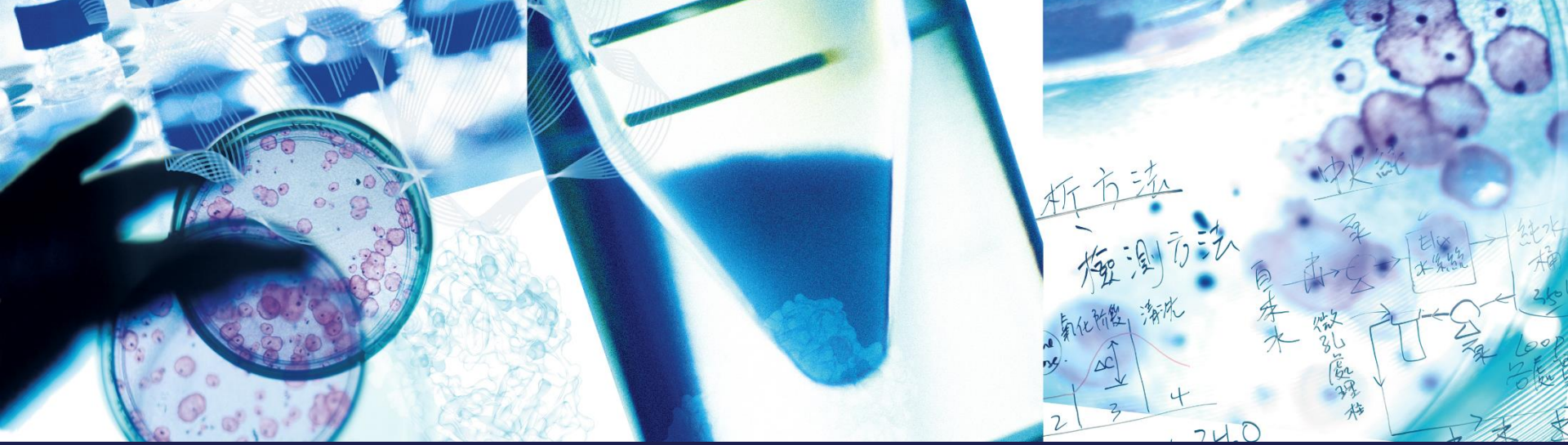


Merck KGaA, Darmstadt, Germany
Healthcare – R&D Update Call

Marcus Kuhnert, CFO

Luciano Rossetti di Valdalabero, Global Head of Research & Development

Andrew Schiermeier, Head of Global Oncology & General Manager Immuno-Oncology Alliance

1 October 2015

Disclaimer

Publication of Merck KGaA, Darmstadt, Germany. In the United States and Canada the subsidiaries of Merck KGaA, Darmstadt, Germany operate under the umbrella brand EMD.

To reflect such fact and to avoid any misconception of the reader of the publication certain logos, terms and business descriptions of the publication have been substituted or additional descriptions have been added. This version of the publication, therefore, slightly deviates from the otherwise identical version of the publication provided outside the United States and Canada.

Disclaimer

Merck KGaA
Darmstadt · Germany

Remarks
All comparative figures relate to the corresponding last year's period.

Important information
This presentation does not constitute an offer of securities for sale or a solicitation of an offer to purchase securities in the United States. The shares referred to herein have not been and will not be registered under the U.S. Securities Act of 1933, as amended (the "Securities Act"), and may not be offered or sold in the United States absent registration under the Securities Act or an available exemption from such registration.
Clinical candidates and early-stage products are currently under clinical investigation and have not been approved for use in the United States (US), Europe, Canada or elsewhere. The clinical candidates have not been proven to be safe or effective, and any claims of safety and effectiveness can be made only after regulatory review of the data and approval of the labeled claims.

Note regarding forward-looking statements
The information in this document may contain "forward-looking statements". Forward-looking statements may be identified by words such as "expects", "anticipates", "intends", "plans", "believes", "seeks", "estimates", "will" or words of similar meaning and include, but are not limited to, statements about the expected future business of Merck KGaA, Darmstadt, Germany. These statements are based on the current expectations of management of Merck KGaA, Darmstadt, Germany and E. Merck KG, Darmstadt, Germany and are inherently subject to uncertainties and changes in circumstances. Among the factors that could cause actual results to differ materially from those described in the forward-looking statements are changes in global, political, economic, business, competitive, market and regulatory forces. Merck KGaA, Darmstadt, Germany and E. Merck KG, Darmstadt, Germany do not undertake any obligation to update the content of this presentation and forward-looking statements to reflect actual results, or any change in events, conditions, assumptions or other factors.

Merck KGaA
Darmstadt · Germany

Agenda

Healthcare – Strategy recap

Progress in the R&D pipeline

Immuno-Oncology and avelumab

Executive Summary

Delivering on promises from Capital Markets Day in September 2014

Merck KGaA
Darmstadt · Germany

Capital Markets Day 2014

Vision 2018

1. ENFORCE STABILITY IN EXISTING BUSINESSES

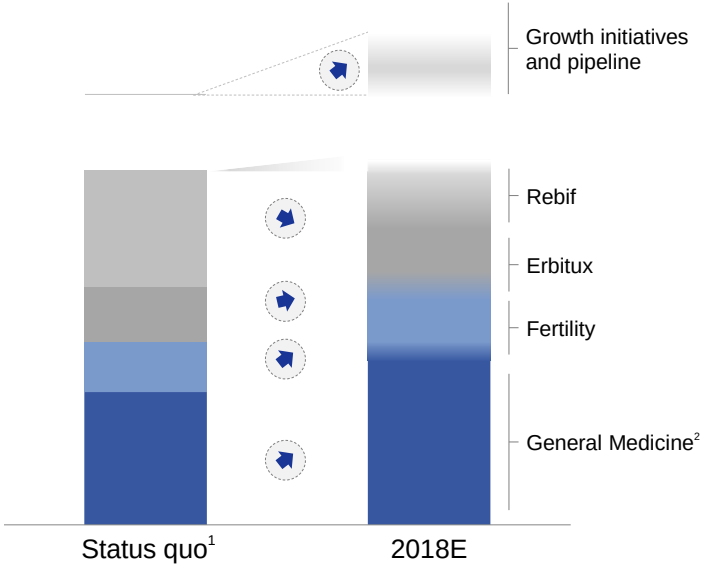
Maximize existing franchises

- 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



[1]FY 2013 Biopharmaceuticals; excludes Allergopharma and Biosimilars; [2]including Cardiometabolic Care, Endocrinology, General Medicine and Others

Maximize existing franchises – delivering stable to slightly growing top-line

Merck KGaA
Darmstadt · Germany

ERBITUX CETUXIMAB

- Taken back full promotional responsibility in Japan
- Liquid biomarker RAS test with Sysmex introduced in testing centre in Spain

Consumer Health

- Ongoing 3x3 strategy implementation
- Strengthened sales activities deliver above-market organic sales growth

Rebif

- Development of Cladribine supports multiple sclerosis franchise
- Restructuring Rebif commercialization in US for post Pfizer era (end Dec 2015)
- Taken further price increases in US (most recent Sept 1, 2015)

GONAL-f, Pergoveris, OVIDREL, Luveris, Cetrotide

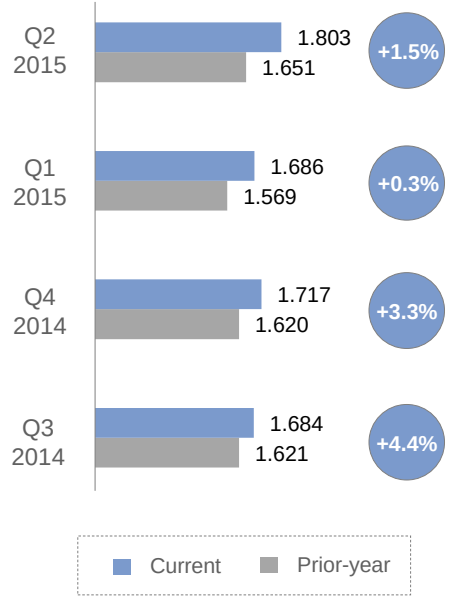
- Enhanced offering of fertility technologies to support established franchise
- Examples: Eeva test, collaboration Genea Biomedx (IVF[1] lab technologies)

- Launch of RebiSmart and MSdialog in 22 additional countries
- Ongoing development of go-to-market model for chronic treatment solution platform

Glucophage, Concor, KUVAN, Euthyrox

- Successful repatriation of businesses (e.g. Glucophage, Thyroids in Russia)
- Lupin partnership to expand portfolio in emerging markets
- Invested €80m in new pharmaceutical manufacturing facility in China

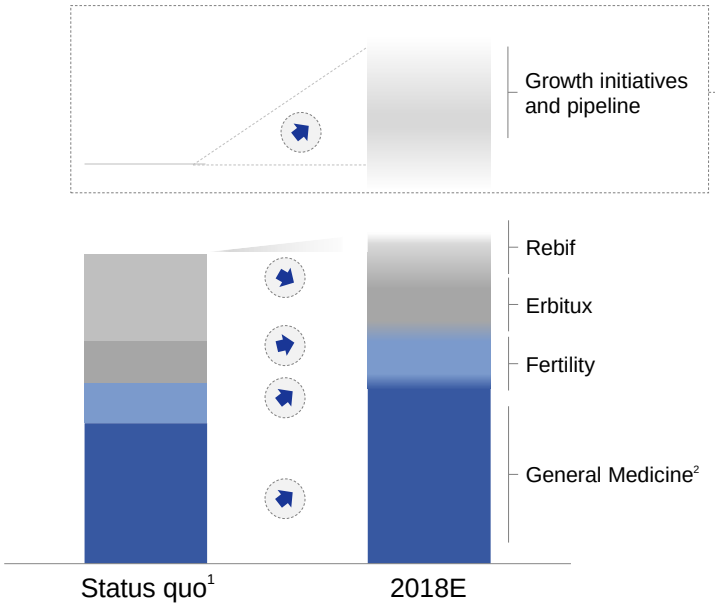
Stable to slight organic growth[2]



[1]IVF = in-vitro fertilization ; [2]Healthcare net sales and organic sales growth rates

New revenue streams from pipeline projects and additional growth initiatives

Merck KGaA
Darmstadt · Germany



Oncology market without I-Onc

Growth[3]

+12%

~ €71.5 bn market 2014[3]

~ €139.4 bn market 2020[3]

Immunology market[4]

Growth[3]

+16%

~ €5.4 bn market 2014[3]

~ €13.5 bn market 2020[3]

Immuno-Oncology market[5]

Growth[3]

+63%

~ €1 bn market 2014[3]

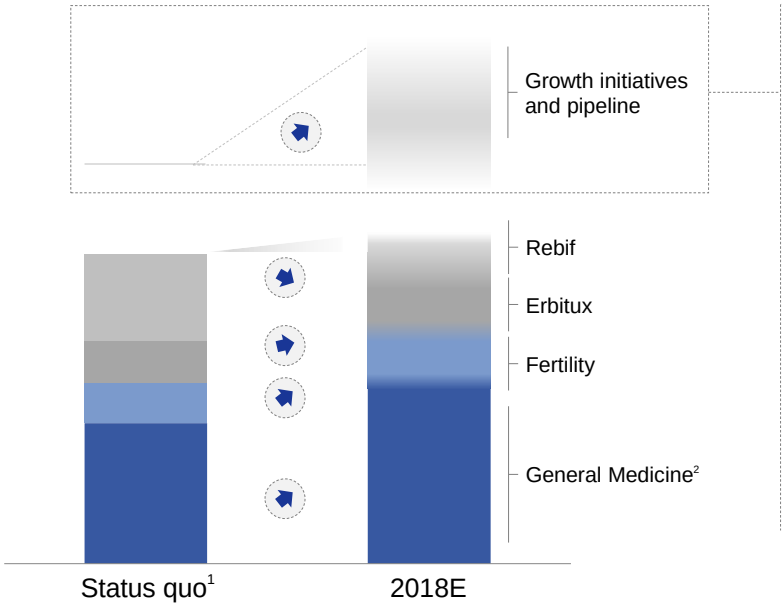
~ €19.9 bn market 2020[3]

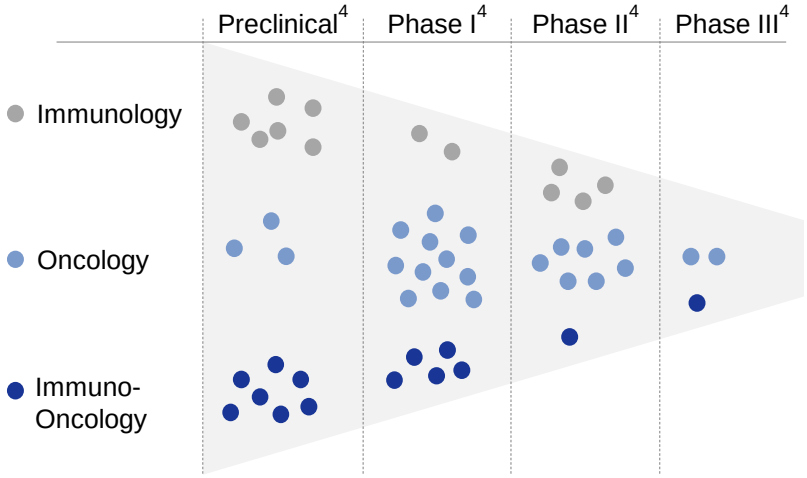
Healthcare investments focused on three attractive market segments

[1]FY 2014; adapted to new Healthcare business sector to include Consumer Health; [2]including Consumer Health, Cardiometabolic Care, Endocrinology, General Medicine and Others; [3]Data for global market 2014, CAGR for 2014-2020; Source: Sales data according to EvaluatePharma® , accessed August 2015; [4]Immunosuppressants Therapeutic Class as defined by EvaluatePharma, excluding ustekinumab; [5]Immuno-oncology (PD-L1, PD-1, CTLA-4, OX-40, IDO, CAR T cells)

New revenue streams from pipeline projects and additional growth initiatives

Merck KGaA
Darmstadt · Germany





Broad and well structured pipeline with promising early-stage compounds[4] in focus areas

[1]FY 2014; adapted to new Healthcare business sector to include Consumer Health; [2]including Consumer Health, Cardiometabolic Care, Endocrinology, General Medicine and Others;
[4]Number of trials initiated/ongoing as of September 2015

Agenda

Healthcare – Strategy recap

Progress in the R&D pipeline

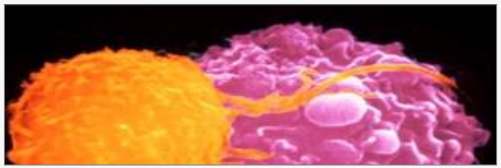
Immuno-Oncology and avelumab

Executive Summary

Focused approach to scientific innovation drives differentiation

Merck KGaA
Darmstadt · Germany

Oncology



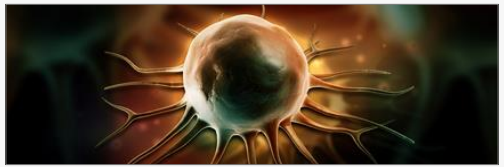
Ambition

- Leverage presence in oncology to deliver the best benefit possible to patients
- Build robust oncology presence across critical innovation platforms

Key projects

- **evofosfamide**
- tepotinib
- DNA-PK inhibitor

Immuno-Oncology



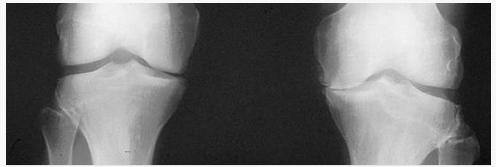
Ambition

- Develop new therapies that will help patients fight difficult-to-treat cancers
- Transform cancer into a chronic disease

Key projects

- **avelumab**
- Intrexon CAR-T
- M7824 Bi-functional immunotherapy

Immunology & Neurology



Ambition

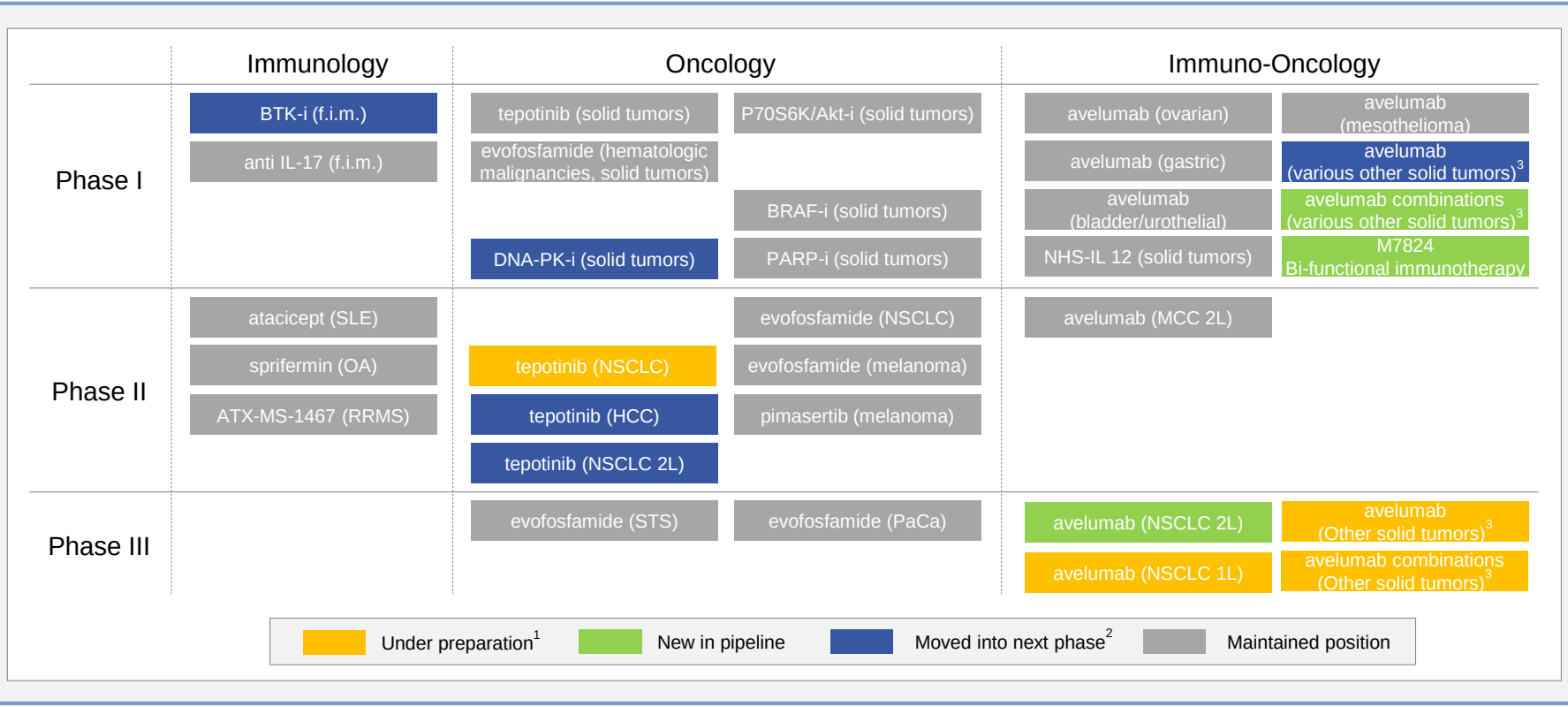
- Become a leader in Lupus with a best-in-disease therapy approach
- Expand immunology presence in other indications, such as multiple sclerosis

Key projects

- **Atacicept**
- BTK inhibitor

Revamped and focused R&D pipeline shows further progress

Merck KGaA
Darmstadt · Germany



As of 1 October 2015; [1]Under preparation for this phase; [2]Since Capital Markets Day in September 2014; [3]See p. 21 for more detailed development program;
Acronyms: f.i.m. = First in man, SLE = Systemic lupus erythematosus, OA = Osteoarthritis, RRMS = Relapse remitting multiple sclerosis, NSCLC = Non-small cell lung cancer, HCC = hepatocellular carcinoma, STS = soft-tissue carcinoma, PaCa = Pancreatic Cancer, MCC = Merkel cell carcinoma

Several pipeline compounds have advanced and will add to long-term momentum

Merck KGaA
Darmstadt · Germany

Avelumab

- Thought to block interaction of PD-L1 with known ligand PD-1
- May enable the activation of T-cells and the adaptive immune system
- Under investigation in more than 15 tumor types

Bi-functional immunotherapy – M7824

- Dual-acting fusion protein neutralizes two immuno-inhibitory pathways
- Expected to control tumor growth by restoring and enhancing anti-tumor immune responses

CAR-T*

- Innovative Chimeric Antigen Receptor T-cell (CAR-T) treatment that is thought to modulate the immune system's natural ability to fight tumors
- Potentially uniquely able to regulate gene expression with proprietary RheoSwitch platform

DNA-PK inhibitor - M3814

- Small molecule inhibitor of key enzyme in double strand break (DSB) repair pathway

Tepotinib/ C-Met Inhibitor

- Investigational small molecule inhibitor of the c-Met receptor tyrosine kinase

BTK inhibitor

- Selective inhibitor of bruton tyrosine kinase (BTK); important in the development of immune cells

*Preclinical phase – alliance with Intrexon

Tepotinib – leveraging biomarker science to achieve growth inhibition and regression of tumors

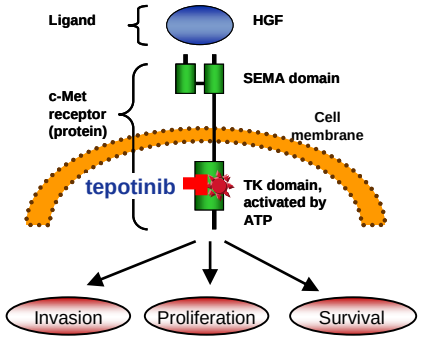
Merck KGaA
Darmstadt · Germany

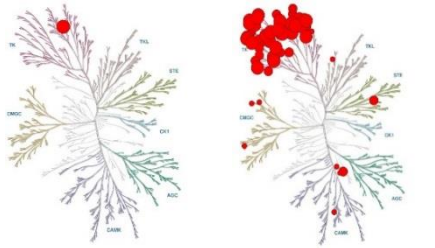
Potential mechanism

- c-Met receptor tyrosine kinase is thought to control key signaling pathway in cancer cells
- Pathway frequently deregulated in human cancer at ligand (HGF) and receptor (c-Met) levels
- In pre-clinical models, tepotinib as small molecule kinase inhibitor of c-Met causes growth inhibition and regression of tumors

Potential for differentiation

- Highly selective and potent kinase inhibitor – only c-Met is completely inhibited at clinically relevant doses
- Biomarker-driven approach for patient selection: only c-Met positive will be enrolled into tepotinib trials
- c-Met amplification and c-Met and HGF (hepatocyte growth factor) overexpression preclinically validated as predictive biomarker





tepotinib[2] alternative inhibitors[2]

Highlights & milestones

- Initiated phase II enrollment in Asia for HCC and EGFR mutant NSCLC, and for HCC in Europe – H1 2015
- Preliminary data show encouraging signs of anti-tumor activity in c-Met positive patients in NSCLC and HCC[3, 4]
- Phase I first-in-man trial: 76% of patients had no drug-related adverse events >Grade 1[5]

Timelines[1]

- Phase II: NSCLC 2L: final analysis expected for end of 2017
- Phase II: HCC 1L , HCC 2L: interim analysis in H2 2016, and final analysis expected for H2 2017
- 2nd NSCLC trial under preparation for Phase II

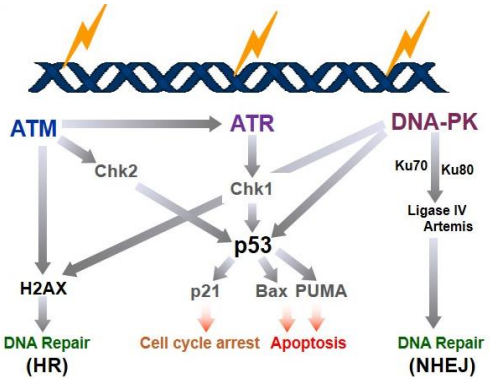
Graphics only illustrative; [1]Note that timelines are event-driven and may change; [2]Biopharmaceuticals data on file; [3]Falchook et al, ASCO 2014, J Clin Oncol 32:5s, 2014 (suppl; abstr 2521); [4]Kim et al, WCLC 2015; [5]Qin et al, CSCO 2014

DNA-PK inhibitor – targeting DNA double strand break (DSB) repair for cancer therapy

Merck KGaA
Darmstadt · Germany

Potential mechanism

- DNA-PK is a relevant enzyme in an important DSB repair pathway
- DNA-PK inhibitor M3814 is thought to delay DNA repair of DSB and may potentiate the antitumor effect of radiotherapy
- M3814 may also have activity as single agent in cancers with dysfunctional DNA repair pathways



Potential for differentiation

- Potential for First-in-Class orally administered selective DNA-PK inhibitor
- Potentially enhances the efficacy of many commonly used DNA damaging agents, such as radiotherapy and chemotherapies
- Strong preclinical proof-of-concept showing complete responses and/or increased progression-free survival in combination with radiotherapy in several xenograft models (SCCHN, NSCLC, CRC, PaCa)

Highlights & milestones

- 100% cure rate in a head & neck cancer model in combination with radiotherapy in a clinically relevant setting (5x2 Gy/week for 6 weeks)
- Combination with radiotherapy may open a broad range of applications
- First in man, Phase Ia monotherapy trial: 3rd dose level completed without DLTs, 4th dose level fully recruited
- Phase Ia dose escalation trial in combination with radiotherapy open for recruitment

Timelines*

- First patient cohort in radiotherapy combination trial (Phase I) to be recruited within next 1-2 quarters
- Phase Ib expansion cohorts: Solid tumors, CLL: First patient in H2 2016; Key data / statistics expected for H2 2017

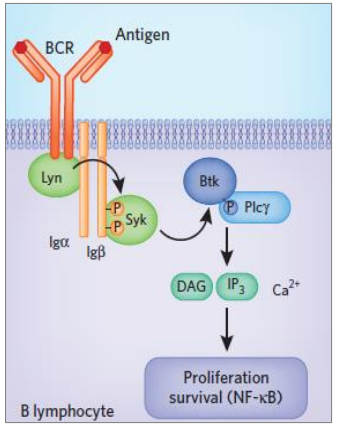
Graphics only illustrative; Acronyms: SCCHN = Squamous Cell Carcinoma of the Head and Neck, CRC = Colorectal Cancer, CLL = Chronic Lymphocytic Leukemia, DLT = dose-limiting toxicity
*Note that timelines are event-driven and may change

BTK inhibitor – selective inhibitor

Merck KGaA
Darmstadt · Germany

Potential mechanism

- BTK is expressed by multiple cell types, including B lymphocytes and macrophages
- BTK may play an important role in B cell development, differentiation, activation, class-switching, proliferation, survival and cytokine release
- BTK-i is thought to suppress autoantibody-producing cells in RA and SLE; preclinical research suggests this may be therapeutically useful in certain autoimmune diseases



Potential for differentiation

- Highly differentiated and selective inhibitor
- BTK inhibitor demonstrates promising kinase selectivity profile
- Good cellular assay target profile for B and T cell interactions
- Aim to achieve best in class through minimization of off-target effects

Highlights & milestones

- BTK seems to prevent immune complex-mediated signalling and production of inflammatory cytokine in macrophages and glycoprotein VI signalling in platelets
- High and differentiated efficacy in preclinical models
- Second differentiated BTK molecule (M7583) moving into oncology clinical development in 2016

Timelines[1]

- Phase I (M2951), SAD/MAD/Food effect studies completed
- Phase Ib SLE start Oct 2015
- Phase IIa RA[2] start H1 2016

Graphics only illustrative; Acronyms; [1]Note that timelines are event-driven and may change; [2]RA = Rheumatoid Arthritis

Merck KGaA
Darmstadt · Germany

Agenda

Healthcare – Strategy recap

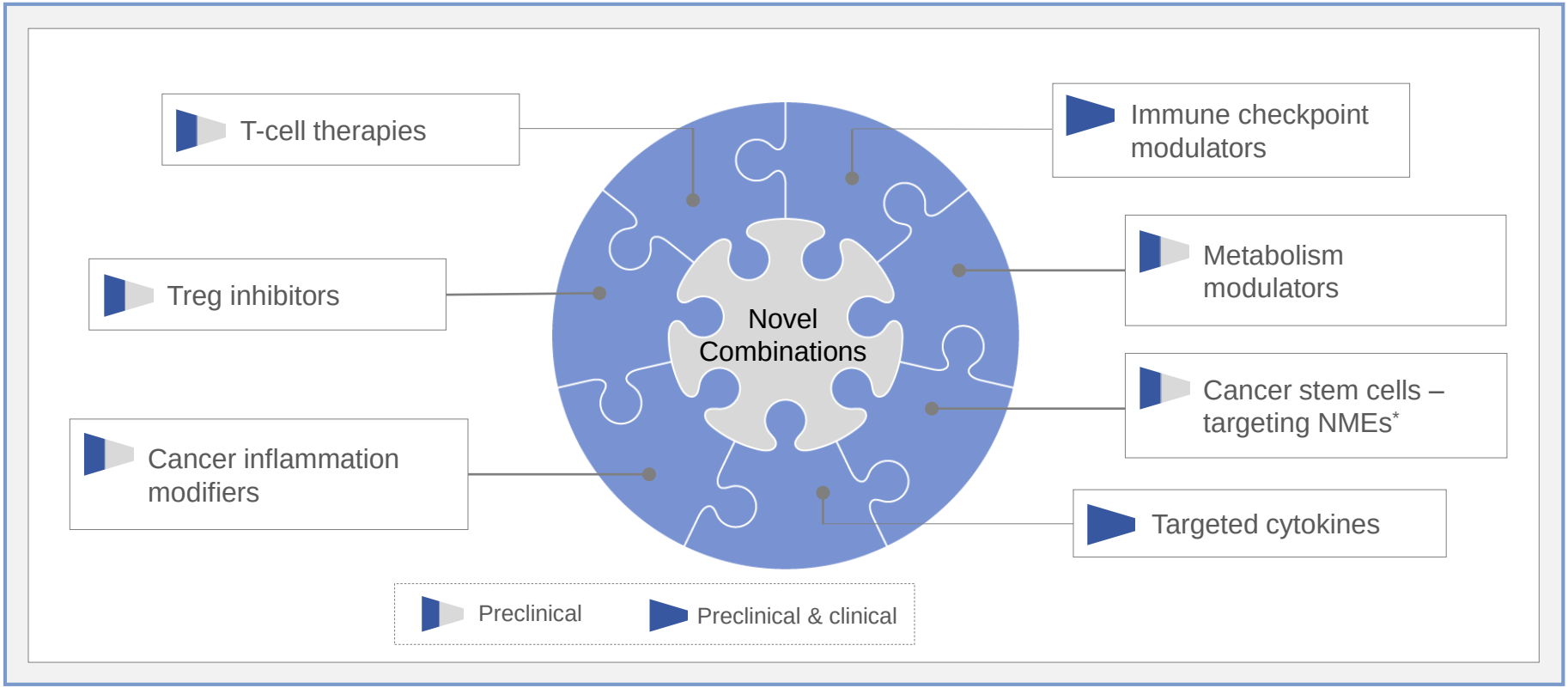
Progress in the R&D pipeline

Immuno-Oncology and avelumab

Executive Summary

Immuno-Oncology pipeline aims to deliver novel combinations from internal and external innovation

Merck KGaA
Darmstadt · Germany

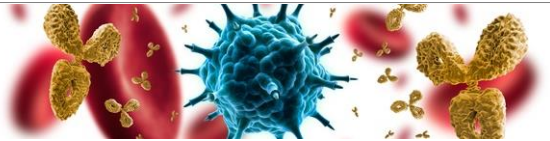


*NMEs = new molecular entities

M7824 – novel bi-functional immunotherapy

Merck KGaA
Darmstadt · Germany

M7824



Potential mechanism

- Novel, first-in-class bi-functional immunotherapy has potential to be a highly efficacious, enhanced therapy
- Dual-acting fusion protein designed to neutralize two immuno-inhibitory pathways
- Thought to control tumor growth by potentially restoring and enhancing anti-tumor immune responses

Potential for differentiation

- Preclinical research indicates enhanced anti-tumor activity, and treatment with bi-functional modulator leads to immunological memory
- 100% complete response as demonstrated in in vivo preclinical models[2]

Highlights & milestones

- Rapid progression through development cycle:
  - Moved from preclinical to First-in-Human within 11 months
  - Expansion cohorts expected to start in H2 2016

Timelines[1]

- Phase I: Solid tumors (September 2015)
- Key data: expected H2 2016

[1]Note that timelines are event-driven and may change; [2]Source: Biopharmaceuticals R&D

CAR-T – T-Cell therapies could be the next cornerstone of cancer immunotherapy

Merck KGaA
Darmstadt · Germany

CAR-T – Intrexon

Potential mechanism

- Chimeric Antigen Receptor T-cell (CAR-T) therapy harnesses a patient's own immune system to direct it specifically against tumor cells
- CAR-T cells are genetically engineered to recognize a specific antigen expressed on tumor cells and trigger immunological attack

Potential for differentiation

- Possibility to improve safety profile of CAR-Ts through switch that could activate/modulate T-cell expression (Intrexon's proprietary RheoSwitch platform)
- Opportunity to solid tumors
- Possible combination with avelumab or next-generation checkpoint inhibitors
- Current CAR-T treatments are unique to each patient; Intrexon therapy is engineered with potential to be infused back to universal, "off-the-shelf" treatment (i.e. allogeneic)

Highlights & milestones

- Considered as next cornerstone of cancer immunotherapy
- CAR T cells have shown clinical response rate with up to 91% complete remission in certain hematological indications (ALL)
- Technology has potential to address limitations of 1st/2nd generation gene and cell-based therapy

Timelines*

- 2016: Preclinical/clinical development to CAR-T cells safer based on existing design targeting hematological tumors
- 2017: Test next-gen CAR-T cells for efficacy in solid tumors

*Note that timelines are event-driven and may change

Avelumab – milestones and next steps

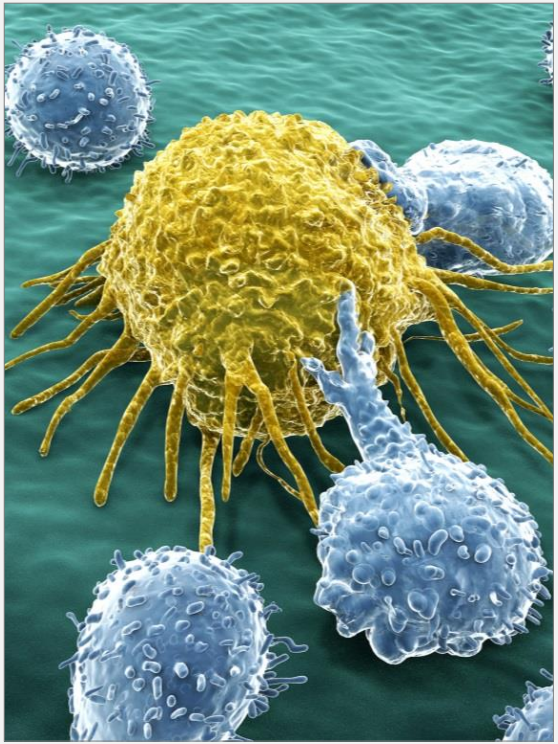
Merck KGaA
Darmstadt · Germany

Key milestones so far

- Development pipeline progressing rapidly; large range of potential combination candidates
- Orphan drug designation for MCC received in September 2015
- Preclinical testing on multiple combinations under way for completion by end-2015 at Merck KGaA, Darmstadt, Germany
- >1,000 patients treated as part of multicenter, dose-escalation and parallel-group dose-expansion phase I trial
- Promising clinical activity in several indications

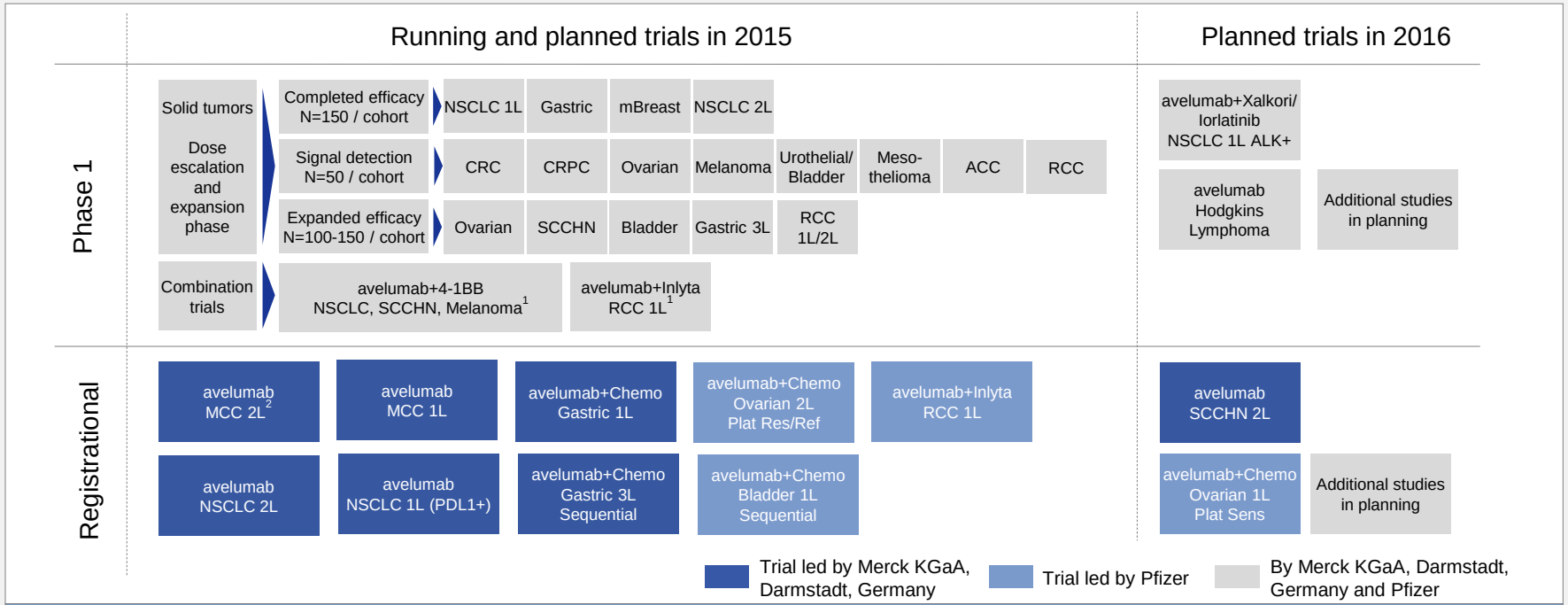
Next steps

- 2 registration trials under way, up to 5 additional Phase III studies to start by December 2015
- New trials include monotherapy or combination trials for NSCLC 1L, Ovarian, Gastric, Merkel Cell and other solid tumors
- Enrolment of ~ 1,500 patients expected for 2015 and >3,000 by 2016
- First potential commercial launch of avelumab in 2017; working toward at least one additional potential launch per year through 2022



Avelumab – JAVELIN clinical development program initiated and planned as of 1 Oct 2015

Merck KGaA
Darmstadt · Germany



Acronyms: CRC = colorectal cancer; CRPC = Castrate Resistant Prostrate Cancer; ACC = Adrenocortical Cancer; SCCHN = Squamous Cell Carcinoma of the Head and Neck, RCC = Renal Cell Carcinoma;
[1]Trials currently initiating; [2]Phase 2 trial

Avelumab shows promising clinical activity in five indications[1] supporting further clinical development

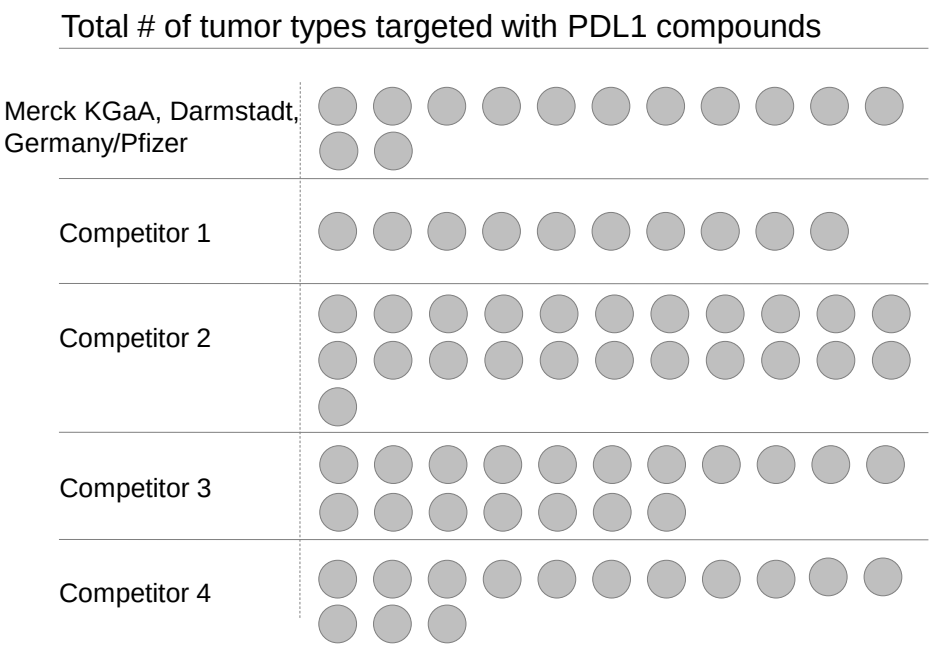
Merck KGaA
Darmstadt · Germany

1.	NSCLC	▪ Treatment with avelumab led to early and durable responses (ORR 14%) as a 2nd line treatment ▪ Longer median PFS and OS were observed for PDL1+ patients ▪ Phase III head-to-head trial of avelumab vs docetaxel in patients with recurrent NSCLC is underway
2.	OVARIAN	▪ Largest reported dataset[2] of patients with advanced ovarian cancer treated with anti-PD-(L)1 ▪ Treatment with avelumab showed clinical activity (ORR 11%) in heavily pre-treated patients ▪ Phase III clinical development is planned
3.	GASTRIC	▪ Largest reported dataset[2] of patients with advanced gastric cancer treated with anti-PD-(L)1 ▪ Treatment with avelumab as a 2nd line treatment showed clinical activity (ORR 15%) ▪ Disease stabilization was also observed in a SwM (switch-maintenance therapy) group
4.	UROTHELIAL / BLADDER	▪ Treatment with avelumab led to early and durable responses (ORR 19%) ▪ Biomarkers from tumor tissue and blood samples are under evaluation
5.	MESOTHELIOMA	▪ Treatment with avelumab in heavily pre-treated patients with advanced unresectable tumors led to: ▪ Partial responses in 3 patients (15.0%); all ongoing at time of analysis ▪ Disease control rate for patients 60.0% (partial response and stable disease)

[1]Phase I trial solid tumors; all response rates refer to all-comer population; [2]To date; source: ECC poster September 2015

Avelumab development program covers a broad range of tumor types

Merck KGaA
Darmstadt · Germany

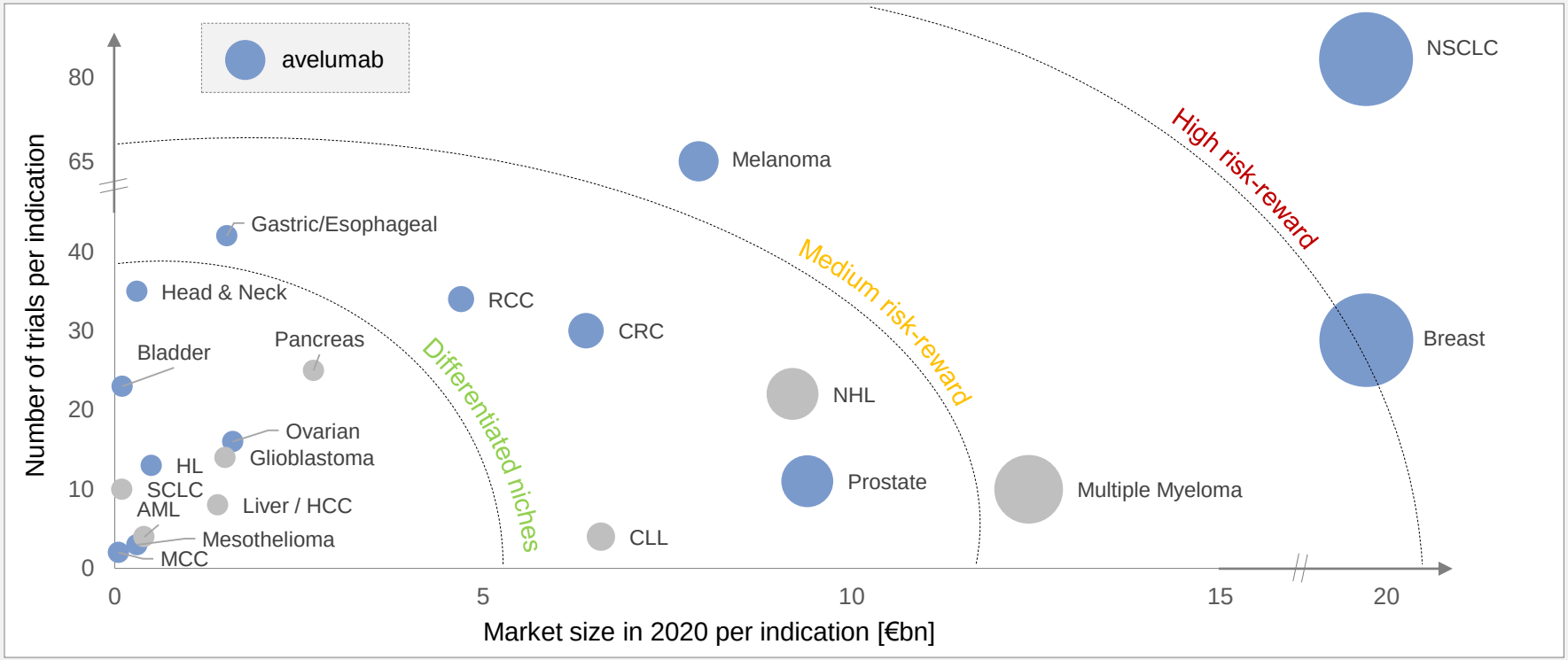


- Avelumab is well represented and is currently investigated across more than 15 tumor types and lines of therapy
- It tackles a similar range as competitive products in the field of checkpoint inhibitors
- Significant progress made until 1 Oct. 2015 and expected to be made until the end of 2015 and into 2016:
  - Confident to start up to 6 registrational trials in 2015
  - Up to 25 trials until ASCO 2016 as single-agent and combination therapy

Source: Merck KGaA, Darmstadt, Germany, Boston Consulting Group

Avelumab plays predominantly in attractive and differentiated niches

Merck KGaA
Darmstadt · Germany



Sources: Trialtrove and Cortellis as of September 2015, Boston Consulting Group, Evaluate Pharma forecast 2020
Acronyms: SCLC = Small Cell Lung Cancer; HL = Hodgkins Lymphoma; NHL = Non Hodgkins Lymphoma; AML = Acute Myeloid Leukaemia

Avelumab – Differentiation strategy varies according to chosen target indication and market

Merck KGaA
Darmstadt · Germany

1. UNSATURATED AND/OR NICHE INDICATIONS

Ambition: Smart leader

- Indications (Merkel cell) or markets (Asia for gastric)
- Quick to market strategy, e.g. ODD for MCC in September 2015
- Small, but unchallenged sales potential with notable impact for Merck KGaA, Darmstadt, Germany
- Strategic strength of Merck KGaA, Darmstadt, Germany in niche markets

2. SATURATED AND/OR MAJOR INDICATIONS

Ambition: Smart follower

- Indications such as NSCLC or Bladder
- Learn from experience of incumbents / early movers
- Differentiate in trial design and use of biomarkers
- Potential for combinations given breadth of our and Pfizer's pipelines, e.g. Lung / Xalkori

Acronym: ODD = Orphan drug designation

Merck KGaA
Darmstadt · Germany

Agenda

Healthcare – Strategy recap

Progress in the R&D pipeline

Immuno-Oncology and avelumab

Executive Summary

Executive Summary

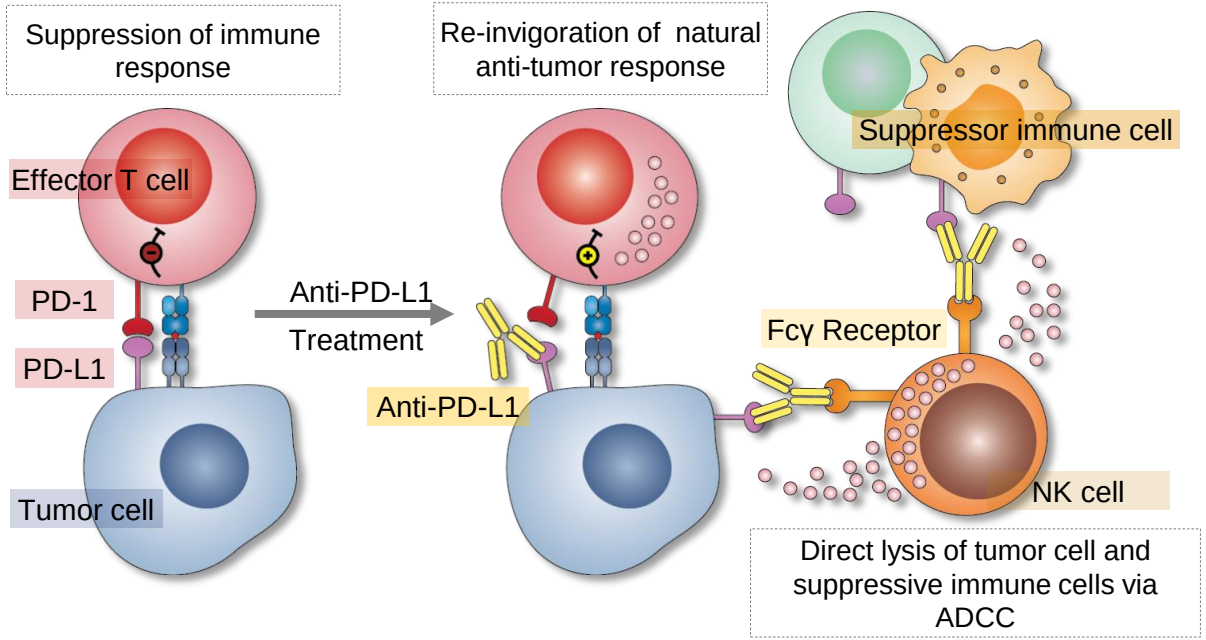
Merck KGaA
Darmstadt · Germany

BROAD R&D PIPELINE	We have a broad and well-structured pipeline in its focus areas Immuno-Oncology, Oncology and Immunology
VISIBLE PROGRESS	Since the Capital Markets Day 2014, several promising earlier-stage assets have made visible progress
BROAD I-ONC PLATFORM	Our immuno-oncology platform extends beyond checkpoint inhibitors and allows for clear differentiation
AVELUMAB DIFFERENTIATION	Combination of our and Pfizer's compounds can be a powerful in the chosen indications and markets
GROWTH TRAJECTORY	The foundation for Healthcare's long-term growth trajectory is being built step-by-step now

Appendix

avelumab – an Anti PD*-L1 drug to improve natural immune response: targeting principle

Merck KGaA
Darmstadt · Germany



- Fully human IgG1
- Blocks interaction of PD-L1 with its known ligands PD-1
- Exhibits Antibody Dependent Cell-Mediated Cytotoxicity (ADCC)
- Binds with high affinity to human, monkey and mouse PD-L1

- Expression of PD-L1 in the tumor microenvironment can inhibit anti-tumor T cell activity

Illustration only; *PD = programmed death