R&D update call 2020

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Today's Call
Participants - R&D and Commercial Leadership

Luciano Rossetti
Global Head of Research & Development

- Joined Merck KGaA, Darmstadt, Germany in 2014 after 8 years at Merck & Co.
- Spent 18 years in academia
- Previously professor of Medicine and Head of the Diabetes Research & Training Center at the Albert Einstein College of Medicine
- MD degree from the Trieste University Medical School, Italy

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Head of the Global Innovative Medicine Franchises & President of EMD Serono

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- Co-founded start-ups in bioinformatics and dermatology R&D
- Ph.D. (Dr. rer. nat.) in Molecular Biology from the University of Konstanz, Germany

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Head of Oncology Development

- Joined Merck KGaA, Darmstadt, Germany in January 2020
- Industry experience at AstraZeneca, GlaxoSmithKline, Sanofi, Genmab
- Previously professor of Experimental Cancer Research/Medicine at Lund University
- MD and PhD degree from the University of Copenhagen

Today's Call
Agenda

1

CMD 2020 Refresher
Healthcare Pipeline –
One of the „BIG3" growth drivers for the Group

2

Healthcare Research at Merck KGaA, Darmstadt, Germany
Early innovation, conscious risk-taking, & rigorous prioritization for value maximization

3

Pre-Clinical & New-to-Clinic
Selected examples of early innovation across our therapeutic focus areas (Oncology, Immuno-Oncology, Immunology)

4

Oncology - Clinical Pipeline & Commercial Update
Bavencio® (Avelumab)
Bintrafusp alfa (anti-PD-L1/TGF-ß Trap)
Tepotinib (MET kinase inhibitor)
DDR Portfolio

5

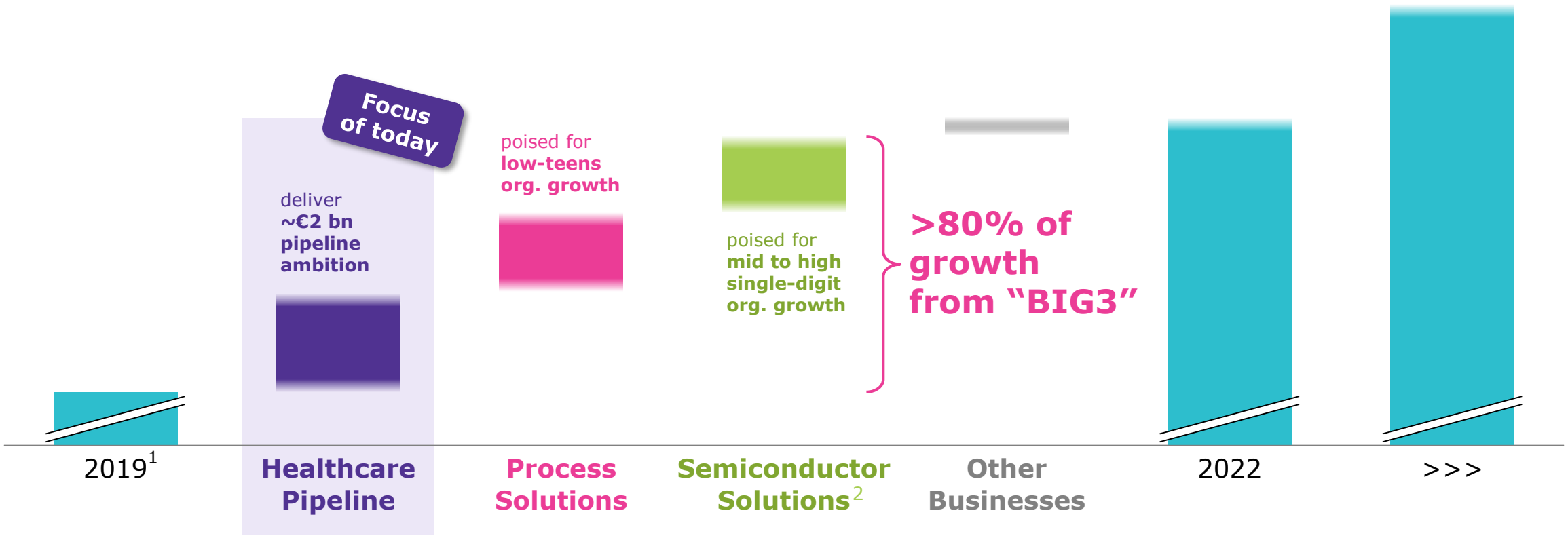
Neurology & Immunology – Clinical Pipeline & Commercial Update
Evobrutinib (BTK-inhibitor)
M5049 (TLR7/8 antagonist)
Mavenclad® (Cladribine)

6

Q&A Session

CMD 2020 Refresher

Group - Three main drivers of growth to 2022 and beyond



Beyond 2022: further significant growth potential from "BIG3" and increasing contributions from other businesses

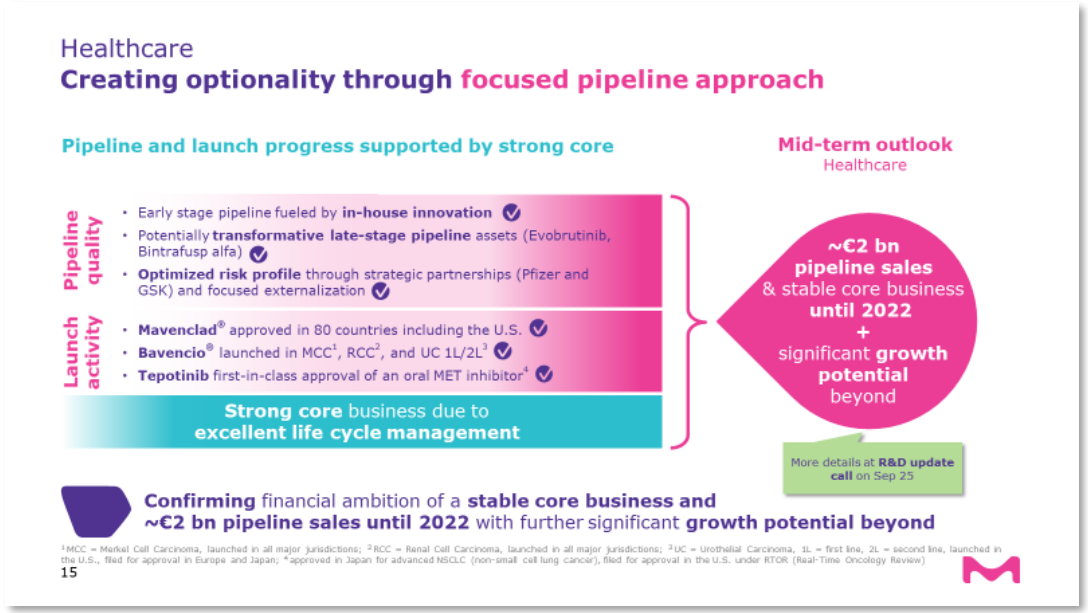
1: 2019 Group sales of €16.2 bn; 2: including Versum portfolio effect

CMD 2020 Refresher
Healthcare – On track to becoming a Global Specialty Innovator

Business today

- H1 2020: **Growing organically**, resilient Oncology and General Medicine portfolio, **visibly strong June** signals COVID-19 recovery
- **Bavencio®: Transformative UC1L data** presented at ASCO; **strong U.S. launch** with positive early feedback, EMA & JP filings accepted
- **Mavenclad®:** Visible **ramp-up recovery** post pandemic starting in June (Rx volumes & share)
- **Tepotinib: First-in-class approval** in Japan, U.S. filing accepted (priority review, under RTOR)
- **Potentially transformative pipeline:** Bintrafusp alfa, Evobrutinib, DDR portfolio

…and tomorrow



Inflection point achieved: reaping the benefits of pipeline investments

Further build & deliver on innovator strategy to drive sustainable success

Acronyms: DDR = DNA Damage Response; EMA = European Medicines Agency; JP = Japan; RTOR = Real-Time Oncology Review; Rx = Prescriptions; UC = Urothelial Cancer

Increasing momentum from R&D
Innovating new medicines

10 NMEs[1] with First-in-Class, Best-in-Disease or Best-in-Class potential progressed to clinic in the last 6 years

Bintrafusp alfa (anti-PD-L1/TGF-β Trap)

Evobrutinib (BTK-inhibitor)

M5049 (TLR7/8 antagonist)

Peposertib (M3814)

M6495 (anti-ADAMTS-5 nanobody)

M8891 (MET AP2i)

M4344 (ATRi)

Berzosertib (M6620)

M3258 (LMP7 inhibitor)

M6223 (anti-TIGIT)

Significant growth in **contribution to prestigious scientific publications**

- Publications in top-quartile (top 25%) medical journals increased from 66 in 2016 to over 100 in 2020 YTD
- 12 publications in world's top medical journals in past 2 years:

JAMA · The New England Journal of Medicine · nature reviews drug discovery · nature genetics · The Lancet Respiratory Medicine · Annals of Oncology · JAMA Oncology · Cell

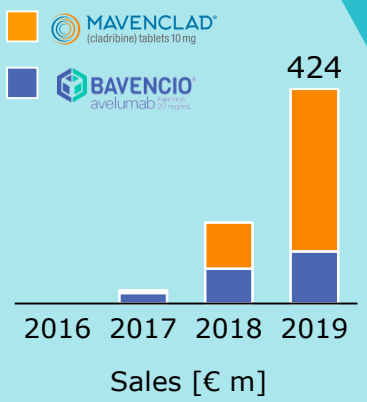
Assets reviewed under **multiple accelerated pathways rewarding innovation**

- 4x Breakthrough Designation (BTD) (Bavencio® UC, RCC & MCC, & Tepotinib)
- 1x Sakigake (Tepotinib)
- 2x US FDA Real-Time Oncology Review (Bavencio® UC1L, & Tepotinib)

3 new medicines approved across 6 indications since 2017

- Relapsing Multiple Sclerosis: MAVENCLAD® (cladribine) tablets 10 mg
- Merkel, Renal & Urothelial Carcinoma 1&2L: BAVENCIO® avelumab Injection 20 mg/mL
- NSCLC with METex14 Skipping Alterations: TEPMETKO® tepotinib

Significant increase in sales & further growth potential from newly launched assets



1: Only NMEs in active development, excludes NMEs with terminated development; Acronyms: MCC = Merkel Cell Carcinoma; NME = New Molecular Entity; NSCLC = Non-small Cell Lung Cancer; RCC = Renal cell carcinoma; UC = Urothelial cancer; YTD = Year to date

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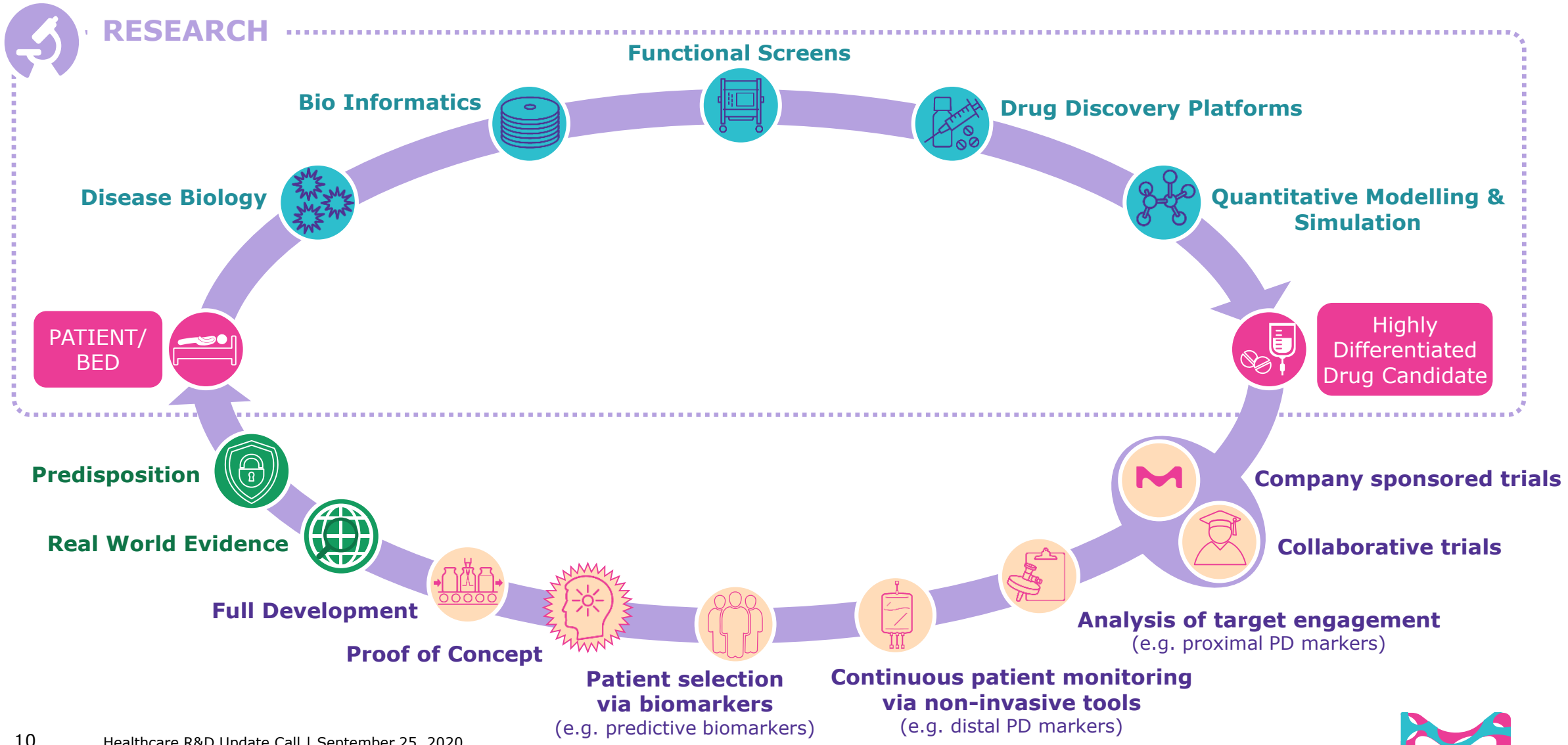
Healthcare Research at Merck KGaA, Darmstadt, Germany
Bedside to Bench and Bench to Bedside



Healthcare Research at Merck KGaA, Darmstadt, Germany

Translational Innovation Platforms (TIPs) advance our science through to first-in-man across our therapeutic areas

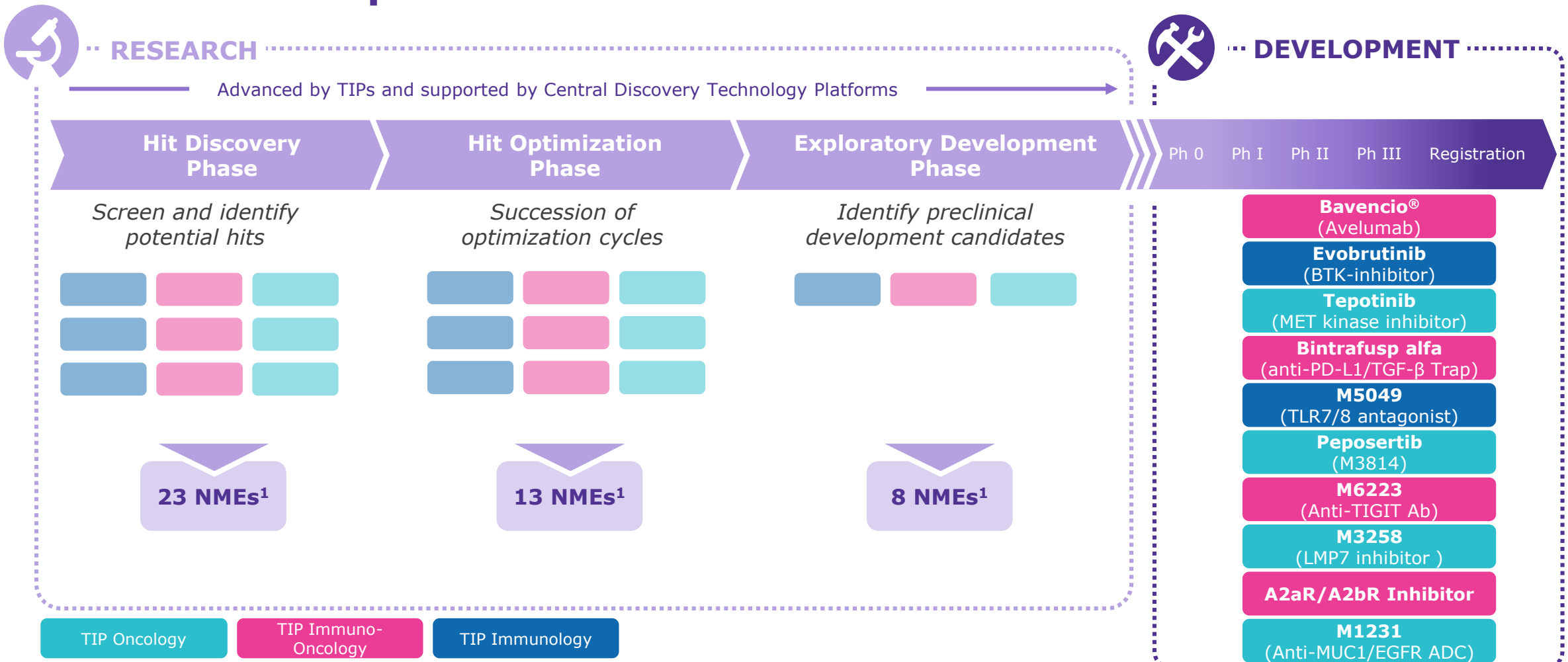
Selected examples – NOT exhaustive

Therapeutic Focus Areas	Disease biology areas[1]	Examples of Output
TIP Oncology – Delivering innovative targeted therapies	Oncogenic Signaling	Tepotinib (MET kinase inhibitor)
	DNA damage response (DDR)	ATR-i (Berzosertib/M6620)
	Next generation Antibody Drug Conjugates (ADC)	Bi-specific MUC1-EGFR-ADC (M1231)
	Stress & Plasticity	Newly established focus area
TIP Immuno-Oncology - Harnessing the immune system and activating or augmenting the body's natural anti-tumor response	Effector T cell modulation	Avelumab, bintrafusp alfa, anti-TIGIT (M6223)
	NK cell biology	ADCC activity avelumab & cetuximab
	Immune suppressive metabolites	adenosine receptor antagonist (M1069)
	Tumor Phagocytosis and Suppressive Myeloid cells	Newly established focus area
TIP Immunology - Modulating key pathogenic mechanisms in autoimmune pathologies and degenerative joint disease	Immune receptor & immune complex signaling	Evobrutinib (BTK-inhibitor)
	Innate immunity and immune complex generation	M5049 (TLR7/8 antagonist)
	Induction of immune tolerance	Newly established focus area
	Epithelial Barrier Homeostasis	Newly established focus area

1: Listed by decreasing maturity/increasing novelty (innovation); Acronyms: ADCC = Antibody-Dependent Cell-mediated Cytotoxicity; ATRi = Ataxia telangiectasia and Rad3 related inhibitor; NK cell = Natural killer cell; TIP = Translational Innovation Platform; TLR = Toll-like Receptors

Innovation Management Process

Fostering innovation at early stage, applying stringent quality criteria to enter development and advance successful clinical candidates

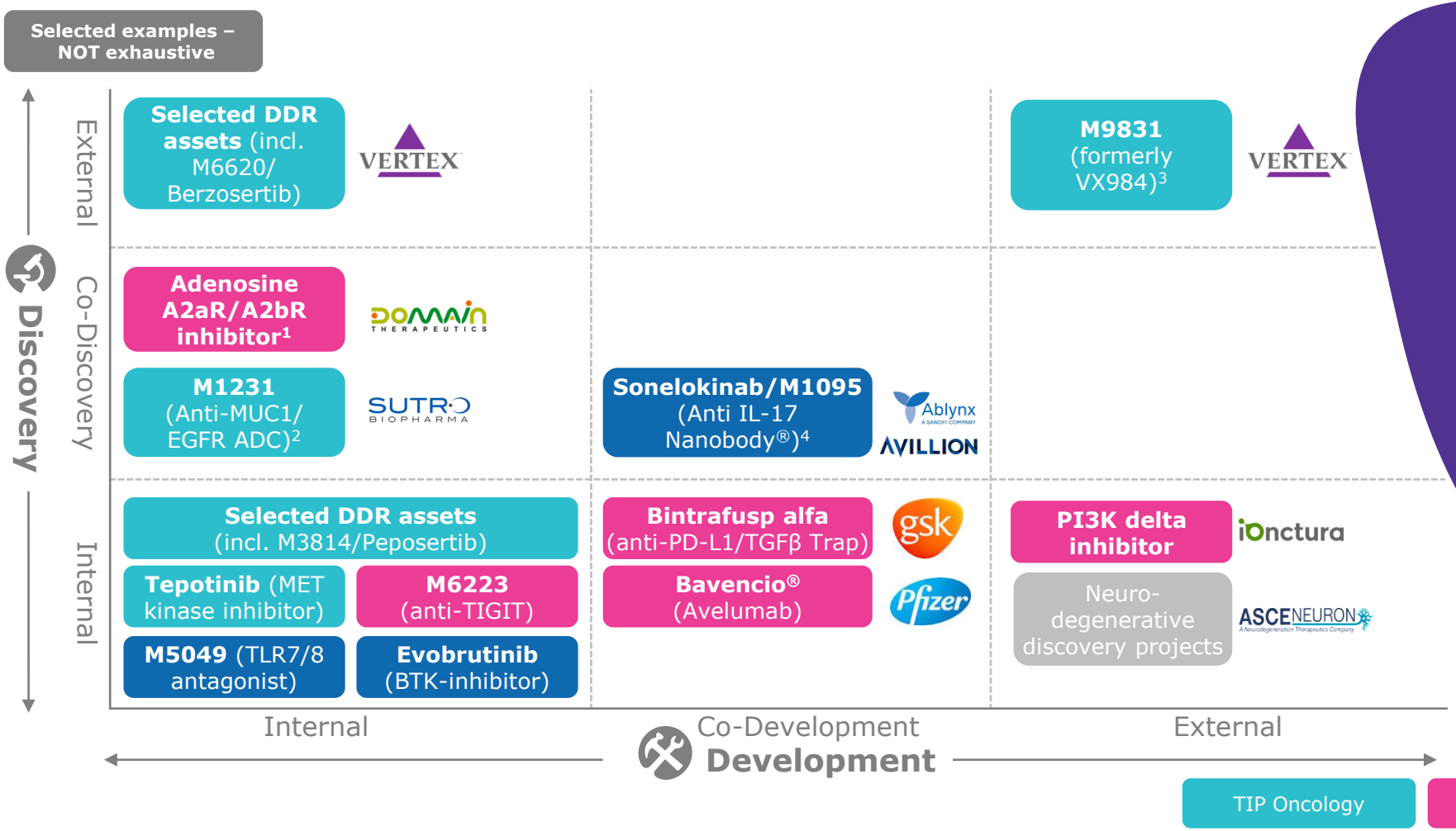


1: As of September 25, 2020; Acronyms: NME = New Molecular Entity; TIP = Translational Innovation Platform

Selected examples of internally and/or jointly (with partners) discovered assets – **NOT exhaustive**

Pipeline Prioritization

Rigorous portfolio & partnering decisions to maximise value



Multi-factorial dimensions assess both scientific rigor and development feasibility:

1. Strategic fit
2. Exploitability
3. Clinical & commercial competencies

1: In 2017, Domain Therapeutics and Merck KGaA, Darmstadt, Germany entered into a collaboration and licensing agreement for the development of adenosine receptor antagonist drugs specifically designed for oncology and immuno-oncology; 2: In 2014, Sutro and Merck KGaA, Darmstadt, Germany initiated a collaboration to discover and develop ADCs utilizing Sutro's cell-free protein synthesis platform, Xpress CF+™. Merck KGaA, Darmstadt, Germany is responsible for drug product, clinical development and commercialization of any resulting products; 3: In 2019, an exclusive license was granted to Vertex for the use of M9831 in gene-editing applications; 4: Avillion conducted Ph II of M1095 in Psoriasis, Merck KGaA, Darmstadt, Germany decided to out license sonelokinab to a new partner to initiate Phase III development in 2021

Pre-Clinical Pipeline

Ph 0 (Pre-clinical)

M1231: Potential first-in-class bispecific antibody-drug conjugate targeting EGFR and MUC1[1]

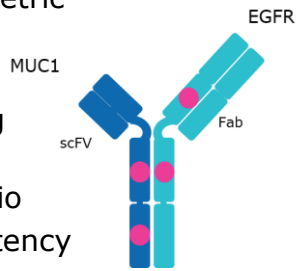
SUTRO BIOPHARMA

Limitations of conventional ADCs

- **Off-target uptake and catabolism**
- **On-target side effects** based on binding to normal cells & tissues
- **Unfavorable PK** and safety profile due to heterogenous structure and influence of hydrophobic payloads
- **Systemic loss of payload** based on linker instability
- **Resistance mechanisms** against payload MoA and ADC processing

M1231: First next generation bispecific targeting EGFR & MUC1 in parallel

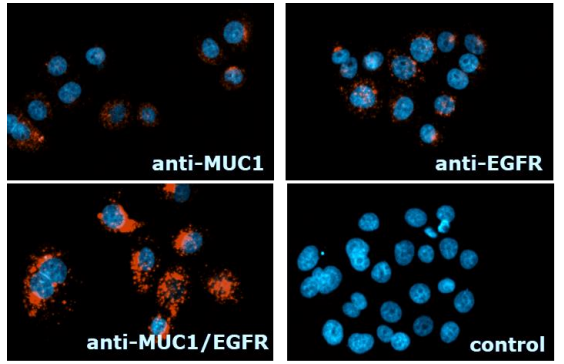
- **Bispecific ADC based on proprietary SEED structure** (Strand-Exchange Engineered Domain) with asymmetric heavy chains
- **XPressCF cell-free expression** system (SUTRO):
  - Non-natural amino acids for stable drug coupling
  - Site-specific conjugation enables structural homogeneity and a consistent drug-antibody ratio
  - Optimized cytotoxin positioning for improved potency and PK

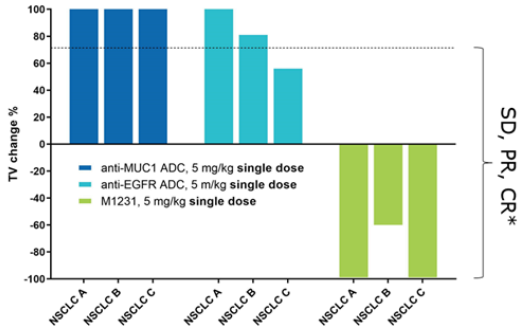


- Proprietary **hemiasterlin-related toxic warhead** with potent tubulin MoA and cleavable Val-Cit module (SUTRO)

Bispecific concept to potentially increase tumor selectivity and payload delivery

1. **Loss of membrane polarization on tumor cells** leads to **EGFR and MUC1 co-localization**
2. **Indication space** & patient population: e.g. NSCLC, esophageal, gastric, ovarian, H&N
3. **Limited co-expression** on normal tissues with potentially **reduced on-target toxicity**
4. **Cooperative binding: higher internalization rate and increased payload disposition in tumors**





First in man study planned in Q1 2021 with focus on NSCLC and esophageal squamous cell carcinoma

1: Knuehl et al., "M1231: A first-in-class bispecific antibody-drug conjugate targeting EGFR and MUC1", AACR 2020; Acronyms: ADC = Antibody-drug conjugate; EGFR = Epidermal Growth Factor Receptor; H&N = Head & Neck; MoA = Mechanism of Action; MUC1 = Mucin-1; NSCLC = Non-small cell lung cancer; PK = Pharmacokinetic

TIP Oncology

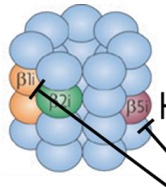
New-to-Clinic (Phase I)

Ph I

M3258: Potent and selective LMP7 Inhibitor demonstrating high efficacy in multiple myeloma models[1]

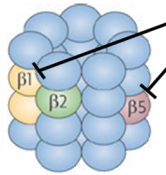
Limitations of current proteasome inhibitors

Immunoproteasome
- Alternate protease subunits
- Hematopoietic expression
- Induced by inflammation
- **Hematopoietic cancers depend on activity**



Selective β5i/LMP7 Inhibitor M3258

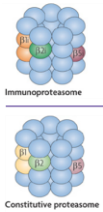
Pan-Proteasome Inhibitors (e.g. Bortezomib, Ixazomib)



Constitutive Proteasome
- Ubiquitous expression
- General protein homeostasis

- LMP7^{high} solid tumors
- Malignant hematopoietic cells
- **Healthy tissue**
  - Toxicity (e.g. hypertension, ischemic heart failure, sensory peripheral neuropathy, anemia, renal failure, dyspnea)
  - Dosing limitations

M3258: A unique profile based on selective LMP7 inhibition

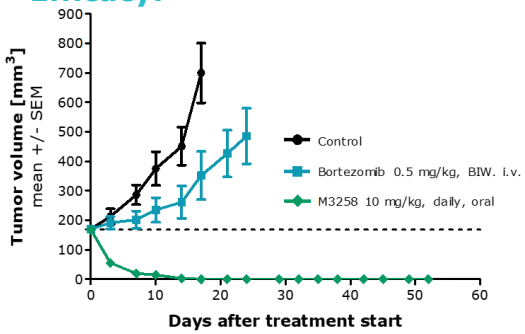


IC_{50} Subunit [nM]	M3258 po, covalent, reversible	Bortezomib iv, covalent, reversible	Ixazomib po, covalent, reversible	Carfilzomib iv, covalent, irreversible
β1i	>30000	4	1	30
β2i	>30000	2100	>30000	19
β5i (LMP7)	**5**	**1**	**5**	**4**
β1c	>30000	26	46	890
β2c	>30000	20500	>30000	66
β5c	2630	4	7	2

IC_{50} > 1000 nM | IC_{50} 100-1000 nM | IC_{50} < 100 nM

Strong scientific data package showing differentiation vs pan-proteasome inhibitors

Efficacy:



Nonclinical Safety:

Organ / System	M3258	Bortezomib
Gastrointestinal tract	Yes	Yes
Hematolymphoid	Yes	Yes
Liver	None	Yes
Cardiac	None	Yes
Lung	None	Yes
Kidney	None	Yes
Nervous system	None	Yes

- **Strong preclinical efficacy**, equal or greater efficacy than pan-proteasome inhibitors
- **More restricted target organ profile** compared to Pan-PIs, i.e. no relevant kidney, cardiovascular, respiratory, central & peripheral nervous system or off-target effects expected
- **Oral once-daily dosing** for improved convenience vs pan-proteasome inhibitors

- Safety & PK/PD assessment ongoing in Phase 1a on MM patients
- Path to clinical Proof-of-Concept in Phase 1b expansion to be finalized upon outcome of Phase Ia

1: Sanderson et al., "First time disclosure of M3258, a selective inhibitor of the immunoproteasome subunit LMP7 with potential for improved therapeutic utility in multiple myeloma compared to pan-proteasome inhibitors", AACR 2019; Acronyms: LMP7 = Low-molecular mass protein-7; MM = Multiple myeloma; PK/PD = Pharmacokinetic/Pharmacodynamic

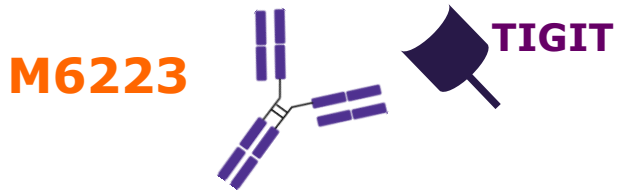
TIP Immunology

TIP Oncology

New-to-Clinic (Phase I)

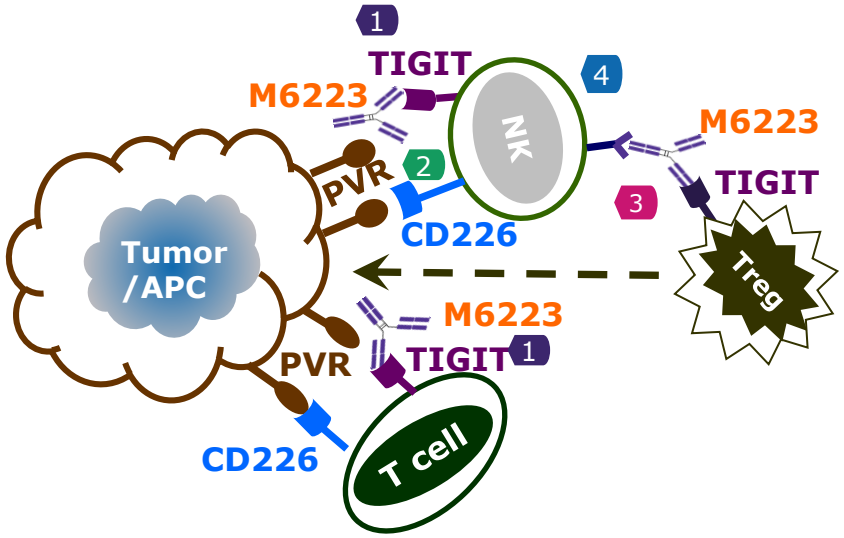
Ph I

M6223: Internally developed IgG1 anti-TIGIT antibody holding combination potential with internal assets and SoC



Fc Effector Competent Fully Human IgG1 Antibody that Recognizes TIGIT

Internally developed



M6223 Preclinical Anti–Tumor Activity

1. Blocking of TIGIT/ligands interaction **counteracts immune suppression** mediated by TIGIT/PVR axis
2. Blockade with M6223 **permits stimulation of CD226** homo-dimerization and immune activation
3. M6223 **depletes TIGIT-expressing** suppressive and **exhausted T cells**
4. Solid combination rational based on **TGF-β and TIGIT are inhibiting NK cell activity** which is required for 3

→ **Publication of preclinical data** planned for H1 2021

First in Human Study in Patients with Metastatic and Locally Advanced Solid Tumors (NCT04457778)

- Initiated in US and Canada
- Monotherapy and in combination with Bintrafusp alfa

Combination potential with internal assets and SoC

Acronyms: APC = Antigen Presenting Cells; CD226 = DNAM-1 (DNAX Accessory Molecule-1); NK = Natural Killer Cells; PVR = poliovirus receptor, CD155 or Necl-5; PVRL2 = CD112 or Nectin2; SoC = Standard of Care; TIGIT = T cell immunoreceptor with Ig and ITIM domains

TIP Immuno-Oncology

New-to-Clinic (Phase I)

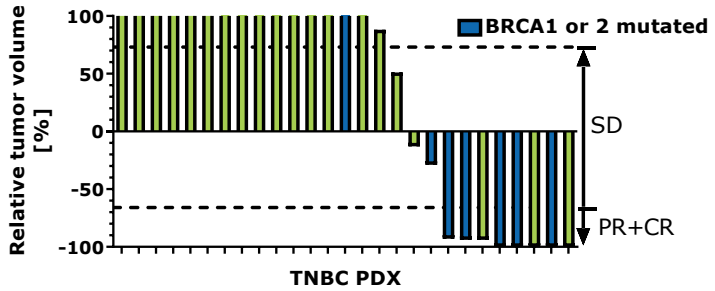
Ph I

M4344 (oral ATRi): Pre-clinical evidence for synthetic lethality in combination with PARPi supports clinical development

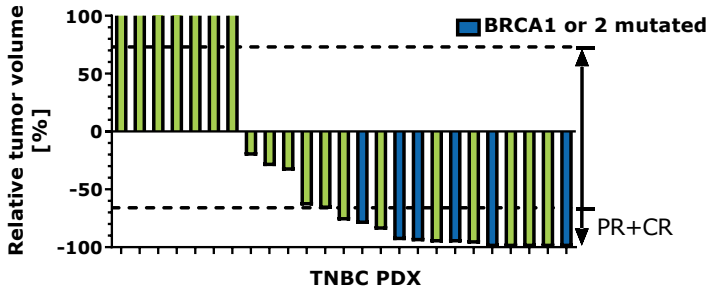
TNBC (PARPi +/- M4344)[1]

Study Design:
M4344 + Talazoparib in TNBC patient-derived xenograft models

Talazoparib (PARP-i) 0.3 mg/kg qd x 28



M4344 10 mg/kg 2qw x 4 & Talazoparib 0.3 mg/kg qd x 28



ATR-i M4344 improves response to Talazoparib in a TNBC PDX study

M4344 Preclinical Anti–Tumor Activity

- ATR kinase is an important regulator of replication stress and double strand break repair
- Demonstrated activity in vitro and in vivo as a single agent and combination with chemotherapy
- Antitumor activity was particularly strong in combination with PARP inhibitors, irrespective of the BRCA1/2 status.

Preclinical Proof-of-Concept established by Group's research after in-licensing of M4344 from Vertex

Phase I Study of the Safety, Tolerability, and PK/PD in Participants With Advanced Solid Tumors (NCT02278250)

- Initiated in US and Europe
- Monotherapy and combination with cytotoxic chemotherapy
- Basis for monotherapy expansion cohorts biomarker-driven, studies in combination with chemotherapy and other DNA repair inhibitors

Combination potential with SoC and beyond

1: Myriad HRD; cut-off = 42 (Telli et al., Clinical Cancer Research 2016); HRD scores kindly provided by J-G Judde, Xentech; Acronyms: ATRi = Ataxia telangiectasia and Rad3-related inhibitors; PK/PD = Pharmacokinetic/pharmacodynamic; SoC = Standard of Care; TNBC = Triple-Negative Breast Cancer

TIP Oncology

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- Joined Serono in 2004 in Medical Affairs
- Previously Managing Director of EMD in Canada, and then Chief Marketing & Strategy Officer
- Master's degree in Molecular & Cellular Biochemistry from the University of Oxford

Joern-Peter Halle
Head of Research

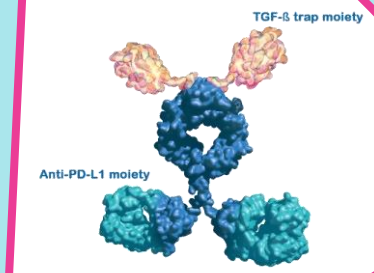
- Joined Merck KGaA, Darmstadt, Germany in 2005 in Business Development before moving on to R&D, most recently Head of TIP Immuno-Oncology & Head of External Innovation
- Co-founded start-ups in bioinformatics and dermatology R&D
- Ph.D. (Dr. rer. nat.) in Molecular Biology from the University of Konstanz, Germany

Klaus Edvardsen
Head of Oncology Development

- Joined Merck KGaA, Darmstadt, Germany in January 2020
- Industry experience at AstraZeneca, GlaxoSmithKline, Sanofi, Genmab
- Previously professor of Experimental Cancer Research/Medicine at Lund University
- MD and PhD degree from the University of Copenhagen

Oncology Portfolio
Update on selected assets

BAVENCIO® avelumab Injection 20 mg/mL



Bintrafusp alfa (anti-PD-L1/TGF-β Trap)

TEPMETKO® tepotinib

DDR (DNA Damage Response) Portfolio

Bavencio® (Avelumab)

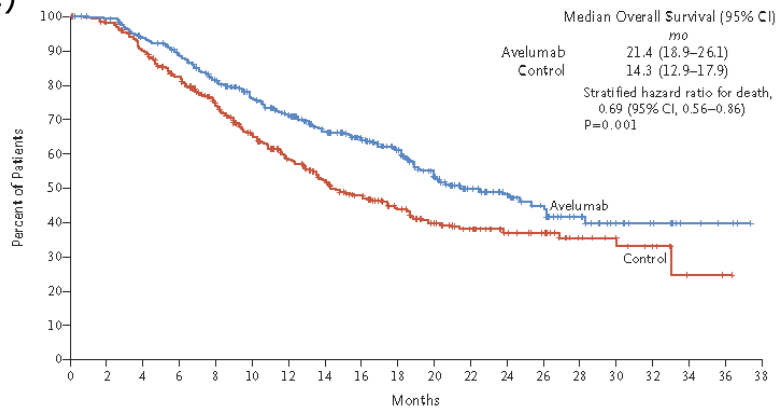
Approved by FDA as UC 1L maintenance treatment on June 30 2020, transformative OS data recently published in NEJM

„Avelumab Maintenance Therapy for Advanced or Metastatic Urothelial Carcinoma", Powles et al., NEJM, published September 18, 2020[1]

New data

ESMO 2020 – Additional analyses support the use of Bavencio® as a new addition and advance to the standard of care[2]

- **31% reduction in risk of death and an increase of 7 months in the median overall survival** (21.4 months for Bavencio® + best supportive care (BSC) versus 14.3 months for BSC alone)



- **OS improvements consistent across pre-specified subgroups**, regardless of the type of platinum-based chemotherapy received and patients' PD-L1 status
- **No new safety signals** were identified, and the safety profile was consistent with previous studies of Bavencio® monotherapy

Broad indication[3]:

- Data demonstrate OS benefits across prespecified subgroups, including patients with CR on chemotherapy, supporting avelumab 1L maintenance as a new treatment option for all platinum-eligible patients, both cisplatin-eligible and ineligible

Important insights for unique MOA of Bavencio® in maintenance[4]:

- Multiple exploratory biomarkers were identified as being potentially predictive of OS in this analysis, including a number of alleles encoding high-affinity FcγRIIA and FcγRIIIA variants, which may indicate FcR-mediated antitumor mechanisms

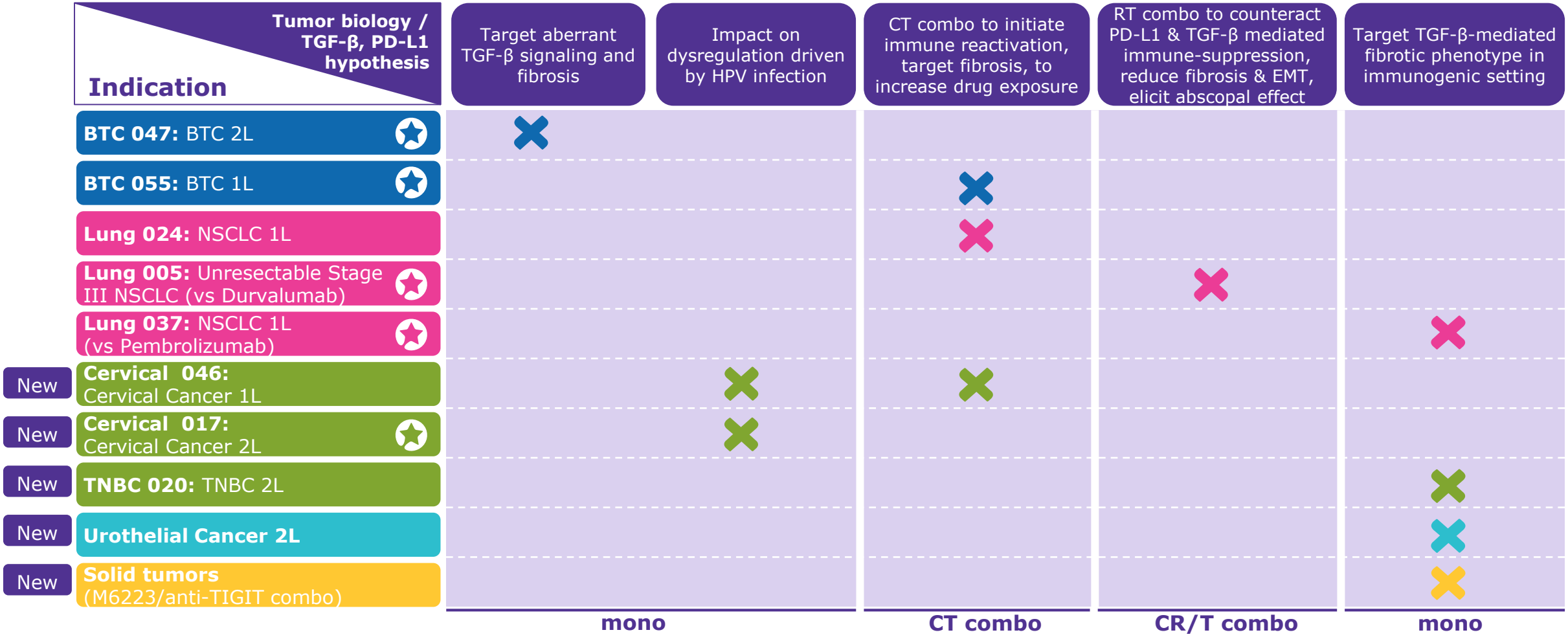
Quality of Life data / Patient-reported outcomes (PROs)[5]:

- Bavencio® 1L maintenance therapy improves OS with no negative effect on clinically relevant PROs, supporting the use of avelumab as a new addition and advance to the standard of care

1: Powles et al., "Avelumab Maintenance Therapy for Advanced or Metastatic Urothelial Carcinoma", published on September 18, 2020 in The New England Journal of Medicine; 2: NCCN July 2020, ESMO Guidelines July 2020; 3: Grivas et al., "Avelumab first-line (1L) maintenance + best supportive care (BSC) vs BSC alone with 1L chemotherapy (CTx) for advanced urothelial carcinoma (UC): Subgroup analyses from JAVELIN Bladder 100", presented at ESMO 2020; 4: Powles et al, "Avelumab first-line (1L) maintenance + best supportive care (BSC) vs BSC alone for advanced urothelial carcinoma (UC): association between clinical outcomes and exploratory biomarkers"; 5: Powles et al., "Patient-reported outcomes (PROs) from JAVELIN Bladder 100: avelumab first-line (1L) maintenance + best supportive care (BSC) vs BSC alone for advanced urothelial carcinoma (UC)", presented at ESMO 2020; Acronyms: NEJM = New England Journal of Medicine; OS = Overall survival; UC = Urothelial cancer

Bintrafusp alfa (anti-PD-L1/TGF-β Trap)

Development approach: Multiple shots-on-goal to evaluate co- localized inhibition of TGF-β / PD-L1 hypotheses



Acronyms: BTC = Biliary Tract Cancer; CT = Chemotherapy; EMT = Epithelial-mesenchymal transition; HPV = Human papillomavirus; NSCLC = Non-small Cell Lung Cancer; RT = Radiation therapy; TNBC = Triple-Negative Breast Cancer

New Study start date imminent OR within the last 6 months

Registrational potential

Bintrafusp alfa (anti-PD-L1/TGF-β Trap)

ESMO 2020: Long-term follow-up data shows encouraging and durable responses across multiple tumor types

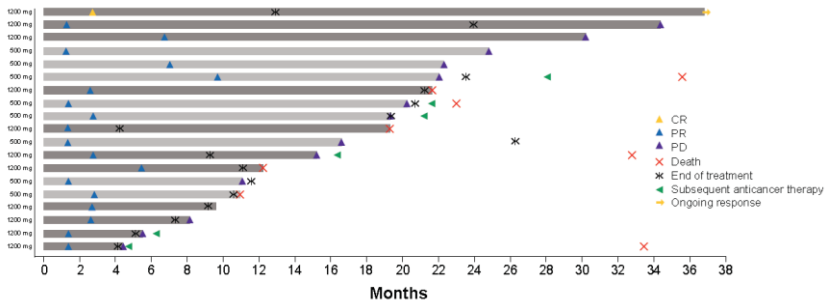
VIRTUAL 2020 ESMO congress

Three-year follow-up for second-line (2L) treatment of non-small cell lung cancer (NSCLC)[1]

After 3 years of follow-up durable responses and long-term survival were observed, especially in patients with high PD-L1 expression:

- Median OS was 21.7 months for PD-L1–positive patients with a 36-month OS rate of 33.6%
- Median OS was not reached for PD-L1–high patients with a 36-month OS rate of 66.7%
- The median DOR was 18.0 months; 21.2% of patients had responses lasting ≥24 months

DOR as assessed by investigator in the overall population



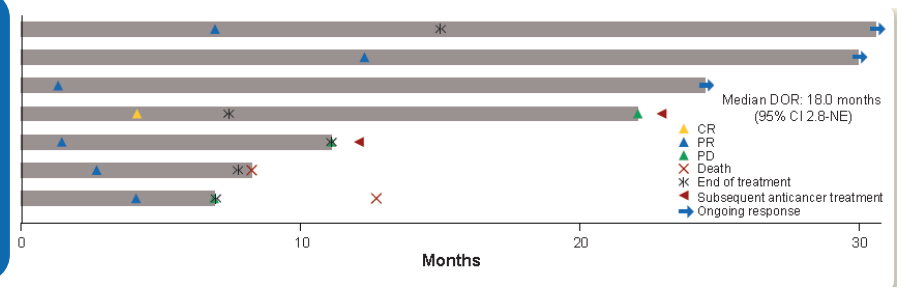
Overall safety profile consistent with results from the two-year follow-up analysis, with **no new safety signals or deaths**

Long-term follow-up of bintrafusp alfa in patients with pretreated biliary tract cancer (BTC)[2]

After 28 months of follow-up, bintrafusp alfa **continues to demonstrate manageable safety with durable, long-lasting responses and long-term survival**

- Bintrafusp alfa showed a 20% response rate with a long duration of response; 42.8% of the patients have an ongoing response after 18 months (18+, 23.5+, and 24+ months)
- The median OS was 12.7 months; 24-month OS and PFS rates were 27.7% and 11.1%, respectively

Time to and duration of response per investigator



No additional safety signals or deaths were observed since the initial analysis

1: Paz-Ares et al., „Three-year follow-up of bintrafusp alfa, a bifunctional fusion protein targeting TGF-β and PD-L1, for second-line (2L) treatment of non-small cell lung cancer (NSCLC)", presented at ESMO 2020 (Poster no.: 1272P); 2: Yoo et al., "Long-term follow-up of bintrafusp alfa, a bifunctional fusion protein targeting TGF-β and PD-L1, in patients with pretreated biliary tract cancer", presented at ESMO 2020 (Poster no: 73P); Acronyms: DOR = Duration of response; OS = Overall survival; PFS = Progression-free survival

Tepotinib (MET kinase inhibitor)

First-in-class launch in MET Exon14 sets foundation for EGFRm/ METamp opportunity and exploration in other tumor types

TEPMETKO® tepotinib

Lay the foundation in NSCLC – MET Exon14
(VISION study, NCT02864992)

- **Highly competitive data** set presented at ASCO 2020 and published in New England Journal of Medicine in May 2020 (99 patients with a follow up ≥9 mths)
- **First-in-class launch** in Japan[1] in March 2020, Sakigake designation[2] granted in 2018
- **US approval expected in Q1 2021** following acceptance of filing on August 25, 2020; granted Priority Review, being evaluated under FDA Real-Time Oncology Review (RTOR) pilot program; previously granted Breakthrough Therapy Designation in 2019

Tap into a growing opportunity in NSCLC – EGFRmut/ METamp
(INSIGHT 2 study, NCT03940703)

- **Increased EGFRm detection** with testing and treatment moving into earlier lines of therapy (ADAURA trial demonstrates a 79% reduction in the risk of death with Osimertinib in the adjuvant setting (ASCO 2020), suggesting an even greater uptake of Osimertinib)
- **METamp as the primary driver of resistance -** Some publications suggest that METamp resistance post-Osimertinib could be ~25%[3]

Explore EGFR resistance in CRC – Tepotinib + Erbitux® combo
(NCT04515394)

- Opportunity for **Tepotinib to address an unmet need in metastatic colorectal cancer (mCRC) together with Erbitux®**

ERBITUX CETUXIMAB

1: second largest Oncology market globally; 2: SAKIGAKE designation promotes research and development in Japan, aiming at early practical application for innovative pharmaceutical products; 3: Piotrowska et al., "Landscape of Acquired Resistance to Osimertinib in EGFR -Mutant NSCLC and Clinical Validation of Combined EGFR and RET Inhibition with Osimertinib and BLU-667 for Acquired RET Fusion", AACR Cancer Discovery 2018; Acronyms: CRC = Colorectal cancer; EGFR = Epidermal Growth Factor Receptor; NSCLC = Non-small cell lung cancer

Tepotinib (MET kinase inhibitor)
Tapping into the rapidly evolving EGFRmut/METamp market - Encouraging INSIGHT 1 data

INSIGHT 2 – Tepotinib + Osimertinib in Osimertinib Relapsed METamp NSCLC

Recruiting

- **Study design recently amended to reflect evolved and future standard of care:**
  - **Target population** – Inclusion criteria adjusted to focus solely on 1L Osimertinib failures
  - **Testing -** Streamline patient enrollment based on current gold standard method (TBx FISH)
  - **Increasing METamp prevalence** - Some publications suggest that METamp resistance post-Osimertinib could be ~25%[1]
- Estimated primary completion date: **November 2022**

Tepotinib + Erbitux® (Cetuximab) - Adressing a significant medical need in 2L metastatic colorectal cancer (mCRC)

NEW – Not yet recruiting

- Opportunity for **Tepotinib to address an unmet need in CRC** together with Erbitux®
- Estimated primary completion date: **March 2023**

A solid foundation - Encouraging INSIGHT 1 data (18-months follow-up presented at WCLC 2019)[1]

Endpoint	Tepotinib + gefitinib	Chemotherapy
Primary - PFS (HR 0.13 [90% CI 0.04, 0.43])	16.6 m	4.2 m
Secondary - ORR (OR 2.67 [90% CI 0.37, 19.56])	66.7%	42.9%
Secondary - OS (HR 0.09 [CI 0.01, 0.54])	37.3 m	13.1 m

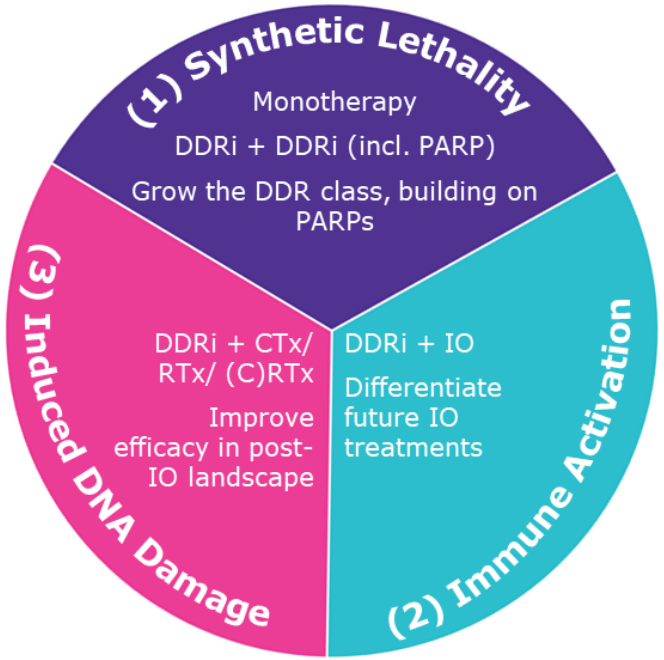
- **Proof of Concept: MET amplification can be considered a suitable biomarker** for treatment with Tepotinib
- **Safety:** generally **well-tolerated,** most adverse events mild to moderate

1: Piotrowska et al., "Landscape of Acquired Resistance to Osimertinib in EGFR -Mutant NSCLC and Clinical Validation of Combined EGFR and RET Inhibition with Osimertinib and BLU-667 for Acquired RET Fusion", AACR Cancer Discovery 2018; 2: Wu et al., „Long term outcomes to tepotinib plus gefitinib in patients with EGFR mutant NSCLC and MET dysregulation: 18 month follow up", presented at WCLC 2019; Acronyms: FISH = Fluorescence in situ hybridization; TBx = Tissue Biopsy

DNA Damage Response (DDR) Portfolio

Leading DDR portfolio with a broad clinical program

Strategy presented at R&D Update Call 2019



ATRi

- **Berzosertib/M6620** (formerly VX-970)
  - Only ATR-inhibitor with a POC from an RCT
  - Multiple NCI studies in various tumor types
- **M4344** (formerly VX-803)
- M1774 (formerly VX-400)
  - Two oral ATR-inhibitors currently in Ph I
  - Provides optionality

DNA-PKi

- **Peposertib/ M3814**
  - Rectal cancer (CRT combo): Ph Ib ongoing, Ph II to enroll approx. 150 patients
  - Combo with Avelumab: Study with and w/o RT ongoing (PhI, solid tumors)
  - Multiple NCI studies in various tumor types
- M9831 (formerly VX984)
  - Exclusive license[1] granted to Vertex in 2019 for use in gene-editing applications

ATMi

- **M4076**
  - Clinical candidate/ready for Phase I trials, chemical structure first disclosed at AACR 2019

1: incl. upfront payment + milestone/royalties on future sales; Acronyms: ATMi = Ataxia telangiectasia-mutated; ATRi = Ataxia telangiectasia and Rad3-related inhibitors; CRT = Chemoradiotherapy; DDR = DNA Damage Response; DNA-PKi = DNA-dependent Protein Kinase Inhibitor; PARP = poly(ADP-ribose) polymerase inhibitor; POC = Proof of concept; RCT = Randomized Controlled Trial; RT = Radiation Therapy

DNA Damage Response (DDR) Portfolio

Berzosertib (M6620) - Promising data in Small Cell Lung Cancer (SCLC) and Ovarian Cancer support further clinical development

First report of an ATRi-chemo combination – SCLC (Berzosertib + Topotecan)[1]

Background: hypothesized that a combination of berzosertib and topotecan, a selective TOP1 inhibitor, would be tolerable and active, particularly in tumors with high replicative stress

Patients and Treatment:
- 21 patients enrolled, combination of M6620 and topotecan tested in 3-week cycles

Results:
- Well tolerated, allowing for highest dose escalation
- 2 partial responses
- 7 stable disease responses ≥3 months
- 3 of 5 patients with SCLC, all of whom had platinum-refractory disease, had a partial response or prolonged stable disease

Promising Phase II data soon to be published in a leading medical journal

First randomized study of an ATR inhibitor in any tumor type – Ovarian Cancer (Berzosertib +/- Gem)[2]

Background: hypothesized that the combination of berzosertib, and gemcitabine could show acceptable toxicity and superior efficacy to gemcitabine alone in high-grade serous ovarian cancer

Patients and Treatment:
70 patients with platinum-resistant epithelial ovarian cancer received:
- Berzosertib + gemcitabine, 21-day cycle (n=34)
- Gemcitabine monotherapy, 21-day cycle (n=36), crossover allowed

Results:

N = 70	Berz. + Gem	Gem	HR
Median PFS (all pts.)	22.9 wks	14.7 wks	*HR 0.57; 90% CI: 0.33-0.98; p=0.044*
Median PFS (pt-free≤3m)	27.7 wks	9.0 wks	HR 0.29; 90% CI: 0.12-0.71; p=0.0087

Results **support further assessment of ATR inhibitor therapy in combination with gemcitabine in Ovarian Cancer and additional tumor types**

1: Thomas et al., " Phase I Study of ATR Inhibitor M6620 in Combination With Topotecan in Patients With Advanced Solid Tumors", published in Journal of Clinical Oncology, June 2018; 2: Konstantinopoulos et al., "Berzosertib plus gemcitabine versus gemcitabine alone in platinum-resistant high-grade serous ovarian cancer: a multicenter, open-label, randomized, phase 2 trial published in Lancet Oncology, 2020

Bavencio® (Avelumab)

Strong early USA launch performance validates significance of 1L UC overall survival (OS) advantage

Bavencio® data ushering in a new era in 1L mUC

Significance of Bavencio® data recognized through major conferences, FDA approval, and publication

May 31	ASCO Presidential Plenary
June 30	**US FDA Approval**
July 16	ESMO guideline inclusion
July 17	**NCCN Level 1 evidence guideline update**
Sep 18	**NEJM publication of primary data analysis**
Sep 19	ESMO oral presentation

Successful introduction in unique COVID context

- **Leading share of voice (SOV):** SOV among IO in UC at **>40%**[1]
- **Broad Rxer reach :** **~70% of priority targets** engaged in first ~2.5 months by field force in spite of COVID constraints[2]
- **Virtual programming:** **robust participation** rates and positive reception to the data

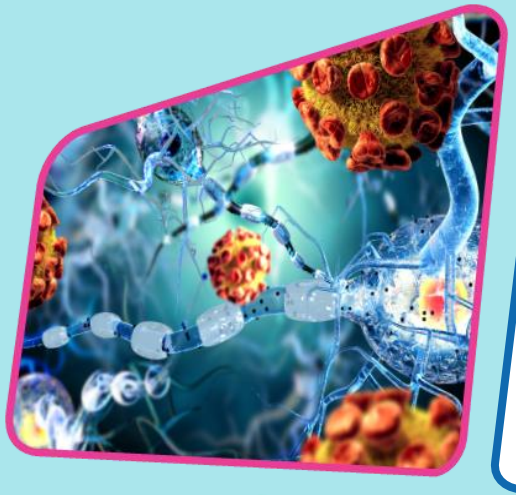
Performance inflection point

- **Strong unit growth:** **+40% vs pre-approval period**[3]
- **Account breadth increasing rapidly:** Progressive acceleration since approval, with **August new accounts 3x above pre-approval level steady state**
- **Penetration into indication:** **~30% penetration into indicated population in first 6 weeks** (July to mid-August) with accelerating penetration in August vs July[4]

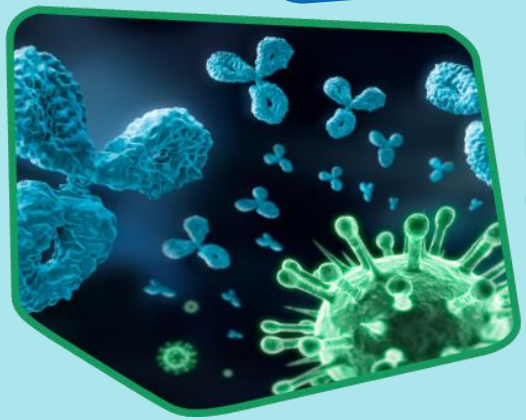
1: Brand impact SOV Report – August 28 2020; 2: Internal CRM data; 3: Internal order data for units – 11 weeks post vs 11 weeks prior; Accounts August vs pre-baseline; 4: Medimix patient charts July-Mid August; Acronyms: ASCO = American Society of Clinical Oncology; ESMO = European Society for Medical Oncology; IO = Immuno-Oncology; mUC = metastatic Urothelial cancer; NCCN = National Comprehensive Cancer Network; NEJM = New England Journal of Medicine; Rxer = Prescriber

Neurology & Immunology
Update on selected assets

Evobrutinib
(oral BTK-inhibitor)



MAVENCLAD®
(cladribine) tablets 10 mg



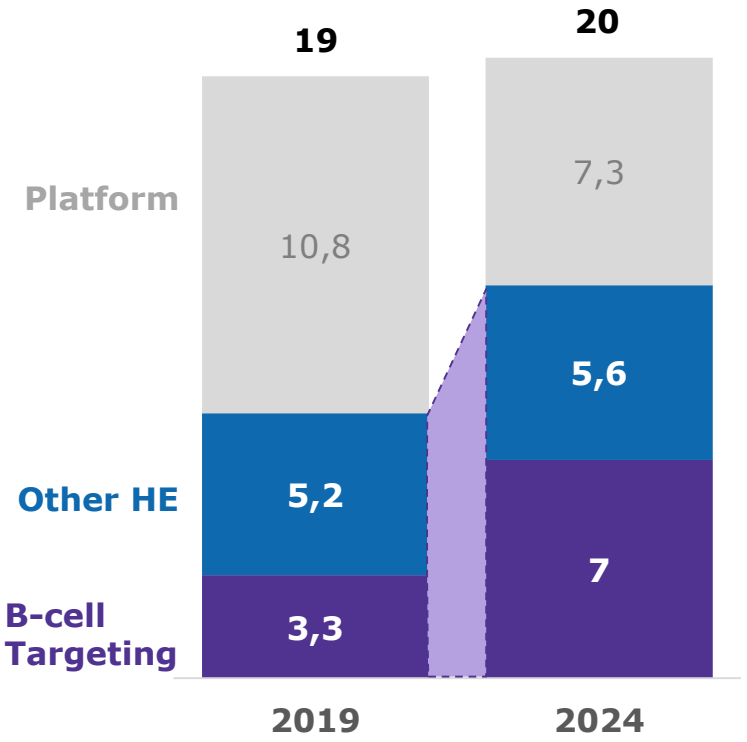
M5049
(TLR7/8 antagonist)

Evobrutinib (Investigational oral BTK-inhibitor)
Leading in a novel class with significant growth potential

Unmet need in Multiple Sclerosis (MS) – Need for new mechanisms to control disease

- **~50% of patients with Relapsing MS (RMS) continue to have ongoing disease activity** over 2 years even when treated with the most effective agents
- No approved oral therapy with **efficacy on progression vs an active control**
- **Systemic side effects** of therapies limit patient acceptance and compliance
- All approved higher efficacy therapies **associated with elevated risk of infection**

Worldwide MS Market [€ bn][1]



B-Cell Targeting + High-Efficacy (HE) Orals represent >60% of MS sales

- **BTKi is a novel class** of non-depleting therapies selectively targeting both B-cells and innate immune cells including disease progression-relevant microglia
- **Merck KGaA, Darmstadt, Germany pioneered BTKi development** for MS with Evobrutinib, **a highly selective covalent BTKi**[2]
- **We are** a **growing MS player** and could have 3 complementary branded products by 2025 – Mavenclad®, Rebif®, Evobrutinib

Platform agents – interferons, copaxone, DMFs and Teriflunomide; Other HE (high-efficacy) - cladribine, S1Ps, alemtuzumab; B-cell Targeting – ocrelizumab, ofatumumab, ublituximab. Includes branded products, generics and biosimilars; 1: Merck KGaA, Darmstadt, Germany internal estimates; 2: Montalban et al. NEJM 2019; 380:2406-2417; Acronyms: BTKi = Bruton's tyrosine kinase inhibitor

Evobrutinib (Oral BTK-inhibitor)

Most extensive efficacy and safety data among BTKis in MS

Efficacy and Safety Profile Maintained Long Term (Ph II)

Phase II: 108 weeks OLE data at EAN 2020[1]

- **Only BTKi to have demonstrated mAb-like efficacy on relapses** maintained over 108 weeks with evobrutinb 75 mg BID
- **Best characterized BTKi in MS on safety:** generally well tolerated and characterized in >1200 patients over 2 years of treatment in RMS, RA & SLE

CNS Effect on Progression

Evobrutinib may impact number of progression-relevant mechanisms

- BTK increased in brains of progressive models and MS patients, primarily in microglia[2]
- BTKi shifts macrophage phenotypes from pro- to anti-inflammatory[3]
- BTKi improves remyelination by microglia[4]
- BTKi reduces B cells and CNS leptomeningeal inflammation[5]

Optimal Dose Selection

The largest and most sustained efficacy on ARR was achieved at >95% steady state BTK occupancy, observed in nearly all patients receiving 75 mg BID[1]

Dose selection based on efficacy and BTK occupancy data from the **largest RCT** that tested both QD and BID BTKi

Highly Selective

Evobrutinib is a potent, highly selective, covalent BTKi[6]

Potent impact on B cell activation and macrophage polarization[3,6]

Only impacts a single off-target kinase out of 267 tested (IC_{50} determination)[6]

Covalent BTKi enabling use at lower exposure levels than non-covalent inhibitors

evolutionRMS

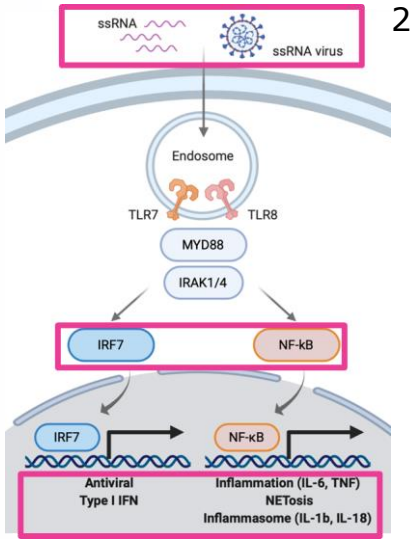
Phase III studies: Recruitment on track → Target data in-house in Q4 2023 and potential filing shortly after

Two randomized, parallel-group, double-blind, active-controlled Phase III studies of oral evobrutinib bid vs oral teriflunomide qd, in patients with RMS, with the objective of evaluating efficacy and safety. *Only BMX was determined to have an IC50 value within 10 fold of the intended target out of 218 tested; 1: Montalban et al. 2020 EAN; 2: Gruber et al. AAN 2020.; 3: Alankus YB et al. ECTRIMS 2018; 4: Aigrot MS et al. AAN 2020; 5: Sol Kim ECTRIMS 2020; 6: Haselmayer et al 2019; Acronyms: ARR = Annual relapse rate; BID = twice daily; BTKi = Bruton's tyrosine kinase inhibitor; CNS = Central Nervous System; mAb = monoclonal antibody; OLE = Open Label Extension; QD = once daily; RA = Rheumatoid arthritis; RCT = Randomized controlled trial; SLE = Systemic lupus erythematosus

M5049 (TLR7/8 antagonist)
TLR7/8 are drivers of SLE pathology and possibly of COVID-19

Mechanism of Action[1]

- M5049 (**discovered in-house**) is a **potentially first-in class small molecule** that blocks activation of Toll-like receptors TLR7 and TLR8, two innate immune sensors that detect single-stranded (ss) RNA from viruses such as SARS-COV-2, the virus responsible for COVID-19, and inflammatory self-RNAs in the context of autoimmunity
- Activation of TLR7/8 leads to immune cell activation and inflammation, which when not properly controlled can cause severe immunopathology



2

Results from Phase I study in healthy volunteers
(NCT03676322)[1]

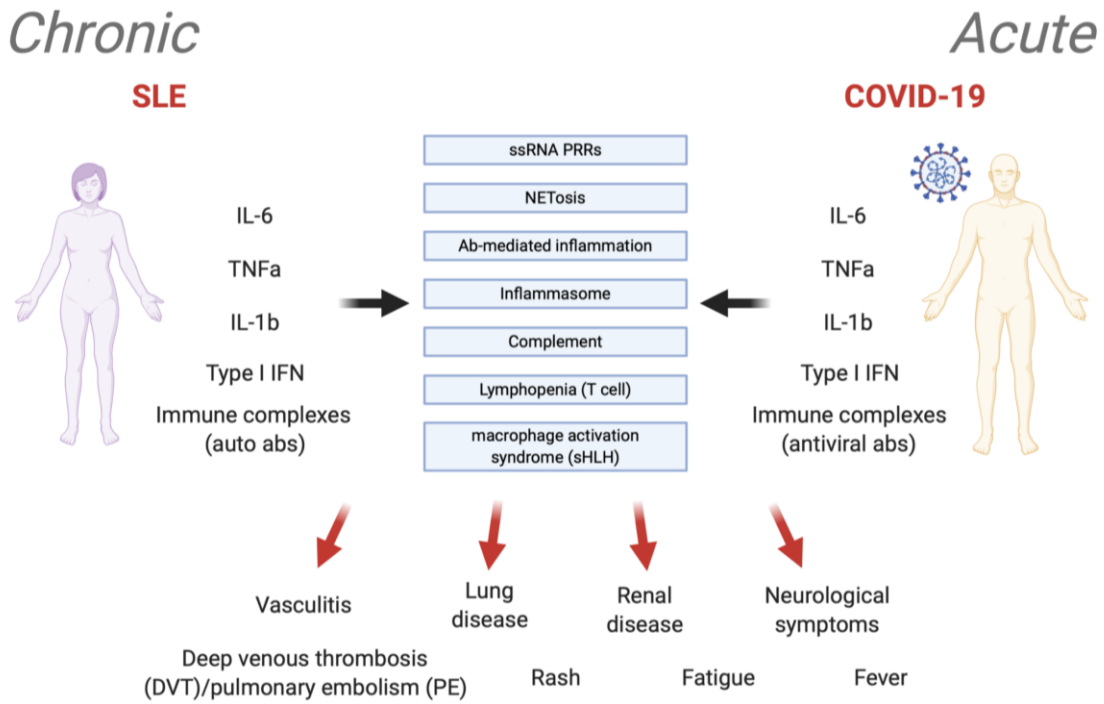
- **Well-tolerated** over the dosing interval, no significant or dose-limiting adverse event
- Pharmacokinetic parameters linear and dose-proportional from 1 to 200 mg
- Exposure-dependent inhibition of ex vivo-stimulated IL-6 secretion observed, with maximum inhibition achieved at 200 mg

Preliminary Phase I data warrant further investigation as a potential treatment for autoimmune diseases including SLE

1: Port et al., A PHASE I, FIRST-IN-HUMAN STUDY TO ASSESS THE SAFETY, PHARMACOKINETICS AND PHARMACODYNAMICS OF SINGLE AND MULTIPLE ASCENDING DOSES OF M5049, A DUAL ANTAGONIST OF TLR7/8, IN HEALTHY SUBJECTS, Lupus Science & Medicine 2020;7(Suppl 1):A1–A131, conference cancelled due to COVID-19; 2 Adapted from ImmunoHorizons July 1, 2018 Dowling, D;
Acronyms: SLE = Systemic lupus erythematosus; TLR = Toll-like receptors

M5049 (TLR7/8 antagonist)
Similarities between SLE and COVID-19

Similarities between SLE and COVID-19[1]



Phase II study started in July 2020

Rational:

- Investigate if M5049 intervention at critical point in course of COVID-19 disease may prevent or ameliorate hyper-inflammatory response in patients with COVID-19 pneumonia and **prevent progression to 'cytokine storm'**
- Successful intervention with investigational drug may reduce life-threatening complications of COVID-19, including severe respiratory symptoms often necessitating further interventions such as mechanical ventilation

Design:

- Phase II randomized, controlled clinical study
- Commenced in July 2020

Results:

→ Dependent on recruitment and COVID-19 infection rates

1: Illustration created in-house; Acronyms: SLE = Systemic lupus erythematosus

Mavenclad®

Data at ECTRIMS further characterize unique profile, and launch momentum is recovering well globally after peak COVID-19 impact

Mavenclad® Real World Evidence

New Mavenclad® data at ACTRIMS-ECTRIMS highlight rapid onset of action and compelling post-approval safety

- **Onset of action:** In MAGNIFY-MS, patients experienced a **rapid onset of action from end of month 1 -** significant in all study periods versus baseline[1]
- **Post-approval safety:** Data on viral respiratory infections and malignancy **from the post-marketing setting** reassure on benefit-risk profile of Mavenclad®[1]
- **COVID-19:** Data from Mavenclad®-treated patients with confirmed or suspected COVID-19 **suggest no increased risk of severe outcomes**[1]
- **Persistence rates on therapy:** UK NHS data demonstrates that **Mavenclad® patients have very high persistence rates on treatment**[2]

US launch progress

- **Prescription trends:** New Rx **regaining momentum**, adding both new Rxer's and increasing Rxer depth in a not-as-yet recovered dynamic HE market[3]
- **Market share:** Mavenclad® has **continued to grow dynamic share** in HE segment and in the Oral segment throughout pandemic: +**1.6% HE dynamic, +3.0% Oral dynamic**[3]
- **Access:** Mavenclad® **reimbursement rate now on par** with established DMDs

Ex-US performance

- **Prescription trends:** **New initiations rebounding** after April low point across all major Ex-US markets, with very **good performance for year 2 return patients**[4]
- **Safety Perception:** Mavenclad® **continuing to improve safety perception as experience increases** vs. Q2 2019, on par with other HE MS treatments[5]
- **France received reimbursement in February: commercial launch preparation for H1 2021** on track

1: ECTRIMS/ACTRIMS 2020; 2: Retrospective real-world analysis conducted on NHS validated data (collected via Blueteq forms, n=1208 patients treated between November 2017 to March 2020); 3: IQVIA Projected National Claims; 4: Local IQVIA or respective in-market data; 5: Ipsos Q2 2020 EU5 & US MS Monitor; Acronyms: DMD = Disease modifying drugs; HE = High-Efficacy; Rxer = Prescriber

Executive Summary
Increasing momentum across the innovative medicines pipeline

- **10 NMEs with First-in-Class, Best-in-Disease or Best-in-Class potential** progressed to the clinic in the last 6 years
- **3 new medicines approved** across 6 indications since 2017

MAVENCLAD® (cladribine) tablets 10 mg
BAVENCIO® avelumab Injection 20 mg/mL
TEPMETKO® tepotinib

- **Confidence to generate ~€2 bn pipeline sales** by 2022
- Transformative early pipeline to **sustain growth beyond 2022**, including Bintrafusp alfa, Tepotinib, Evobrutinib, M5049 (TLR7/8), and DDR portfolio

Q&A
Participants - R&D and Commercial Leadership

Luciano Rossetti
Global Head of Research & Development

- Joined Merck KGaA, Darmstadt, Germany in 2014 after 8 years at Merck & Co.
- Spent 18 years in academia
- Previously professor of Medicine and Head of the Diabetes Research & Training Center at the Albert Einstein College of Medicine
- MD degree from the Trieste University Medical School, Italy

Rehan Verjee
Head of the Global Innovative Medicine Franchises & President of EMD Serono

- Joined Serono in 2004 in Medical Affairs
- Previously Managing Director of EMD in Canada, and then Chief Marketing & Strategy Officer
- Master's degree in Molecular & Cellular Biochemistry from the University of Oxford

Joern-Peter Halle
Head of Research

- Joined Merck KGaA, Darmstadt, Germany in 2005 in Business Development before moving on to R&D, most recently Head of TIP Immuno-Oncology & Head of External Innovation
- Co-founded start-ups in bioinformatics and dermatology R&D
- Ph.D. (Dr. rer. nat.) in Molecular Biology from the University of Konstanz, Germany

Klaus Edvardsen
Head of Oncology Development

- Joined Merck KGaA, Darmstadt, Germany in January 2020
- Industry experience at AstraZeneca, GlaxoSmithKline, Sanofi, Genmab
- Previously professor of Experimental Cancer Research/Medicine at Lund University
- MD and PhD degree from the University of Copenhagen

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Appendix

- Healthcare pipeline
- Additional information on selected assets
- Trial summaries by asset

Healthcare Pipeline
As of July 31, 2020

Phase I

berzosertib (M6620)
ATR inhibitor
Solid tumors

peposertib (M3814)
DNA-PK inhibitor
Solid tumors[1]

M1774
ATR inhibitor
Solid tumors

M3258
LMP7 inhibitor
Multiple myeloma

M4344
ATR inhibitor
Solid tumors

M8891
MetAP2 inhibitor
Solid tumors

bintrafusp alfa
TGFbeta trap/anti-PD-L1
Solid tumors

M9241 (NHS-IL12)
Cancer immunotherapy
Solid tumors[1]

M5049
TLR7/8 antagonist
Immunology

M6495
anti-ADAMTS-5 nanobody
Osteoarthritis

M5717
PeEF2 inhibitor
Malaria

Phase II

peposertib (M3814)
DNA-PK inhibitor
Rectal cancer

tepotinib
MET kinase inhibitor
Non-small cell lung cancer

bintrafusp alfa
TGFbeta trap/anti-PD-L1
Non-small cell lung cancer 1L

bintrafusp alfa
TGFbeta trap/anti-PD-L1
Non-small cell lung cancer 1L/2L

bintrafusp alfa
TGFbeta trap/anti-PD-L1
Locally advanced non-small cell lung cancer

bintrafusp alfa
TGFbeta trap/anti-PD-L1
Biliary tract cancer 1L

bintrafusp alfa
TGFbeta trap/anti-PD-L1
Biliary tract cancer 2L

bintrafusp alfa
TGFbeta trap/anti-PD-L1
Cervical cancer 2L

avelumab
anti-PD-L1 mAb
Solid tumors[2]

avelumab
anti-PD-L1 mAb
Non-small cell lung cancer[2]

avelumab
anti-PD-L1 mAb
Urothelial cancer[2]

M5049
TLR7/8 antagonist
Covid-19 pneumonia

atacicept
anti-BlyS/APRIL fusion protein
Systemic lupus erythematosus

atacicept
anti-BlyS/APRIL fusion protein
IgA nephropathy

sprifermin
fibroblast growth factor 18
Osteoarthritis

M1095 (ALX-0761)[3]
anti-IL-17 A/F nanobody
Psoriasis

Phase III

avelumab
anti-PD-L1 mAb
Non-small cell lung cancer 1L

evobrutinib
BTK inhibitor
Multiple sclerosis

Registration

tepotinib
MET kinase inhibitor
Non-small cell lung cancer, *MET*ex14 skipping[4]

avelumab
anti-PD-L1 mAb
Urothelial cancer 1L-M[5]

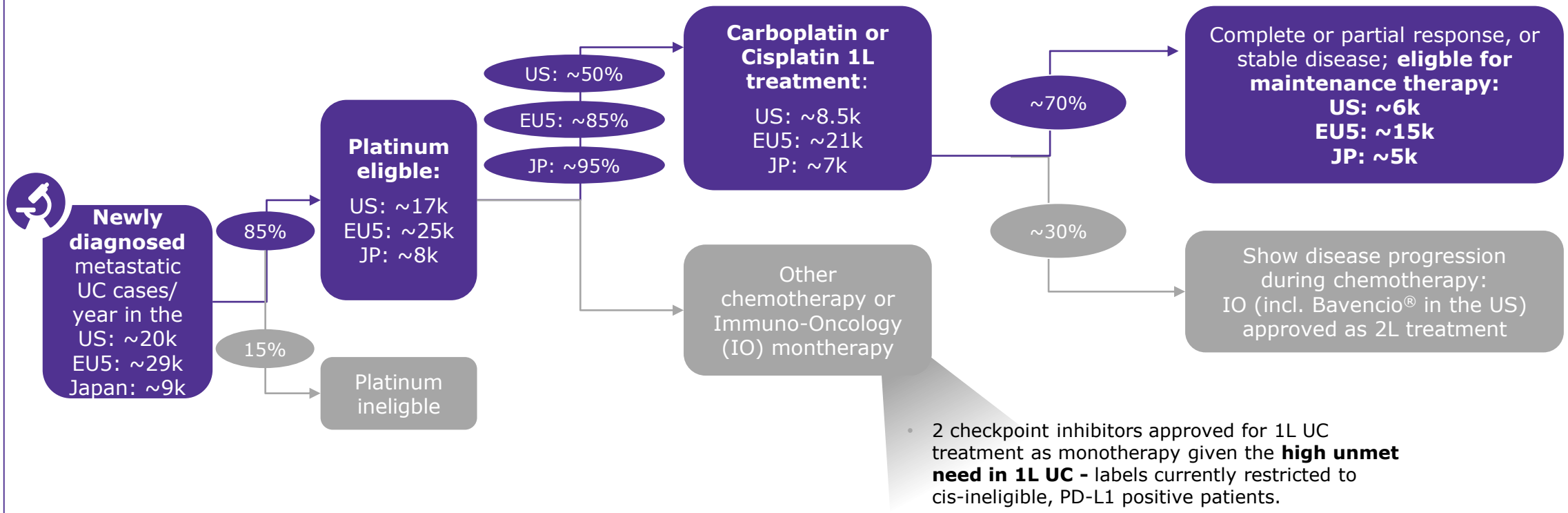
- Oncology
- Immuno-Oncology
- Immunology
- Neurology
- Global Health

1L, first-line treatment; 1L-M, first-line maintenance treatment; 2L, second-line treatment.1: Includes studies in combination with avelumab. 2: Avelumab combination studies with talazoparib, axitinib, ALK inhibitors, cetuximab, or chemotherapy. 3: As announced on March 30 2017, in an agreement with Avillion, anti-IL-17 A/F nanobody will be developed by Avillion for plaque psoriasis and commercialized by Merck KGaA, Darmstadt, Germany. 4: As announced on March 25 2020, tepotinib was approved in Japan for the treatment of patients with non-small cell lung cancer harboring *MET*ex14 skipping. 5: As announced on June 30, 2020, Avelumab was approved in US for maintenance treatment of patients with locally advanced or metastatic urothelial carcinoma (UC) that has not progressed with first-line platinum-containing chemotherapy.

Bavencio® (Avelumab)

Urgent need for a 1L treatment strategy that maintains and reinforces the initial benefit of induction chemotherapy

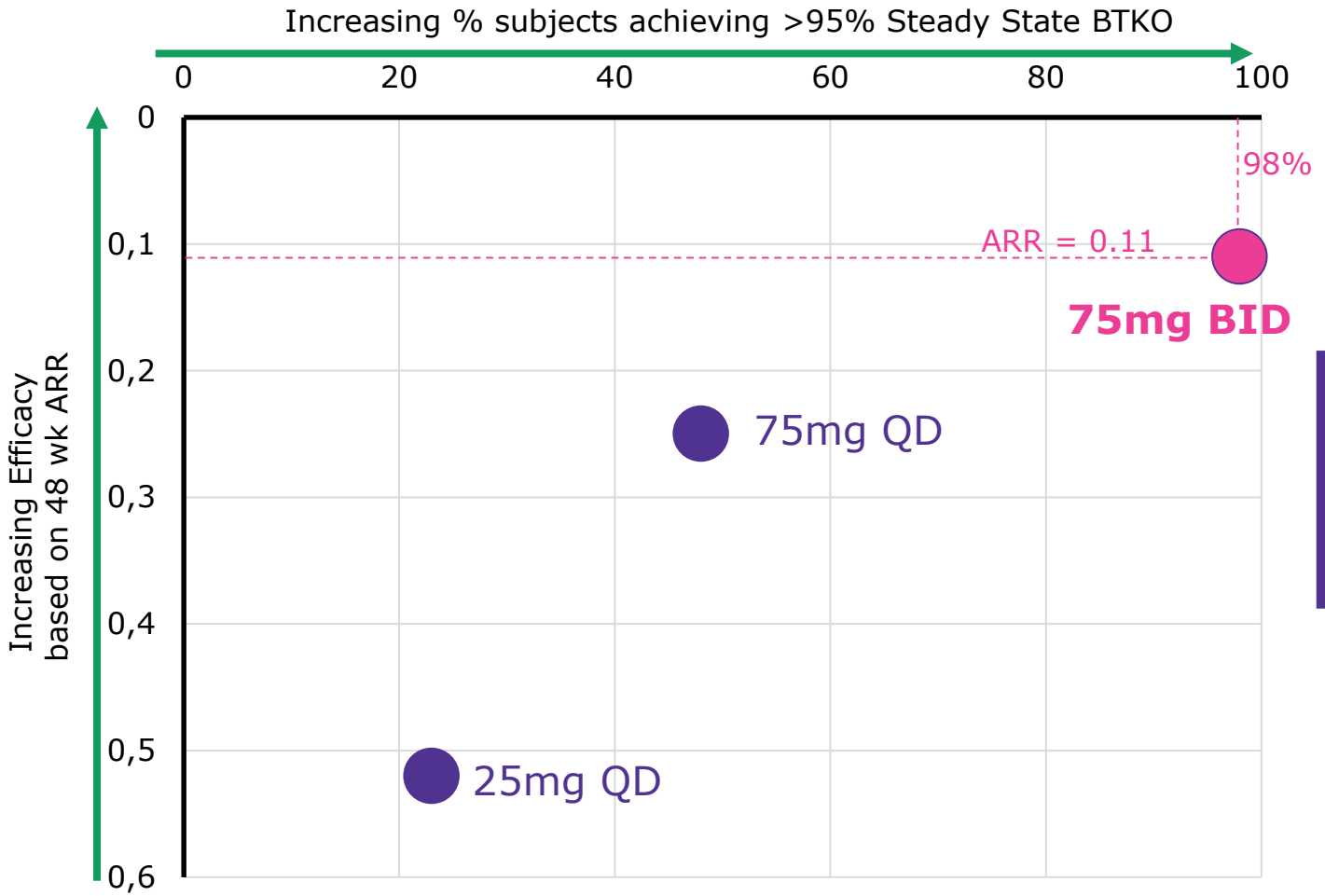
Durable responses to standard of care (1L chemotherapy) are rare with most patients experiencing progression within 9 months of treatment[1]



1: Kantar Health Patient Metrics & Kantar Health Treatment Architecture for epidemiological data; IMS Claims, Kantar and IPSOS for triangulation of market shares

Evobrutinib (Oral BTK-inhibitor)

Superior efficacy with BID dosing, based on the most comprehensive BTKi Phase 2 in Multiple Sclerosis[1]



Only BTKi Phase 2 study in MS that studied both QD and BID dosing

98% of subjects receiving evobrutinib 75mg BID achieved >95% Steady State BTKO

Median Steady State BTKO did not separate between doses - Values across doses were 90%, 96% and 98% for 25mg QD, 75mg QD and 75mg BID, respectively

1: Based on exposure:response modelling and 124 (35/46/43) pre-dose observations from 11–17 fasted patients per dose level on Weeks 4/12/24; Acronyms: ARR = annualized relapse rate; bid = twice daily; BTK = Bruton's tyrosine kinase; BTKO = BTK occupancy; RMS = Relapsing MS; qd = once daily; SS = steady-state. Montalban X et al. EAN 2020 & Data on file

Bavencio® (Avelumab)
Phase III Clinical Trials

Selected trials – List not exhaustive

Phase	Study	NCT number (hyperlinked)	Recruitment Status	Est. Primary completion date
III	Avelumab in First-line Non-Small Cell Lung Cancer (JAVELIN Lung 100)	NCT02576574	Active, not recruiting	April 23, 2021
III	A Study of Avelumab With Axitinib Versus Sunitinib In Advanced Renal Cell Cancer (JAVELIN Renal 101)	NCT02684006	Active, not recruiting	May 21, 2024

Bintrafusp alfa (anti-PD-L1/TGF-β Trap)
Clinical Trials

Selected trials – List not exhaustive

Phase	Study	NCT number (hyperlinked)	Recruitment Status	Est. Primary completion date
I	MSB0011359C (M7824) in Subjects With Metastatic or Locally Advanced Solid Tumors	NCT02699515	Active, not recruiting	December 31, 2020
I	Bintrafusp Alfa Combination Therapy in Participants With Cervical Cancer	NCT04551950	Not yet recruiting	May 28, 2022
I	First in Human Study of M6223 in Participants With Metastatic or Locally Advanced Solid Unresectable Tumors	NCT04457778	Recruiting	September 14, 2022
Ib	A Study to Evaluate the Efficacy and Safety of Bintrafusp Alfa (M7824) Monotherapy in Metastatic or Locally Advanced Urothelial Cancer	NCT04349280	Not yet recruiting	August 5, 2022
Ib/II	M7824 in Combination With Chemotherapy in Stage IV Non-small Cell Lung Cancer (NSCLC)	NCT03840915	Recruiting	October 28, 2021
II	M7824 Monotherapy in Locally Advanced or Metastatic Second Line (2L) Biliary Tract Cancer (Cholangiocarcinoma and Gallbladder Cancer)	NCT03833661	Active, not recruiting	November 9, 2020
II	M7824 With cCRT in Unresectable Stage III Non-small Cell Lung Cancer (NSCLC)	NCT03840902	Recruiting	March 4, 2024

Bintrafusp alfa (anti-PD-L1/TGF-β Trap)
Clinical Trials (continued)

Selected trials – List not exhaustive

Phase	Study	NCT number (hyperlinked)	Recruitment Status	Est. Primary completion date
II	Bintrafusp Alfa Monotherapy in Platinum-Experienced Cervical Cancer	NCT04246489	Recruiting	May 16, 2022
II	Bintrafusp Alfa in High Mobility Group AT-Hook 2 (HMGA2) Expressing Triple Negative Breast Cancer	NCT04489940	Not yet recruiting	February 23, 2023
II/III	Gemcitabine Plus Cisplatin With or Without Bintrafusp Alfa (M7824) in Participants With 1L Biliary Tract Cancer (BTC)	NCT04066491	Recruiting	November 24, 2022
Adaptive Phase III	M7824 Versus Pembrolizumab as a First-line (1L) Treatment in Participants With Programmed Death-ligand 1 (PD-L1) Expressing Advanced Non-small Cell Lung Cancer (NSCLC)	NCT03631706	Recruting	April 30, 2023

Tepotinib (MET kinase inhibitor)
Clinical Trials

Selected trials – List not exhaustive

Phase	Study	NCT number (hyperlinked)	Recruitment Status	Est. Primary completion date
II	Tepotinib Phase II in Non-small Cell Lung Cancer (NSCLC) Harboring MET Alterations (VISION)	NCT02864992	Recruiting	December 9, 2021
II	A Study of Tepotinib Plus Osimertinib in Osimertinib Relapsed Mesenchymal-epithelial Transition Factor (MET) Amplified Non-small Cell Lung Cancer (NSCLC) (INSIGHT 2) (INSIGHT 2)	NCT03940703	Recruiting	November 30, 2022
II	Study of Tepotinib Combined With Cetuximab in Participants Left-Sided Metastatic Colorectal Cancer (mCRC) Acquired Resistance Due to Mesenchymal Epithelial Transition (MET) Amplification	NCT04515394	Not yet recruiting	March 23, 2023

DNA Damage Response (DDR) Portfolio
Selected Clinical Trials – Berzosertib (M6620)

Selected trials – List not exhaustive

Phase	Study	NCT number (hyperlinked)	Recruitment Status	Est. Primary completion date
I	M6620 and Irinotecan Hydrochloride in Treating Patients With Solid Tumors That Are Metastatic or Cannot Be Removed by Surgery	NCT02595931	Recruiting	April 30, 2021
II	Gemcitabine Hydrochloride Alone or With M6620 in Treating Patients With Recurrent Ovarian, Primary Peritoneal, or Fallopian Tube Cancer	NCT02595892	Active, not recruiting	March 19, 2021
II	Randomized Trial of Topotecan With M6620, an ATR Kinase Inhibitor, in Small Cell Lung Cancers and Small Cell Cancers Outside of the Lungs	NCT03896503	Recruiting	September 1, 2023

DNA Damage Response (DDR) Portfolio
Selected Clinical Trials – Peposertib (M3814)

Selected trials – List not exhaustive

Phase	Study	NCT number (hyperlinked)	Recruitment Status	Est. Primary completion date
I/II	Study of M3814 in Combination With Capecitabine and Radiotherapy in Rectal Cancer	NCT03770689	Recruiting	July 31, 2021
I	Study of Avelumab-M3814 Combinations	NCT03724890	Recruiting	April 13, 2021
I	Phase 1 Trial of MSC2490484A, an Inhibitor of a DNA-dependent Protein Kinase, in Combination With Radiotherapy	NCT02516813	Recruiting	December 16, 2020
I/II	Testing the Addition of a New Anti-cancer Drug, M3814 (Peposertib), to Radiation Therapy for Localized Pancreatic Cancer	NCT04172532	Not yet recruiting	November 1, 2022
I/II	Testing the Combination of New Anti-cancer Drug Nedisertib With Avelumab and Radiation Therapy for Advanced/Metastatic Solid Tumors and Hepatobiliary Malignancies	NCT04068194	Recruiting	December 3, 2022
I/II	Radiation Medication (Radium-223 Dichloride) Versus Radium-223 Dichloride Plus Radiation Enhancing Medication (M3814) Versus Radium-223 Dichloride Plus M3814 Plus Avelumab (a Type of Immunotherapy) for Advanced Prostate Cancer Not Responsive to Hormonal Therapy	NCT04071236	Recruiting	January 31, 2023

DNA Damage Response (DDR) Portfolio
Clinical Trials – Oral ATRi's M4344 & M1774

Phase	Study	NCT number (hyperlinked)	Recruitment Status	Est. Primary completion date
I	First in Human Study of M4344 in Participants With Advanced Solid Tumors	NCT02278250	Recruiting	June 30, 2021
I	M1774 in Participants With Metastatic or Locally Advanced Unresectable Solid Tumors	NCT04170153	Recruiting	September 13, 2021

Evobrutinib (oral BTKi)
Clinical Trials

Selected trials – List not exhaustive

Phase	Study	NCT number (hyperlinked)	Recruitment Status	Est. Primary completion date
III	Study of Evobrutinib in Participants With Relapsing Multiple Sclerosis (evolutionRMS 1)	NCT04338022	Recruiting	September 18, 2023
III	Study of Evobrutinib in Participants With Relapsing Multiple Sclerosis (RMS) (evolutionRMS 2)	NCT04338061	Recruiting	September 18, 2023
I	Effect of Hepatic Impairment on M2951 (Bruton's Tyrosine Kinase [BTK] Inhibitor) Pharmacokinetics (PK)	NCT04546789	Not yet recruiting	June 29, 2021

M5049 (TLR7/8 antagonist)
Clinical Trials

Phase	Study	NCT number (hyperlinked)	Recruitment Status	Est. Primary completion date
I	Single Ascending Dose (SAD) and Multiple Ascending Dose (MAD) Study of M5049 in Healthy Participants	NCT03676322	Completed	Actual: July 26, 2019
II	M5049 Study in Participants With Coronavirus Disease 2019 (COVID-19) Pneumonia (ANEMONE)	NCT04448756	Recruiting	November 13, 2020