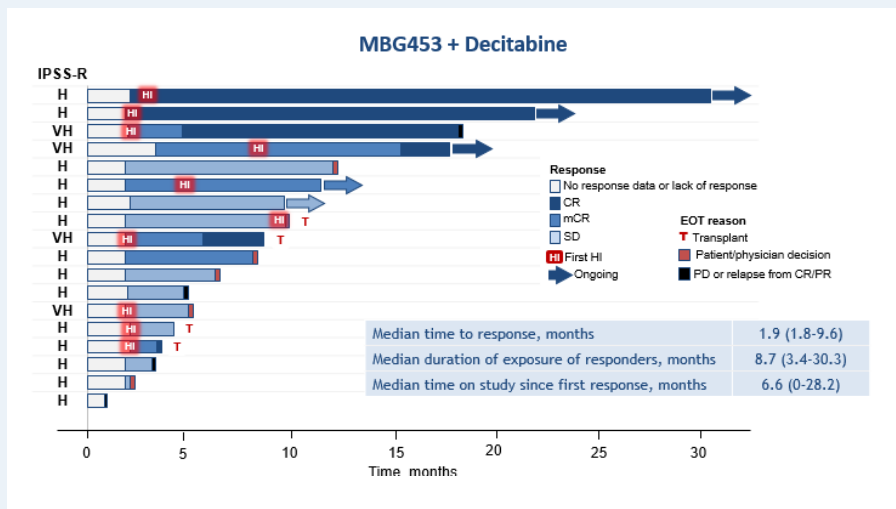
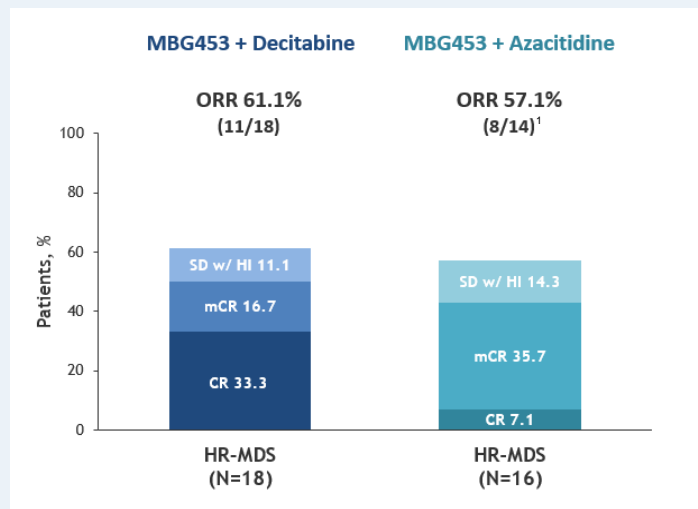
*Multi-arm, open-label, phase 1b dose escalation and expansion study of MBG453 as a single-agent or in combination with HMAs or spartalizumab.

1. Kikushige Y et al., Cell Stem Cells, 2010. 2. Dama P et al., J. Immunotherapy Cancer, 2019. 3. Kong Y et al., Blood Cancer J., 2015.

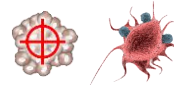
MBG453+HMA provides promising and durable response rates in ongoing Phase 1 trial



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

HR-MDS

STIMULUS-MDS-1

Phase 2 ongoing, enrollment expected to complete in 2020

STIMULUS-MDS-2

Phase 3 ongoing, enrollment started in June 2020

Unfit AML

STIMULUS-AML-1

Phase 2 combo HMA + venetoclax, enrollment expected to start H2 2020

Novel combinations

MDS/AML

Phase 1 combo with HDM201¹ ongoing

Myelofibrosis

Phase 1b/2 combo with Jakavi[®] ongoing

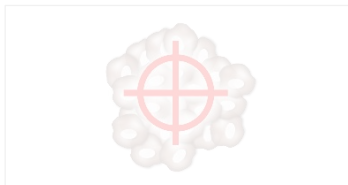
Phase 1 combo without Jakavi[®] in post-JAKi patients

1. HDM201: MDM2 inhibitor

Four therapeutic modalities to drive future growth

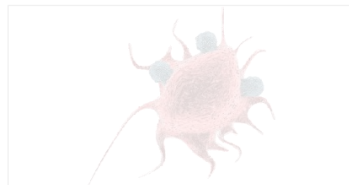
Select pipeline assets and opportunities

Targeted Therapies



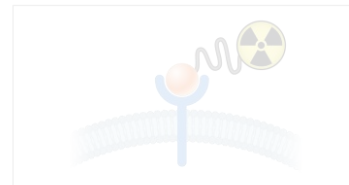
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 ▪ TNBC
 ▪ Head & neck
 ▪ Ovarian cancer
 ▪ PROS
Adakveo® in sickle cell disease
Tabrecta™ in NSCLC, single agent and combinations
Jakavi® in GvHD, and combinations (platform) in MF
Asciminib in CML
LXH254 in RAS/RAF mutant melanomas and lung cancer
TNO155 in solid tumors

Immunotherapies



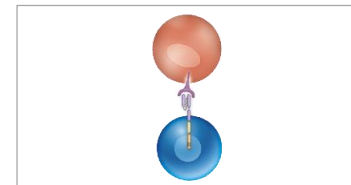
Canakinumab in
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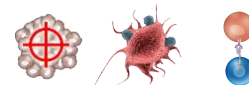
Lutathera® in 1st line grade 2/3 advanced GEP-NET
¹⁷⁷Lu-PSMA-617 in prostate cancer
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¹⁷⁷Lu-NeoB in multiple solid tumors
¹⁷⁷Lu-FF58 in glioblastoma

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
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YTB323 in
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 ▪ 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

90%
final products

made available to patients globally, including OOS

25
countries

where Kymriah® is available and reimbursed

240+
qualified

treatment centers worldwide

RWE

demonstrated comparable efficacy and improved safety versus pivotal trials

Expanding manufacturing

7
global sites

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

125%
capacity increase

Q1 2020 vs. Q1 2019

2800+
therapies

delivered for patients cumulatively

Moving into new indications

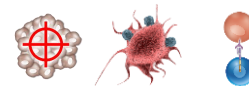
7
clinical trials

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

FDA
designation

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

Advancing our cell therapy pipeline



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

Cell therapy pipeline

Study	Indication	Phase I	Ph II/Pivotal	Phase III	Submitted	Approved
CAR-T CD19 (Kymriah®)	ELIANA CTL019B2202	Pediatric & young adult r/r ALL				US, EU, CH, CA, AU, JP
	JULIET CTL019C2201	r/r DLBCL				US, EU, CH, CA, AU, JP
	BELINDA CTL019H2301	DLBCL in 1 st relapse			STARTED 2019	
	ELARA CTL019E2202	r/r FL		STARTED 2018		
	OBERON CTL019J2101	Adult r/r ALL			STARTING 2020	
	PORTIA CTL019J2101	r/r DLBCL combo with pembrolizumab		STARTED 2018		
	CTL019L12101C	r/r DLBCL combo with ibrutinib		STARTED 2019		
	BIANCA CTL019C2202	Pediatric NHL			STARTED 2019	
CASSIOPEIA CTL0198G2201J	1L high risk pediatric & young adult ALL			STARTED 2019		
CAR-T CD19 YTB323	YTB323A12101	r/r DLBCL, r/r CLL combo with ibrutinib		STARTED 2019		
CAR-T BCMA PHE885	PHE885 ADPT07A12101	r/r MM		START Q2 2020		
Other targets		CD19, BCMA, CD22, CD123, EGFRvIII		STARTED 2018		

Four therapeutic modalities to drive future growth

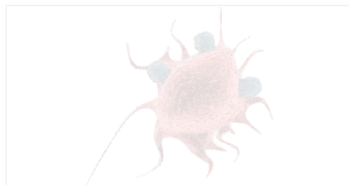
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Targeted Therapies



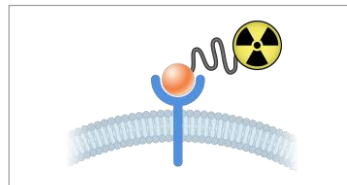
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Cell & Gene



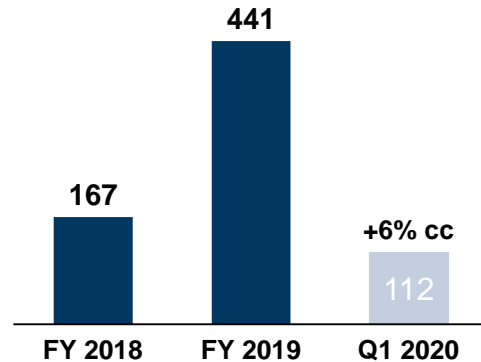
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YTB323 in
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 ▪ r/r CLL combination with ibrutinib
PHE885 in r/r MM
Other targets: BCMA&CD19, CD22&CD19, CD123, EGFRvIII



Lutathera[®]: On track for blockbuster status in NET; real-world safety data featured at ASCO

Net sales

USD million,
growth in % cc vs. PY period



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 ¹⁷⁷Lu-PSMA-617 for mCRPC, including earlier lines, along with moving to alpha emitters and new targets

ASCO²⁰ Virtual

- 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



TheraP: First randomized trial with ^{177}Lu -PSMA-617, initiated and sponsored by ANZUP, presented at ASCO

TheraP study design

ANZUP ASCO20 Virtual
Cancer Trials Group Limited

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 \geq 20 ng/mL
- Adequate renal, hematologic and liver function
- ECOG performance status 0-2



^{68}Ga -PSMA + ^{18}F -FDG PET/CT

- PSMA SUV_{max} > 20 at any site
- Measurable sites SUV_{max} > 10
- No FDG positive/PSMA negative sites of disease
- Centrally reviewed



^{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

200 men 1:1 randomization 11 sites in Australia

Stratified by:

- Disease burden (>20 sites vs. \leq 20 sites)
- Prior enzalutamide or abiraterone
- Study site

CABAZITAXEL

20mg/m² IV q3 weekly,
Up to 10 cycles

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.

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.

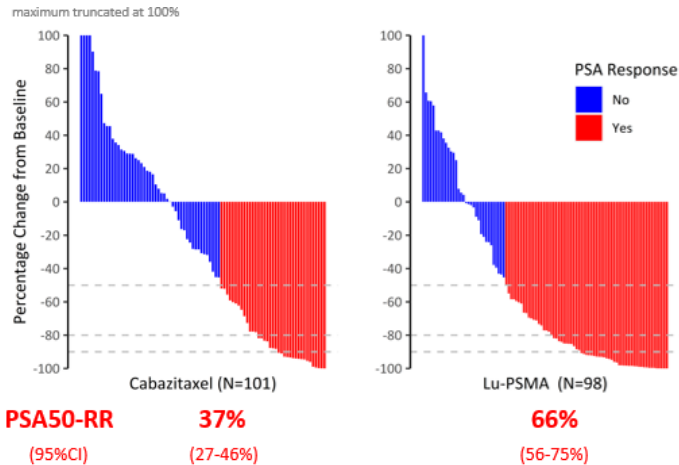


TheraP IIT showed higher PSA activity and less toxicity vs. an active comparator

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

ANZUP ASCO20 Virtual
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Best PSA Response



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

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

Promising PSA response rate, awaiting radiographic endpoint

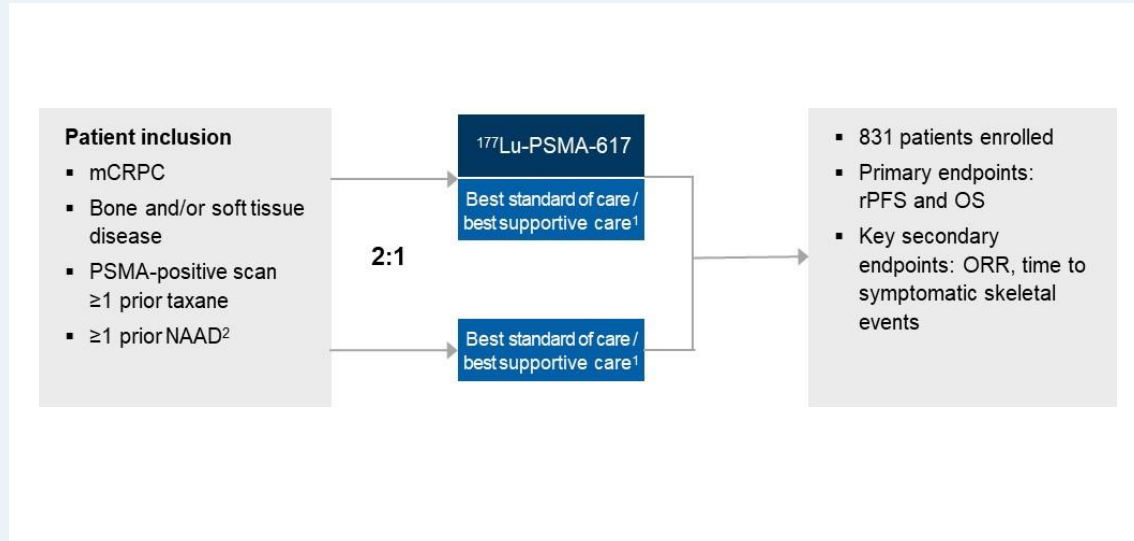
Results highlight potential clinical activity of ^{177}Lu -PSMA-617

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.



Pivotal Phase 3 VISION study of ¹⁷⁷Lu-PSMA-617 on track to read out in H2 2020

VISION study design



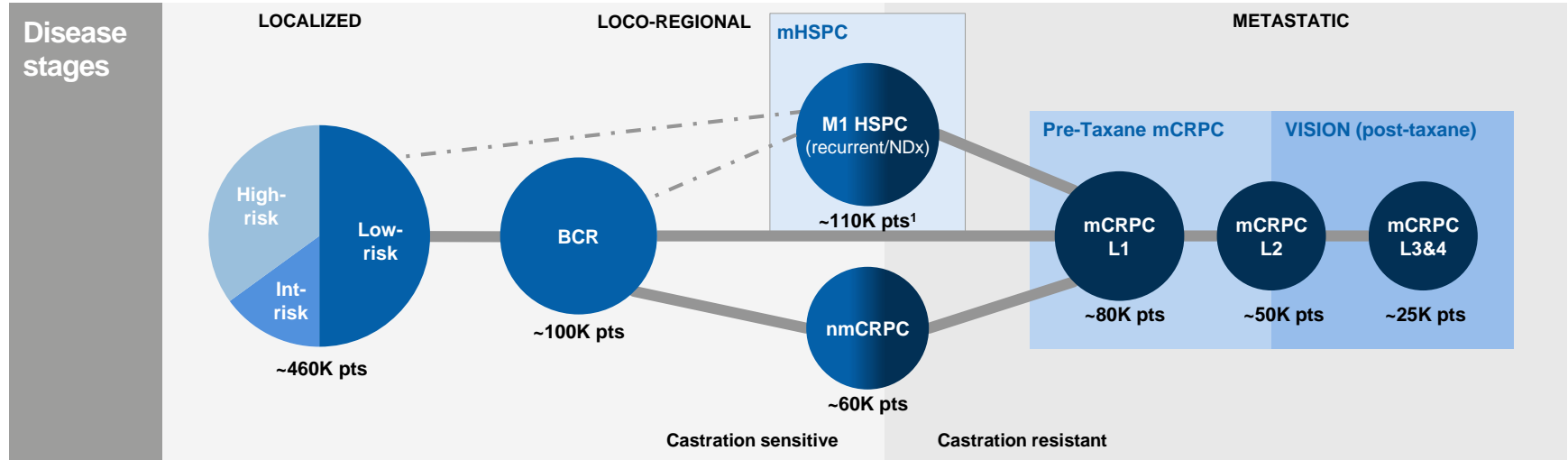
Important differences vs. TheraP study

	TheraP	VISION
Comparator	Head-to-head vs. cabazitaxel	Versus best standard of care (excluding cabazitaxel)
Patient population	Eligible for cabazitaxel and not FDG+/PSMA-; one prior taxane regimen	One or two prior taxane regimens, not currently candidate for cabazitaxel; not CT+/PSMA-
Primary endpoints	PSA response	rPFS & OS

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)

Sources: J Clin Oncol. 2016 Apr 20; 34(12): 1402–1418; Aggarwal, Rahul R., et al. "Emerging Categories of Disease in Advanced Prostate Cancer and Their Therapeutic Implications." 15 June 2017; Kantar Health CancerMPact: US, EU5 & JP, Incidence 2020, w/ tx rate applied. 1. Incl 1L & 2L mHSPC



Q&A