MOLOGEN AG
THE POWER OF IMMUNOTHERAPIES

# 8. DVFA FRÜHJAHRSKONFERENZ

## DR. MARIOLA SÖHNGEN – VORSTANDSVORSITZENDE

## FRANKFURT, 9. MAI 2017

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# Agenda

# MOLOGEN Snapshot

- Based in Berlin, Germany; founded 1998
- Approx. 50 employees
- One of the pioneers in immunotherapies
- Focus on family of TLR9 agonists:
  - Immunotherapy lefitolimod
  - Next-generation technology EnanDIM®
- Highly attractive markets: A multi-billion US$ market
- Network with scientific institutions and experts



Aarhus University Hospital

CHARITÉ

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center

Freie Universität Berlin

MDC MAX DELBRÜCK CENTER FOR MOLECULAR MEDICINE BERLIN-BUCH

# MOLOGEN Summary Highlights

| | |
|---|---|
| Advanced immunotherapy player | • Management with clear commercial focus and strong track record of previous successes<br>• Leading German research player transitioning to global market-ready company<br>• Strong value-generating pipeline with lead product lefitolimod in two late-stage trials and two earlier clinical programs, as well as follow-up compounds being qualified for trials in man |
| Safe & well tolerated lead product | • Lefitolimod has the potential to re-activate the immune system<br>• Single-agent potential in oncology as well as infectious diseases<br>• Combination therapy potential augmenting other existing effective treatments |
| Multi-billion dollar target markets | • mCRC (phase III): sizeable market; immunogenic disease<br>• SCLC (phase II): highly lethal; limited treatment advances; short survival times, exploratory study; 04/17: top-line results<br>• Combination treatment in solid tumors (phase I): broad market opportunity including potential for collaborations<br>• HIV (phase I): potential to eradicate rather than manage infection |
| Value-generating milestones ahead | • Advanced clinical development of lefitolimod (2 study read-outs in 2017: TEACH & IMPULSE)<br>• Progress follow-up compounds<br>• Adjust organization to late-stage development needs (esp. manufacturing scale-up)<br>• Propel outlicensing activities |



**Legend: HIV** human immuno-deficiency virus | **mCRC** metastatic colorectal cancer I **SCLC** small cell lung cancer

# Strengthened Executive Board:
# Clear Commercial Focus & Successful Track Record

**Dr Mariola Söhngen, CEO**

- 29 years biotech industry and corporate leadership experience as founder and former Board Member of Paion
- 15 key successful out-licensings at Paion across the globe

**Walter Miller, CFO**

- 21 years industry as well as financial expertise from leadership positions at Nuvisan and Santhera Pharmaceuticals AG
- Successful IPO of Santhera

**Dr Matthias Baumann, CMO**

- 27 years industry expertise from medical leadership positions in pharma and biotech, most recently at Noxxon and Focus Clinical Drug Development (a CRO)

- Highly experienced senior leadership team focused on value generation

**Legend: IPO** initial public offering | **CRO** contract research organization

# Next Level Strategy:
# Transition to Commercial Enterprise


*Focus on basic research*

- Broad pipeline comprised of three technology platforms
- Own in-house R&D-scale production (trials fully stocked)

*Focus on commercial activities*

- Pipeline focus on lead compound & follow-up
- Streamlined structure, operational efficiency
- Structured partnering/ licensing activities
- US strategy being defined

*Harvest lefitolimod potential*

- Expansion of business development activities with the aim to conclude a license or cooperation agreement
- Enable commercial-scale production; transition to CMO
- Enhance flexibility of cost structure
- (Pre-) clinical development of projects

**Legend: CMO** Contract Manufacturing Organization

# Advanced Immunotherapy Pipeline: Late-Stage Lefitolimod & Follow-Up EnanDIM®

| | Indication[1] | PC | Ph I | Ph II | Ph III | Timeline[2] | Exclusivity[3] |
|---|---|---|---|---|---|---|---|
| Lefitolimod | **Metastatic colorectal cancer (mCRC)** | | | | IMPALA (MGN) | LPI: first months'17<br>Data: '19<br>Filing: '19/'20 | EU: 2030<br>US: 2028 |
| Lefitolimod | **Small-cell lung cancer (SCLC)** | | | IMPULSE (MGN) | | 04/17: top-line results | EU: 2030<br>US: 2028 |
| Lefitolimod | **Advanced solid malignancies** (+ ipilimumab) | | MD Anderson | | | LPI: '18<br>Data: '19 | EU: 2036<br>US: 2036 |
| Lefitolimod | **Human immunodeficiency virus (HIV)** | | TEACH (Aarhus) | | | LPI: '16<br>Data: '17 | EU: 2036<br>US: 2036 |
| EnanDIM® | **Cancer/ infect. diseases** | | | | | Pre-clinical | EU: 2035<br>US: 2035 |
| MGN1601 | **Renal cell carcinoma (RCC)** | | ASET (MGN) | | | Ph I / II data available<br>backup compound | EU: 2036<br>*orphan drug status*<br>US: 2038 |



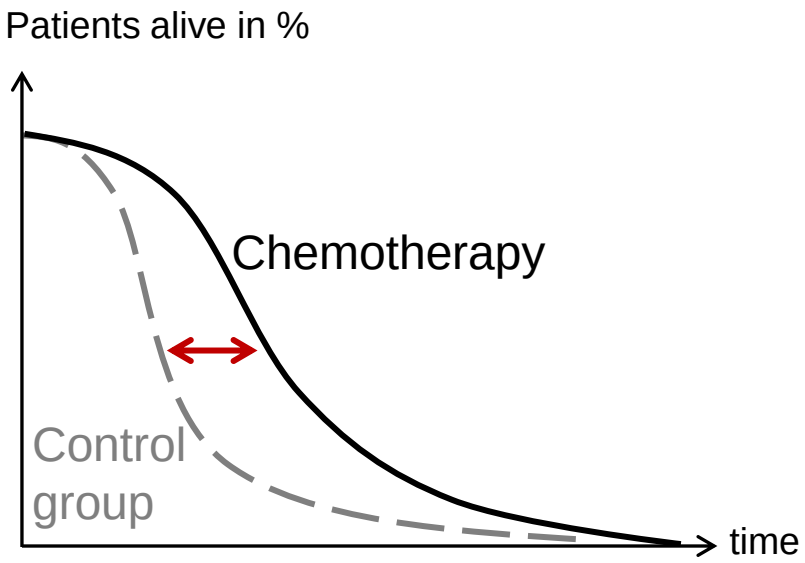
**Notes:** (1) Pipeline overview excludes MIDGE platform | (2) **Timeline** Denotes latest estimated timeline of upcoming milestones | (3) **Exclusivity** Denotes estimated minimum market exclusivity horizon based on patent and data protection

**Legend**: PC Pre-clinical | Ph Phase | LPI last patient in

# Cancer Immunotherapy Value Proposition: Improve Long-Term Overall Survival

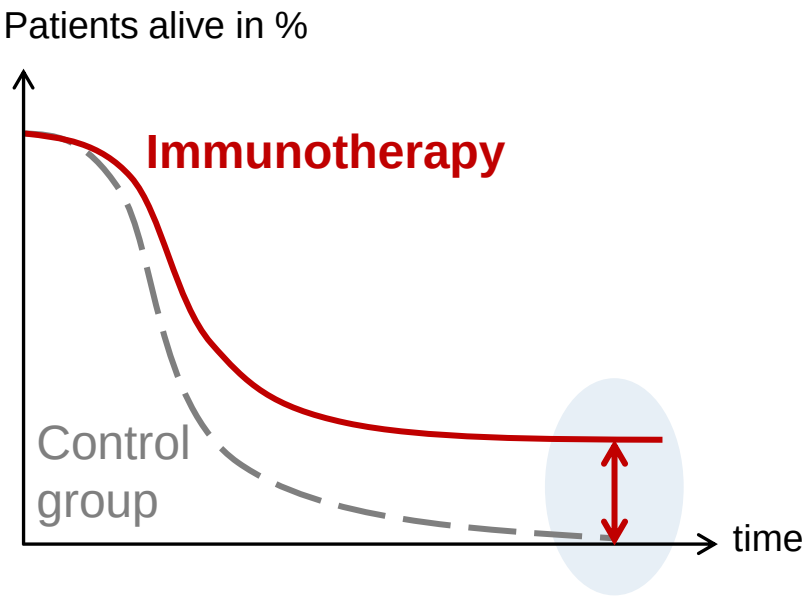
**Traditional Chemotherapy**

- Fast effect in many patients
- Effect not lasting




**Immunotherapy**

- Needs time to be effective
- Long-lasting effect in a subgroup of patients



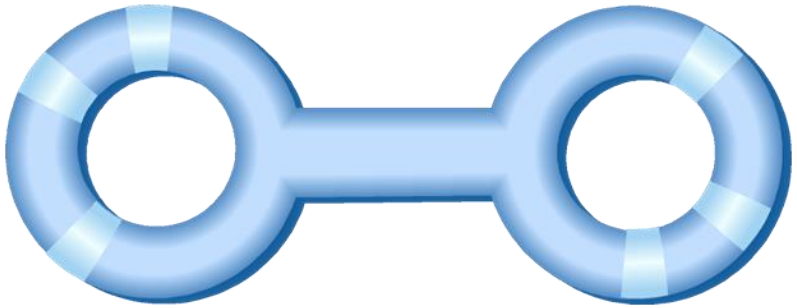

- Immunotherapies target improving OS at the long end of the curve



**Source:** "Immuno-oncology: The new weapon in the war against cancer", Alistair Campbell; Berenberg Equity Highlights, February 2014. **Legend: OS** overall survival.

# Safe and Well Tolerated Immunotherapy: “Best in Class“ TLR9 Agonist Lefitolimod

**Molecular Structure**



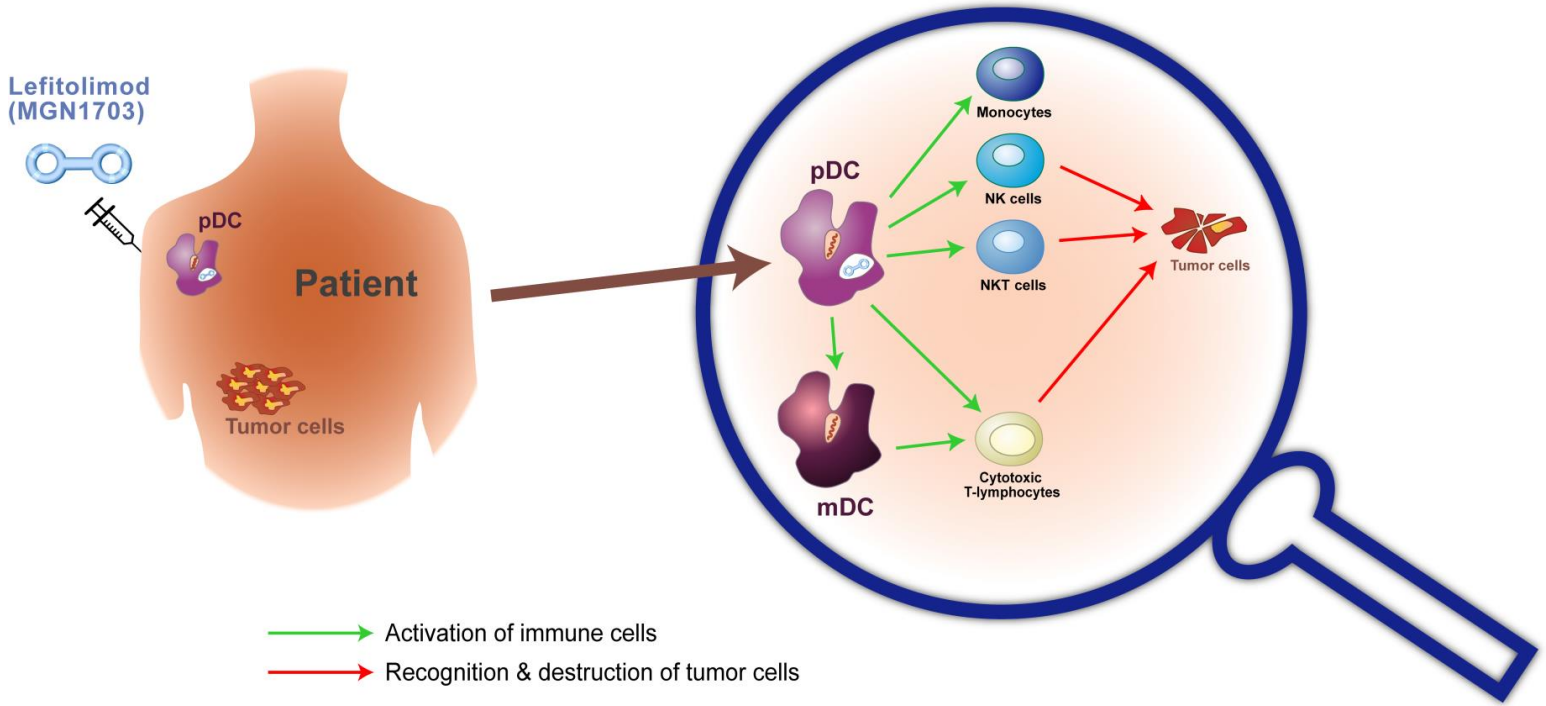
**Commentary**

- Immunologic activation and good safety profile due to molecular composition
  - Safety established in ~400 patients to date
- High dosing over long periods of time – as required to trigger clinical benefit – possible without major toxic effects
- Clinical strategy optimized for lefitolimod TLR9 activation pattern

- Lefitolimod is geared to success given its combination of safety and tolerability by design with large potential for clinical benefit

**Light blue area**: Motifs recognized by TLR9 receptor

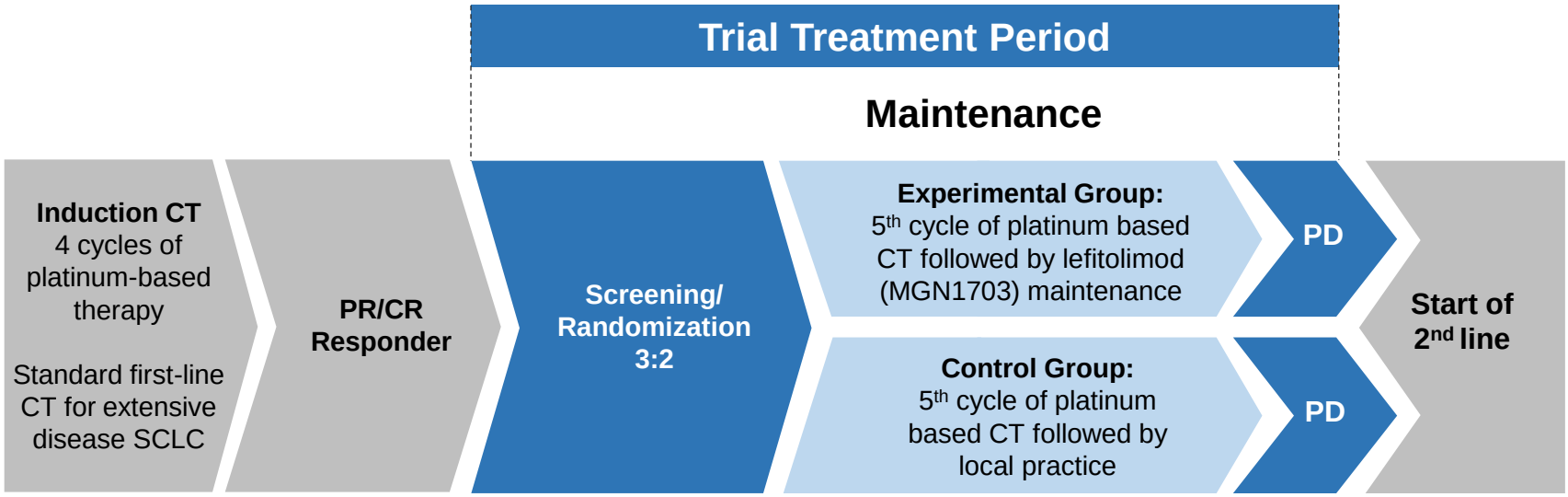
# Safe and Well Tolerated Lead Product: Mode of Action in Oncology




- The patient's immune system generally polices the development of cancer cells – occasionally, cells evade that system, developing into cancer
- Lefitolimod reactivates the patient's own immune system for anti-cancer surveillance
- Lefitolimod can work safely alongside other treatments leveraging the body's own immune surveillance system

**Legend: mDC** myeloid dendritic cell I **NK cell** natural killer cell I **NKT cell** natural killer T cell I **pDC** plasmacytoid dendritic cell

# IMPULSE: Exploratory Phase II Randomized Study in Small Cell Lung Cancer (SCLC)




**Study design**

- Controlled, two-arm, multinational trial with 102 pts in Belgium, Austria, Germany and Spain
- Biomarkers used as stratification factors: NSE level and NKT activation

**Efficacy**

- Primary endpoint: overall survival (OS)
- Secondary endpoints: progression-free survival (PFS), best objective response rate (ORR), quality of life (QOL), biomarkers

**Safety**



**CR** complete response | **CT** chemotherapy | **NKT** Natural Killer T cells | **NSE** neuron specific enolase - a tumor marker for lung cancer
**PD** progressive disease | **PR** partial response | **SCLC** small cell lung cancer

# IMPULSE: Positive Results in Two Subgroups of Patients Treated with lefitolimod

IMPULSE: Exploratory phase II controlled, two-arm, multinational trial with 102 patients with extensive disease small cell lung cancer (SCLC) to evaluate efficacy and safety of lefitolimod in comparison to control group (standard therapy)

- Primary endpoint “overall survival” (OS) not met in the overall study population in this challenging indication
- Positive results in two pre-defined and clinically relevant **subgroups of patients:** Notably, a strong overall survival (OS) benefit was shown in comparison to the control arm (local standard of care):

  1. Patients with a **low count of activated B cells**, an important immune parameter:

     Hazard ratio “HR”: 0.59; 95% confidence interval “CI”: 0.29–1.21

  2. Patients with reported **Chronic Obstructive Pulmonary Disease (COPD)**, a frequent underlying disease:

     Hazard ratio “HR”: 0.54; 95% confidence interval “CI”: 0.21–1.38

- Additional, potentially promising subgroups will be explored
- In this highly challenging indication the primary endpoint OS was not met in the overall study population

Results provide significant guidance for defining patient populations most likely to benefit from lefitolimod

# Favorable Safety Profile of Lefitolimod

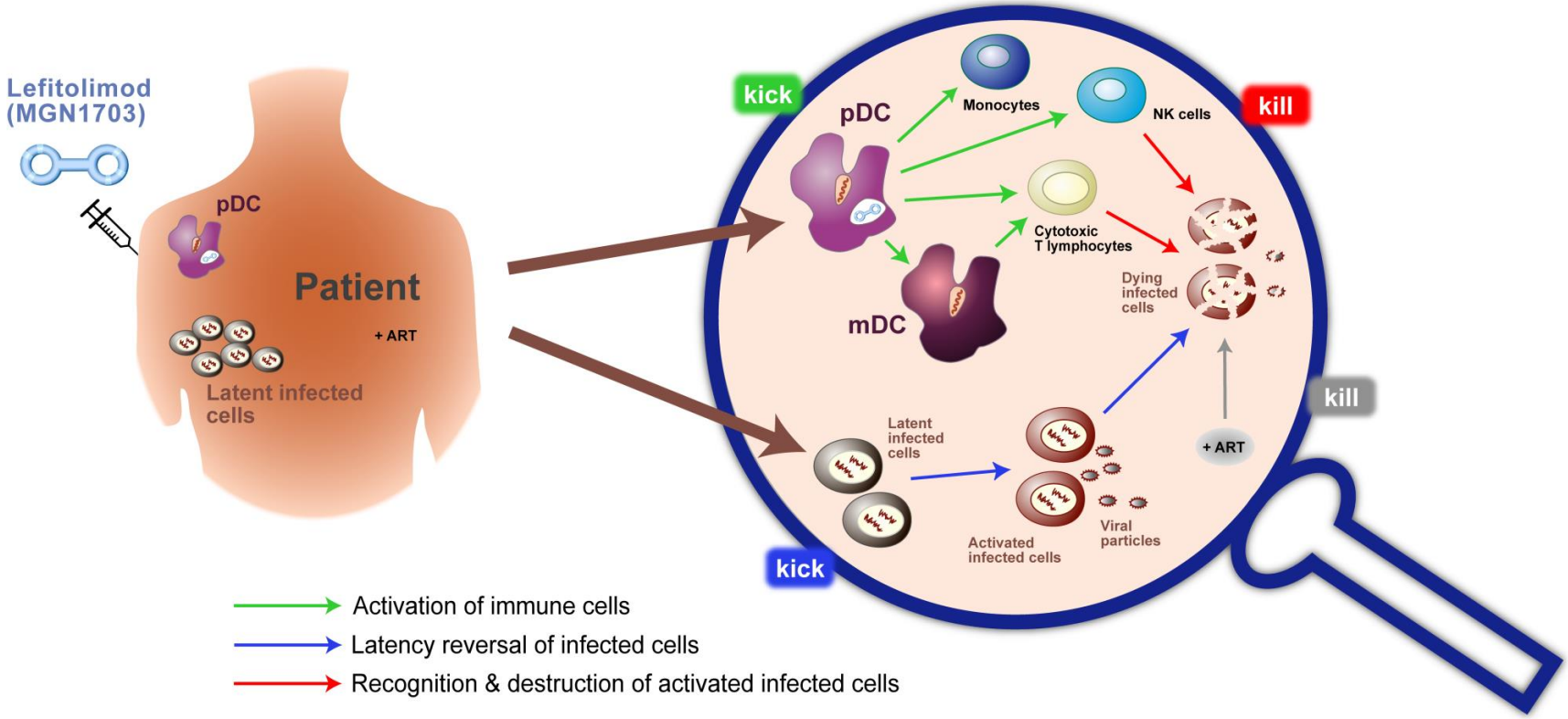
The most common adverse events (AE) in the IMPULSE population were:

| Adverse events | Lefitolimod | Control Group |
|---|---|---|
| Cough | 25.0% | 7.7% |
| Asthenia | 13.3% | 17.9% |
| Headache | 21.7% | 5.1% |
| Nausea | 11.7% | 20.5% |
| Back pain | 13.3% | 12.8% |

# Next Steps

- Extensive evaluation of the data is ongoing
- More detailed results will be presented at international scientific congresses
- Positive study results are important asset in ongoing partnering discussions
- Final read out probably in the first quarter 2018; approximately 24 months following the recruitment of the last patient

# Safe and Well Tolerated Lead Product: Mode of Action in HIV



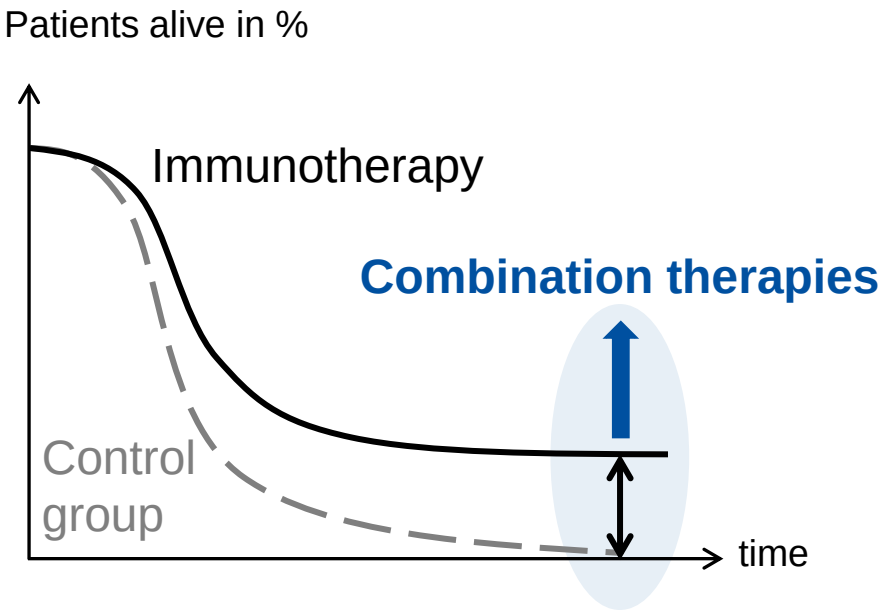

- Patients on ART are cleared from actively-infecting HI viruses, but T cells keep the remaining virus load in its latent stage (no immune response against the virus)
- Lefitolimod as “kick & kill” agent kicks the virus from latency into active infection, and reactivates immune surveillance to kill infected cells by NK cells and CTL



**Legend: ART** anti-retroviral therapy | **HIV** human immuno-deficiency virus | **pDC** plasmacytoid dendritic cell | **mDC** myeloid dendritic cell | **NK cell** natural killer cell | **CTL** cytotoxic T lymphocytes

# Safe and Well Tolerated Lead Product: Combination Therapies Represent the Next Opportunity

**Combination Therapy Potential**




**Commentary**

- Combination treatments aim to combat a disease through various synergistic ways
- Expected to play integral role in future new immunotherapy approaches or breakthrough outcomes
- Increased research – and business development – across the market
- Lefitolimod uniquely positioned as potential “combination partner of choice”

- Combination therapies are the latest advancement in the fight against several global diseases including cancer & HIV

**Source:** "Immuno-oncology: The new weapon in the war against cancer”, Alistair Campbell; Berenberg Equity Highlights, Feb 2014

# Lefitolimod: Clinical Trials

## **HIV:** *Phase I*

- Two-stage single-center "TEACH" trial
  - Aarhus University Hospital (DEN)
- *Status:* started Jun-2015
  - Stage 1 successfully completed (13 patients)
  - Stage 2 first patient Jun-2016 (13 patients)
- *Aim:* to define value in kick and kill concept in HIV / infectious diseases
- *Target:* read-out 2017

## **mCRC:** *Phase III*

- Pivotal multicenter (122) EU (8 countries) study "IMPALA"
- *Status:* started Sep-14; target 540 patients
- Patient recruitment to be finalized shortly
- *Aims:* to compare OS vs. local standard of care & to enable regulatory approval
- *Targets*[(1)]*:* read-out 2019 (event driven), filing 2019/ 2020

**Lefitolimod**
(MGN1703)

## **SCLC:** *Phase II*

- Multicenter (41) EU (4 countries) study "IMPULSE"
- *Status:* started Mar-14 with recruitment of 102 patients completed Oct-15;
  Apr-17: Positive results in two pre-defined subgroup of pts.
- *Aims:* to compare OS vs. local standard of care, to inform development pathway in SCLC, to further support safety data base

## **Solid Tumors:** *Phase I*

- Single-center proof-of-concept trial combining lefitolimod with checkpoint inhibitor ipilimumab (Yervoy®)
  - MD Anderson (US)
  - 50-60 patients envisaged
- *Status:* started Jul 2016 (first patient in)
- *Aim:* to inform development pathway in combination treatments
- *Target:* read-out 2019

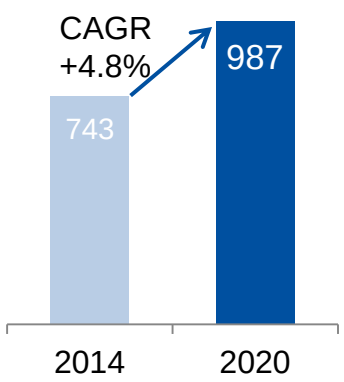
- MOLOGEN is developing its lead compound in various directions



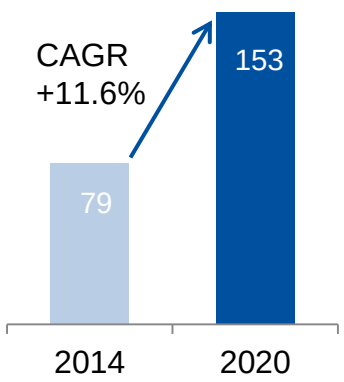
**Legend: HIV** human immune deficiency virus | **mCRC** metastatic colorectal cancer | **SCLC** small-cell lung cancer
**Note:** (1) Subject to actual overall survival (amongst others)

# Multi-Billion US$ Markets in Oncology: Strong Fundamentals and Significant Unmet Needs

**WW Prescription Drugs[1]**



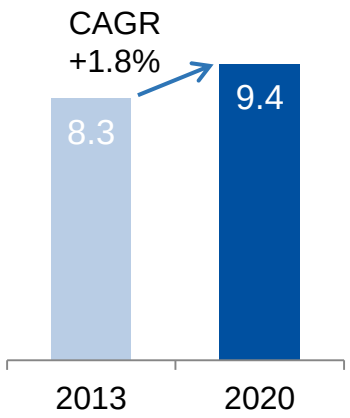

**WW Oncology Drugs[1]**



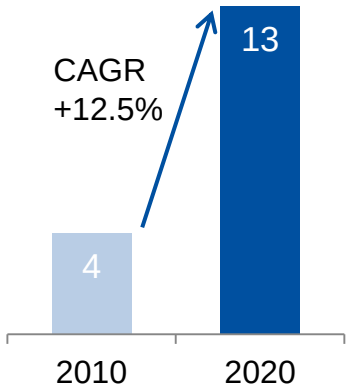

**Sales in US$ bn**

- Oncology is expected to be among the largest and fastest growing therapeutic areas worldwide
- Cancer immunotherapies represent a huge market potential: ~US$ 35 bn

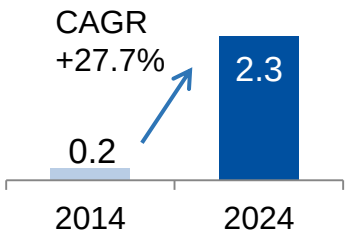
**Colorectal Cancer[2]**




**Lung Cancer[3]**




**SCLC[4]**

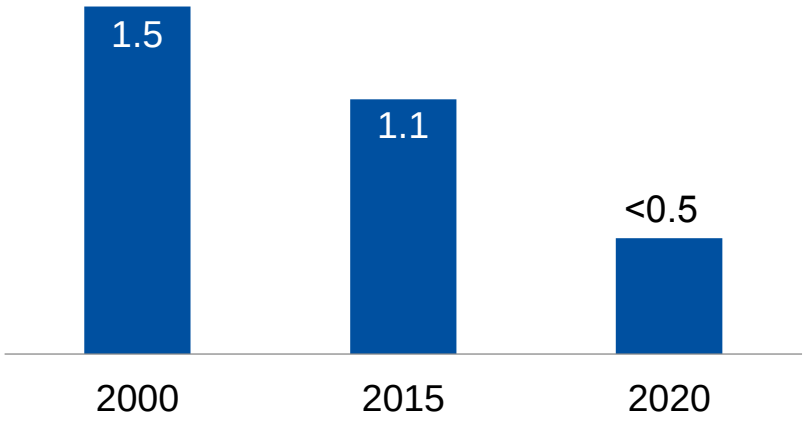





**Source:** [1]EvaluatePharma 2015 | [2]ResearchandMarkets Jan 2015 (5 EU, US, Japan & Canada) | [3]MarketsandMarkets Nov 2011 (G7 Countries) | [4]GlobalData, Jan 2016 (5 EU, US, Japan) | **Legend: CAGR** Compound Annual Growth Rate I **WW** worldwide

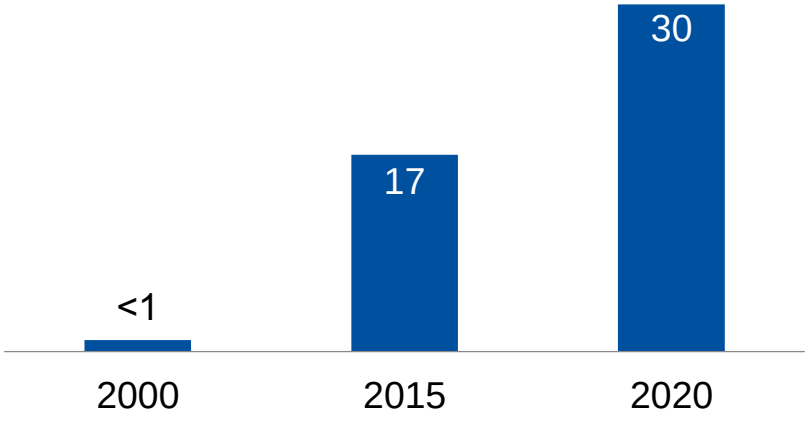
# Multi-Billion Dollar Markets in HIV: Increasing Number of Patients Living with HIV

**AIDS-Related Deaths (in million)**




- Better diagnostics
- Improved treatment regimens
- Price reductions of medicines

**People Living with HIV on ART (in million)**




- Growing patient population
- ART represents no cure
- Patients remain infectious

- People living with HIV have opened a market for drugs like lefitolimod
- Eradicating HIV would prevent risks of further transmission and of viremia, while improving QOL



**Source**: UNAIDS; “Global AIDS Update” (worldwide), 2016 | **ART** antiretroviral therapy | **QOL** Quality of Life

# Follow-Up Molecules EnanDIM®: Next-Generation TLR9 Agonists

| Linear DNA-structure | Lefitolimod | EnanDIM® |
|---|---|---|
|  |  |  |
| • Linear molecules<br>– Simple, cost-effective production<br>• Stability through chemically modified structure<br>– Usually unfavorable risk / benefit ratio | • Stability through closed, dumbbell-shaped structure<br>– Complex production<br>• Only natural DNA components<br>– Good safety and tolerability profile | • Linear molecules; stability through specific feature<br>– Simple, cost-effective production<br>• No chemical modifications<br>– Good safety and tolerability profile expected |

- New family of linear TLR9 agonists, combining safety of molecules containing only natural DNA components with simple production process of linear molecules
  - Allow drug differentiation on molecular level
- Broad immune activation and anti-tumor effect shown in pre-clinical models
- Potential application in cancer and in anti-infective therapies



**Legend: EnanDIM®** Enantiomeric DNA-based ImmunoModulator | DNA sequence essential for function (so-called “CG motifs”) | new structural feature in EnanDIM providing protection against degradation | phosphorothioate backbone (chemical modification)

# Key Financials 2016

| In € million | FY 2016 | FY 2015 | Δ |
|---|---|---|---|
| R&D expenses | 17.0 | 16.8 | 1% |
| EBIT | -21.0 | -20.5 | 2% |
| Cash flows from operating activities | -19.3 | -15.1 | 28% |
| Cash flows from financing activities | 15.2 | 26.2 | -42% |
| Monthly cash burn | 1.7 | 1.4 | 21% |
| **In € million** | **31 Dec 2016** | **31 Dec 2015** | **Δ** |
| Total assets | 21.4 | 26.4 | -19% |
| Cash & cash equivalents | 20.5 | 24.6 | -17% |
| Equity ratio | 55% | 74% | -26% |

- Slightly increased R&D expenses and related cash outflows due to advanced study program
- Next-level strategy including upscaling: increased R&D expenses in the mid- and long-term

# Refinancing -
# Current Shareholder Structure

**Capital Measures**

| | |
|---|---|
| • Capital increase: Oct 2016 (~11 m new shares) | €13.60 m |
| • Convertible bond 2016/2024 (8 years, 6% interest rate) | €2.54 m |
| • Convertible bond 2017/2025 (8 years, 6% interest rate) | €4.99 m |
| **Total gross proceeds** | **~ €21.10 m** |

➔ **Cash reach until early 2018**

Shareholder Structure as at December 31, 2016 (estimates)

# Key Data of Convertible Bonds

| | 2016/2024 | 2017/2025 |
|---|---|---|
| Amount | €2.54 million | €4.99 million |
| Issue date | 25 Nov 2016 | 20 Jan 2017 |
| Maturity date | 29 Oct 2024 | 20 Jan 2025 |
| Coupon | 6% | 6% |
| Interest payment date | Quarterly | Quarterly |
| Conversion price | €1.50 | €1.60 |
| ISIN | DE000A2BPDY4 | DE000A2DANN4 |
| Listing | no | no |
| Holder at issuance date | Global Derivative Trading GmbH (GDT) | GDT: approx. 70% |

# Outlook 2017

- Advance product development
  - Focus on lead compound lefitolimod and successor molecules EnanDIM®
    - IMPALA: Finalize patient recruitment short-term
    - IMPULSE: Present study results in Q2 ✓
    - TEACH study results extension phase by mid-year
    - Ongoing recruitment for combination study with ipilimumab (Yervoy®)
    - Advance pre-clinical study program for EnanDIM®
- Production: Execute tech transfer and start upscaling
- Partnering discussions / Out-licensing activities to accelerate
- Ensure financing beyond early 2018
- R&D expenses will further increase due to study progress; operating results below FY 2016 expected - dependent on financing structure

# Financial Calendar 2017 and Contact Details

**22 March 2017**
Full Year Report 2016

**28 April 2017**
Annual General Meeting

**11 May 2017**
Quarterly Statement as of 31 March 2017

**10 August 2017**
Half-Yearly Financial Report as of 30 June 2017

**9 November 2017**
Quarterly Statement as of 30 September 2017

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**FRANKFURT, 9. MAI 2017**