



# BIOPHARMA PIPELINE UPDATE

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# Vision 2018 – Delivering on promises

**1**  
**Enforce stability  
in existing  
businesses**

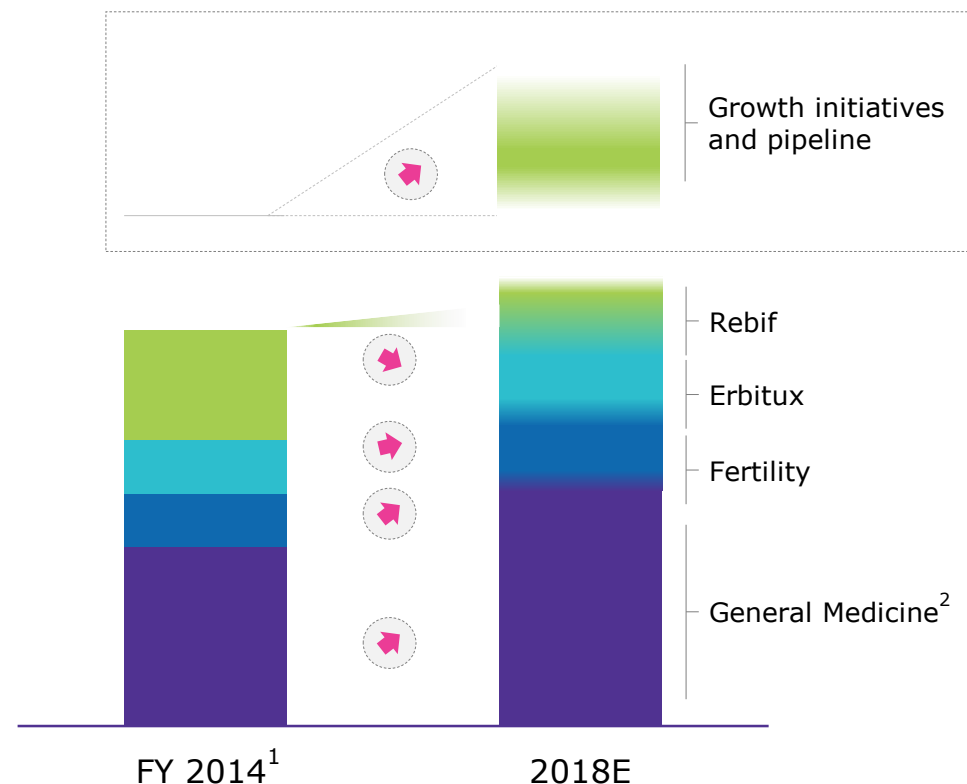
## Maximize existing franchises

- ▶ Market positioning
- ▶ Regions / emerging markets capabilities
- ▶ Life-cycle management including superior devices

**2**  
**Create  
sustained  
growth**

## Generate new revenue streams

- ▶ Deliver on R&D pipeline
- ▶ Payor-centric devices strategy
- ▶ Expand regional portfolio through in-licensing

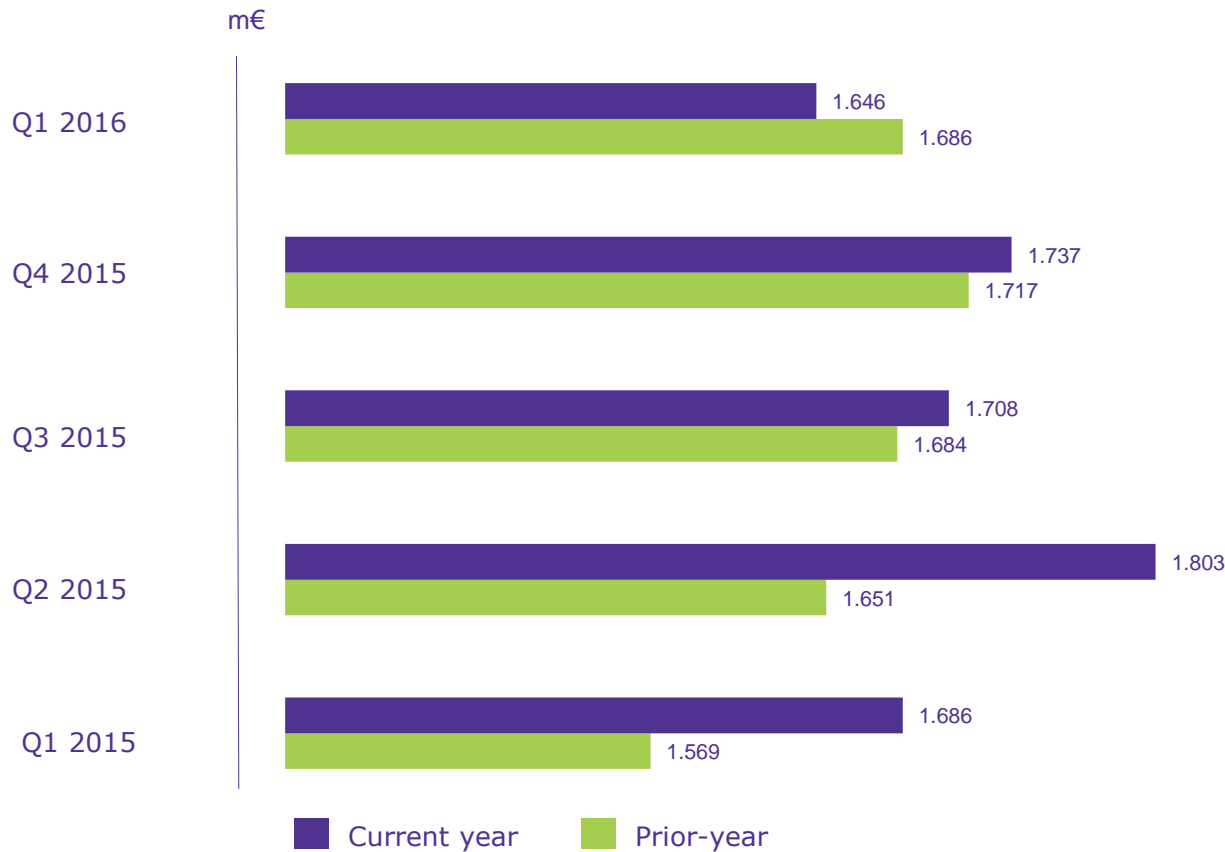


<sup>1</sup> Adapted to new Healthcare business sector to include Consumer Health

<sup>2</sup> Including Consumer Health, Cardiometabolic Care, Endocrinology, General Medicine and Others

# Existing product portfolio delivers stable to slight organic growth

## Sales



## Org. growth rate

## Product portfolio

**ERBITUX®**  
CETUXIMAB

Consumer Health

**Rebif®**

**GONAL-F®** **Pergoveris®**  
(hullitropin alfa and lutropin alfa for injection)

**VIDREL®** **Luveris®** **Cetrotide®**



**Glucophage®**

**Concor®**

**Euthyrox®**

# Our pipeline (focus today)

## Phase I

**Tepotinib**  
c-Met kinase inhibitor  
Solid tumors

**M2698**  
p70S6K & Akt inhibitor  
Solid tumors

**M3814**  
DNA-PK inhibitor  
Solid tumors

**Beigene-283**  
BRAF inhibitor  
Solid tumors

**Avelumab<sup>1</sup>**  
Anti-PD-L1 mAb  
Solid tumors

**M9241 (NHS-IL12)<sup>2</sup>**  
Cancer immunotherapy  
Solid tumors

**M7824**  
Bifunctional immunotherapy  
Solid tumors

**M1095 (ALX-0761)**  
Anti-IL-17 A/F nanobody  
Psoriasis

**M2951**  
BTK inhibitor  
Systemic lupus erythematosus

## Phase II

**M2736 (ATX-MS-1467)**  
Immune tolerizing agent  
Multiple sclerosis

**Tepotinib**  
c-Met kinase inhibitor  
Non-small cell lung cancer

**Tepotinib**  
c-Met kinase inhibitor  
Hepatocellular cancer

**Avelumab<sup>1</sup>**  
Anti-PD-L1 mAb  
Merkel cell carcinoma 2L

**Sprifermin**  
Fibroblast growth factor 18  
Osteoarthritis

**Atacicept**  
Anti-Blys/anti-APRIL fusion protein  
Systemic lupus erythematosus

## Phase III

**Avelumab<sup>1</sup> - Anti-PD-L1 mAb**  
Non-small cell lung cancer 1L<sup>3</sup>

**Avelumab<sup>1</sup> - Anti-PD-L1 mAb**  
Non-small cell lung cancer 2L<sup>4</sup>

**Avelumab<sup>1</sup> - Anti-PD-L1 mAb**  
Gastric cancer 1L<sup>3</sup>

**Avelumab<sup>1</sup> - Anti-PD-L1 mAb**  
Gastric cancer 3L<sup>5</sup>

**Avelumab<sup>1</sup> - Anti-PD-L1 mAb**  
Bladder cancer 1L<sup>3</sup>

**Avelumab<sup>1</sup> - Anti-PD-L1 mAb**  
Ovarian cancer platinum resistant/refractory

**Avelumab<sup>1</sup> - Anti-PD-L1 mAb**  
Renal cell carcinoma 1L<sup>3</sup>

**MSB11022**  
Proposed biosimilar of Adalimumab  
Chronic Plaque Psoriasis

## Pending Submission/Review

**Cladribine Tablets – Lymphocyte targeting agent**  
Relapsing-remitting multiple sclerosis

- Neurodegenerative Diseases
- Oncology
- Immunology
- Immuno-Oncology
- Biosimilars

Note: timelines are event-driven and may change

Pipeline products are under clinical investigation and have not been proven to be safe and effective. There is no guarantee any product will be approved in the sought-after indication.

<sup>1</sup>avelumab is the proposed nonproprietary name for the anti-PD-L1 monoclonal antibody (MSB0010718C)

<sup>2</sup>Sponsored by the National Cancer Institute (USA)

<sup>3</sup>First Line treatment

<sup>4</sup>Second Line treatment

<sup>5</sup>Third Line treatment

# Cladribine tablets – MAA submission to EMA planned for H1 2016

## Background

- Targets lymphocytes (both B and T cells), integral to MS pathogenesis
- Two Phase III and one Phase IIIb extension studies conducted in RRMS and early MS<sup>1,2,3</sup>; Phase II study in patients failing IFN beta therapy<sup>5</sup>
- Substantial new efficacy & safety characterization including data from long-term follow up (>10,000 patient-years)
- Most recent analyses provide relevant information on benefit/risk profile of cladribine tablets in RRMS:
  - ARR reduction (58%)
  - Risk of disability progression (33% reduction)
  - Relative reduction in mean number of lesion (86% reduction in T1 gadolinium-enhanced lesions)
  - 47% of patients experience NEDA over 2 years<sup>4</sup>

## Potential for differentiation

- We aim to address significant unmet needs for agents delivering high efficacy with favorable safety profile in a convenient dosing regimen
- Administered orally (tablet formulation)
- Extremely short treatment courses (8–10 days per year) leading to long-term efficacy<sup>1</sup>

Note: timelines are event-driven and may change

EMA = European Medicines Agency; ARR = Annualized Relapse Rate; MAA = Marketing Authorization Application; MS = multiple sclerosis; NEDA = no evidence of disease activity; RRMS = relapsing-remitting multiple sclerosis. <sup>1</sup> Giovannoni G et al. *New Engl J Med* 2010;362:416–26; <sup>2</sup> Giovannoni G et al. 65th annual meeting of the American Academy of Neurology 2013. P07.119. <sup>3</sup> Leist TP et al. *Lancet Neurol* 2014;13:257–67. <sup>4</sup> Giovannoni G et al. *Lancet Neurol*. 2011;10:329–37. <sup>5</sup> Montalban X et al. 65th annual meeting of the American Academy of Neurology 2013. P07.099.

# MCC 2L: Clinical results support avelumab as potential therapeutic option – planned to apply for marketing authorization in H2 2016

## Encouraging response rates<sup>1</sup>

- ORR: 31.8%
  - 9.1% complete response
  - 22.7% partial response
  - Rapid (78.6% responding within 7 weeks of treatment)
  - Durable (82.1% still responding at time of analysis)
- 6-mo OS: 69% (median OS: 11.3 months)
- 6-mo PFS rate: 40%
- Manageable safety profile; no unexpected safety signals



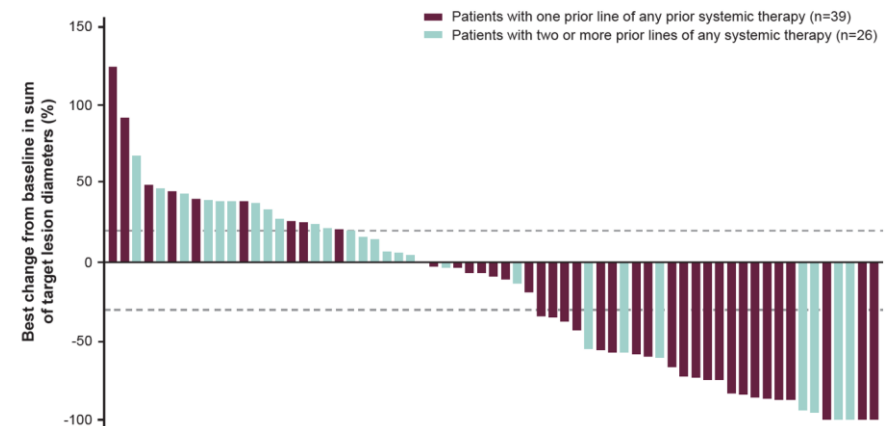
Note: timelines are event-driven and may change

Note: avelumab is the proposed nonproprietary name for the anti-PD-L1 monoclonal antibody (MSB0010718C)

<sup>1</sup>Avelumab (MSB0010718C; anti-PD-L1) in patients with metastatic Merkel cell carcinoma previously treated with chemotherapy: results of the phase 2 JAVELIN Merkel 200 trial\* / Oral Presentation at the 52nd ASCO Annual Meeting, June 3-7, 2016; Chicago, Illinois. Abstract No. 9508; Howard Kaufman et al.

## Potential for differentiation

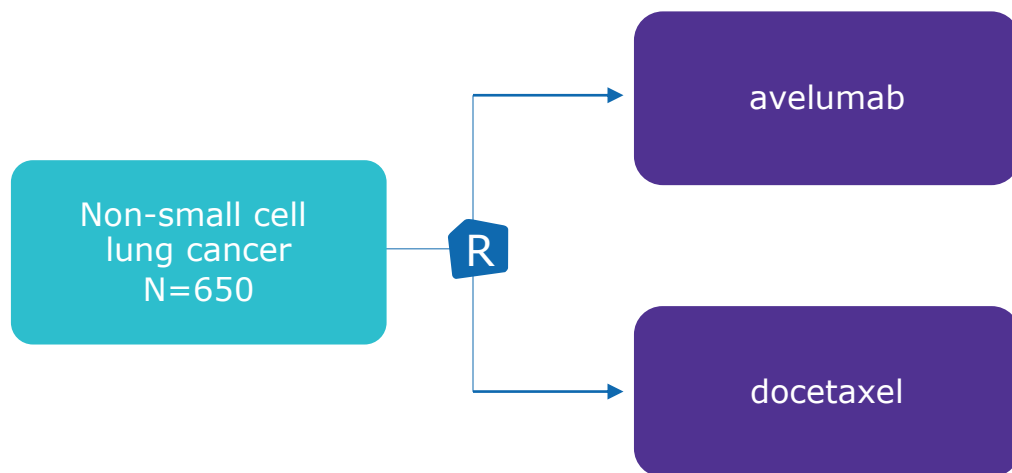
- Largest international multicenter, open-label study of anti-PD-L1/PD-1 reported in this patient population (88 patients) – Responses observed in large number of patients
- Improved response rates observed when used earlier, i.e. fewer lines of prior chemotherapy appeared to be associated with better response to avelumab in MCC 2L and beyond
  - ORR of 40.4% for patients with one prior systematic treatment
  - ORR of 19.4% for patients with two and more prior treatments





# Execution of Phase III trials progressing as planned (example NSCLC<sup>1</sup> 2L)

## Study design



## Status and outlook

- High unmet medical need
- Open-label, multicenter trial in subjects with NSCLC that has progressed after a platinum-containing doublet
- Primary endpoint: Overall survival in patients with PD-L1+ stage IIIb/IV NSCLC
- Study recruitment across 290 sites in over 30 countries – 70% recruitment completed
- Estimated primary completion H2 2017 (final data collection date for primary outcome measure)

Note: timelines are event-driven and may change

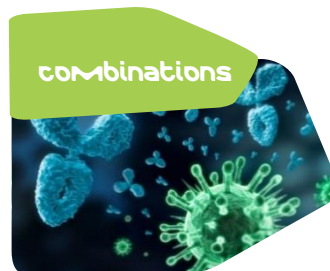
Note: avelumab is the proposed nonproprietary name for the anti-PD-L1 monoclonal antibody (MSB0010718C)

<sup>1</sup> Non Small Cell Lung Cancer

## Going forward, avelumab combinations will drive differentiation strategy



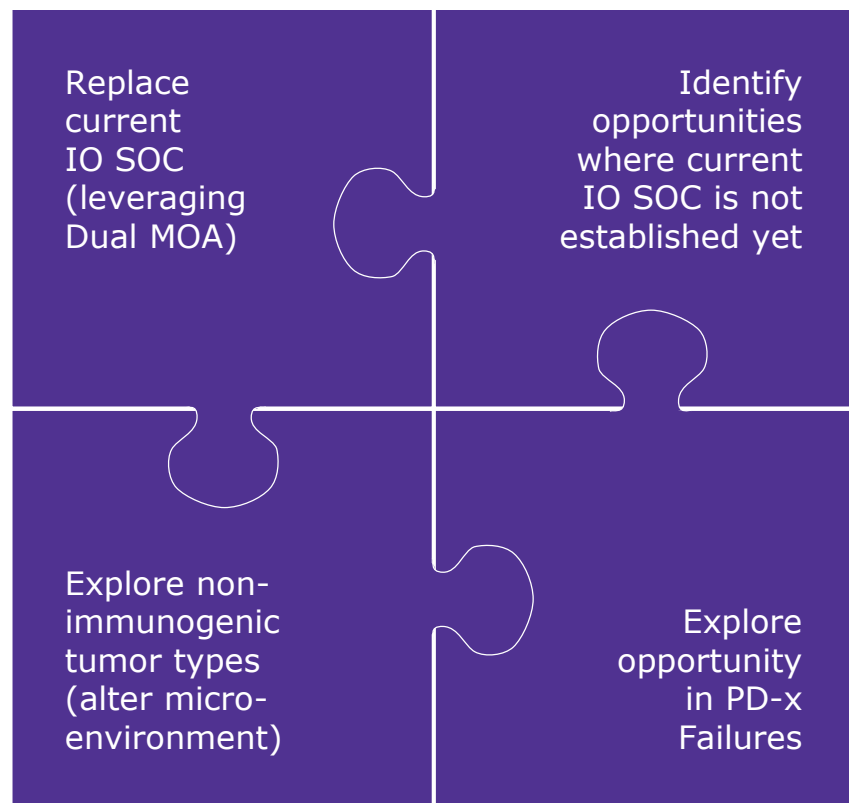
- Phase II 2L MCC (BTD, ODD and FTD)
- Phase III 1L and 2L Plat res/ref ovarian
- Phase III 1L MN and 3L gastric
- Phase III 1L and 2L NSCLC
- Phase III 1L MN bladder
- Phase I Hodgkins Lymphoma
- Multiple other tumor types



- Phase III, RCC 1L (avelumab + Inlyta)
- Phase Ib/II, NSCLC 1L ALK+ (avelumab + Xalkori/Lorlatinib)
- Phase I/II (avelumab + 4-1BB)
- Phase Ib/II, ovarian (avelumab + Entinostat; Syndax collaboration)
- Phase I/Ib, ovarian (avelumab + VS-6063; Verastem collaboration)
- Further combination trials under consideration

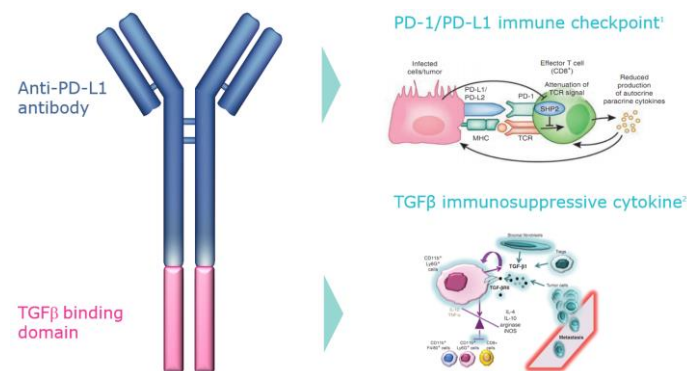
# PD-L1–TGF-beta indicates potential to move beyond checkpoint inhibitors

## Four focus areas for exploration



## Status and next steps

- Novel, first-in-class bifunctional immunotherapy
- Bifunctional mode should result in broader application vs. respective mono-functional agents
- Great potential when combined with Standard of Care, immunotherapy and internal pipeline drug candidates
- Dose level finding of Phase I completed
- Expansion into Ib cohorts expected for Q3 2016

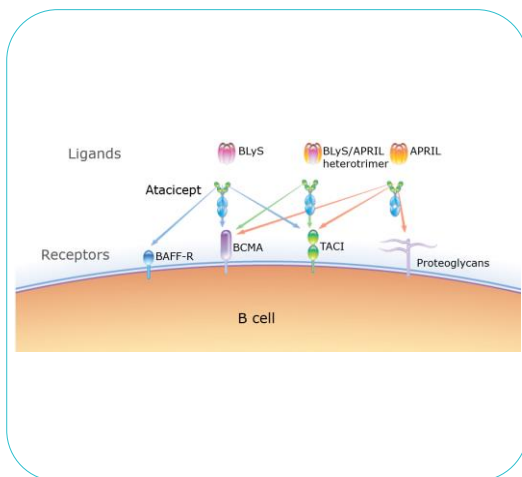


Note: timelines are event-driven and may change

<sup>1</sup> Okazaki T et al., Nature Immunology, 2013; <sup>2</sup> Souza-Fonseca-Guimaraes F and Smyth M, Cancer Discovery, 2013

## Update on selected assets (1/2)

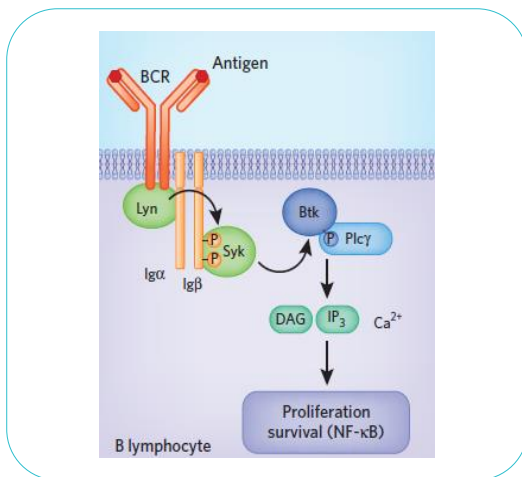
### Atacicept



- Binds to receptors of two cytokines regulating maturation, function, and survival of B cells (B-lymphocyte stimulator (BlyS) & a proliferation-inducing ligand (APRIL))
- ADDRESS II (Ph IIb) in SLE patients aiming to show reduction in disease activity – 279 patients enrolled
- 24-week, randomized, double-blind, placebo-controlled Subcutaneous injection, once-a-week dosing
- Primary outcome: Percentage of patients with SLE responder index (SRI) response at week 24 compared to screening

Phase III decision expected in H2 2016

### BTK

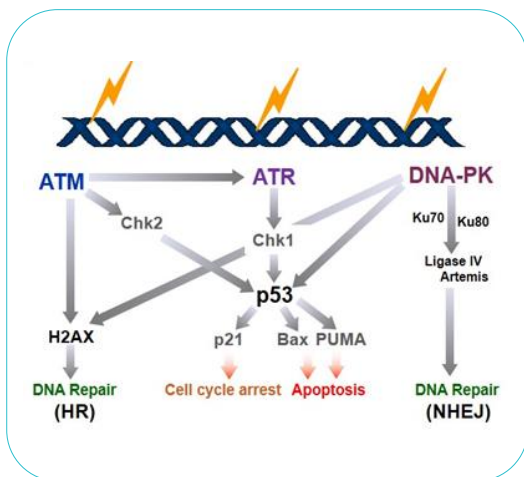


- Suppress autoantibody-producing cells
- Preclinical research suggests therapeutic use in certain autoimmune diseases
- High and differentiated efficacy in preclinical models; promising kinase selectivity profile
- Aim to achieve best in class through minimization of off-target effects
- 2<sup>nd</sup> dose level of Phase I completed
- Partnering opportunities under consideration

Three phase II trials expected to be started until end of 2016 (e.g. RA, SLE)

## Update on selected assets (2/2)

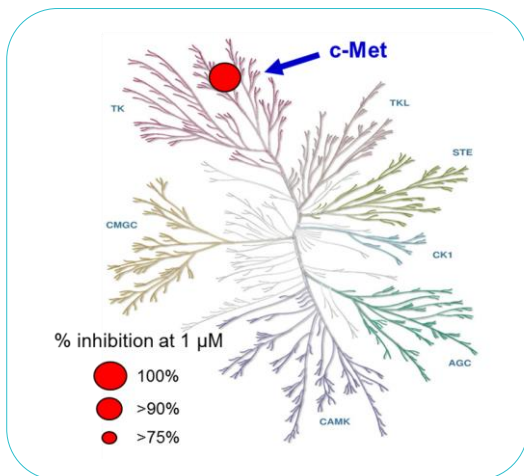
### DNA-PK inhibitor



- M3814 is a selective and potent inhibitor of DNA-PK, a kinase mediating DNA double strand break repair<sup>1</sup>
- Preclinical PoC showing complete responses and/or increased PFS in combination with radiotherapy in several xenograft models (SCCHN, NSCLC, CRC, PaCa) and strong pre-clinical combination data with SoC chemotherapies
- Two Phase Ia trials ongoing: FIM (monotherapy): 5<sup>th</sup> dose level completed, MTD not yet reached; RT combination: recruitment ongoing

Analysis of Phase I data for RT combination expected in H2 2017

### Tepotinib



- Highly selective small molecule c-Met inhibitor
- Active in ligand-dependent and ligand-independent tumor models
- Biomarker-driven approach for patient selection
- Preliminary data show encouraging signs of anti-tumor activity in c-Met positive patients in NSCLC and HCC<sup>2,3</sup>
- Phase II trials in progress in NSCLC and HCC

Analysis of Phase II data for HCC and NSCLC expected in H1 2018

Note: timelines are event-driven and may change

<sup>1</sup> Graphics only illustrative; Acronyms: SCCHN = Squamous Cell Carcinoma of the Head and Neck, NSCLC = Non-small Cell Lung Cancer, CRC = Colorectal Cancer, PaCa = Pancreatic Cancer, HCC = Hepatocellular Cancer, PFS = Progression-free Survival, SoC = Standard of Care, FIM = First-in-Man, RT = radiotherapy, CT = chemotherapy, MTD = maximum tolerated dose; <sup>2</sup>Qin, ECC 2015, (3) Kim et al, IASCL-WCLC 2015

## Outlook – Two submissions planned in 2016

Cladribine	Expected submission	H1 2016
Avelumab (MCC 2L)	Expected submission	H2 2016
Atacicept	Phase III decision	H2 2016
BTK	Start three Phase II trials	H2 2016
PD-L1-TGF-beta	Signals of activity in cohorts	H1 2017
DNA-PK inhibitor	Analysis of Phase I data	H2 2017
Tepotinib	Analysis of Phase II data	H1 2018

Note: timelines are event-driven and may change

Note: avelumab is the proposed nonproprietary name for the anti-PD-L1 monoclonal antibody (MSB0010718C)

## Healthcare is well set for future growth

Stable existing business

Business and market specific initiatives in place to maximize existing business franchises

Strong R&D pipeline

Diversified but focused pipeline with high quality assets in the areas Immuno-Oncology, Oncology and Immunology healthily spread across all clinical phases

Successful collaborations

Proven success in partnering through joint investments and collaborations – maximizing potential of assets in competitive space

Promising late stage progress

Two expected submissions in 2016 may potentially result in product launches in 2017

Disciplined execution

Systematic pipeline review and timely decision making allow efficient resource and budget allocation



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