

# inspired by immunotherapies

**MEDIGENE AG ANNUAL REPORT 2014**

Press & Analyst Conference Call

Dr. Frank Mathias, CEO

Peter Llewellyn-Davies, CFO

Prof. Dolores J. Schendel, CSO

This presentation contains forward-looking statements - that is, statements related to future, not past, events. These statements may be identified either orally or in writing by words as "expects", "anticipates", "intends", "plans", "believes", "seeks", "estimates", "will", "may" or words of similar meaning. Such statements are based on our current expectations and assumptions, and therefore are subject to various risks and uncertainties that could cause the actual results, performance or achievements to differ materially from any future results, performance or achievements that may be expressed or implied by such forward-looking statements. These factors include, without limitation, those discussed in our public reports filed with the Frankfurt Stock Exchange. The company does not assume any obligations to update or revise any of these forward-looking statements, even if new information becomes available in the future.

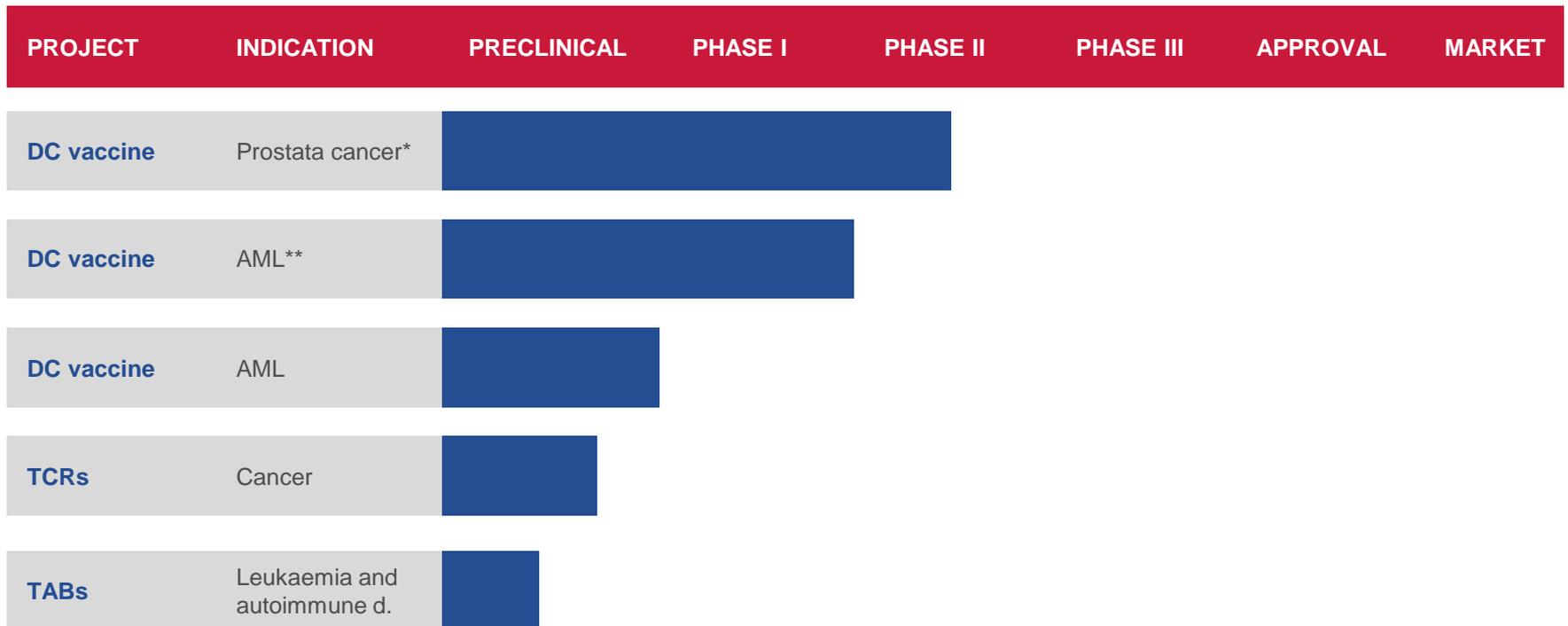
## 2014 - A transformative year at a glance

- Acquisition & integration of Trianta (now Medigene Immunotherapies)
- RhuDex<sup>®</sup> outlicensed for hepatology and gastroenterology
- Prof. Dolores J. Schendel appointed as Chief Scientific Officer
- Repositioning as an immunotherapy company
- €15.9 m secured with capital increase
- New key investors on board
- Market capitalisation increased from € 37m to € 52m average enterprise value (currently ~ €170 m)

## 2014 – Advancing our immunotherapy pipeline

- Integration of highly qualified R&D team
- Development of 3 innovative platforms to combat cancer and autoimmune diseases
  - DCs – start of Phase I/II vaccine study in AML
  - TCRs – preparation for first clinical trial
  - TABs - development of T cell specific monoclonal antibodies continues

# Pipeline focus – innovative immunotherapies



\* investigator initiated trial Oslo University Hospital

\*\* investor initiated trial Ludwig-Maximilians University Hospital

# Transition of business model created by successful partnering

- **Numerous marketing partnerships for Veregen® in place**
  - Currently marketed in the US, Canada, 15 European countries and Taiwan
  - Further market launches planned
  
- **Exclusive global license and development agreement for EndoTAG® in May 2013 with SynCore Biotechnology**
  - Complete financing for phase III trial in return for EndoTAG® global marketing rights
  - Phase III trial in preparation under the responsibility of SynCore
  
- **Licence agreement with Falk Pharma for RhuDex® in hepatology and gastroenterology in March 2014**
  - Falk Pharma receives global rights for development and commercialisation in PBC
  - Medigene retains RhuDex® rights for rheumatoid arthritis and other autoimmune diseases



**inspired by  
immunotherapies**

# Financial Report 2014

# Financial overview for 2014

## - Significant improvement in revenue, EBITDA and net result

### ■ Increase in revenue:

- Total revenue increased by 82% to €13.8m (€7.6m)
- Veregen<sup>®</sup> revenue increased by 23% to €5.2m (€4.2m)

### ■ Reduction of loss:

- EBITDA improved by 75% to €-2.1m (€-8.3m)
- Net loss reduced by 44% to €-5.8 m (2013: € -10.3 m)

### ■ Capital increase:

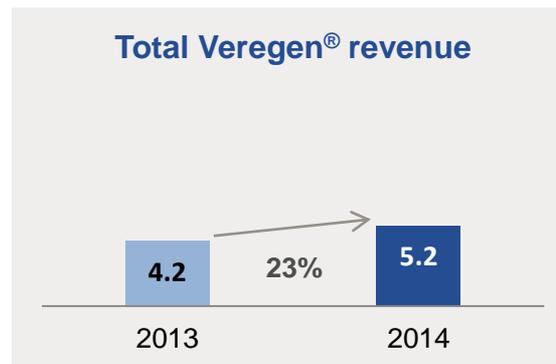
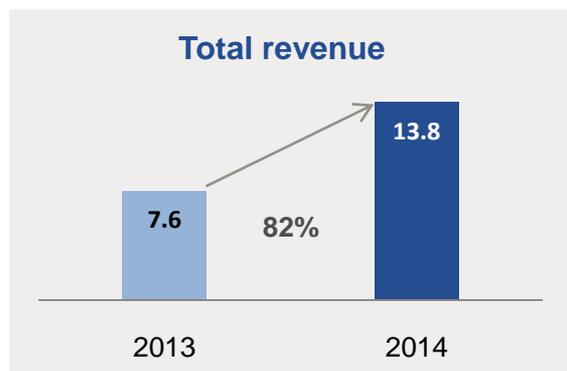
- Funding of €15.9 m for immunotherapy platforms

### ■ FTE total: 65 (31 Dec 2013: 48)

### ■ Integration of 16 Trianta employees

# Revenue increased substantially

In €m



Revenue (in € k)		2013	2014	Change
Veregen®	Product revenue (supply chain)	1,326	2,118	60%
	Royalties	2,585	2,352	-9%
	Milestones	298	725	143%
<b>Veregen® revenue</b>		<b>4,209</b>	<b>5,195</b>	<b>23%</b>
Other operating income		3,383	8,589	154%
<b>Total revenue</b>		<b>7,592</b>	<b>13,784</b>	<b>82%</b>

## Other operating income increased significantly

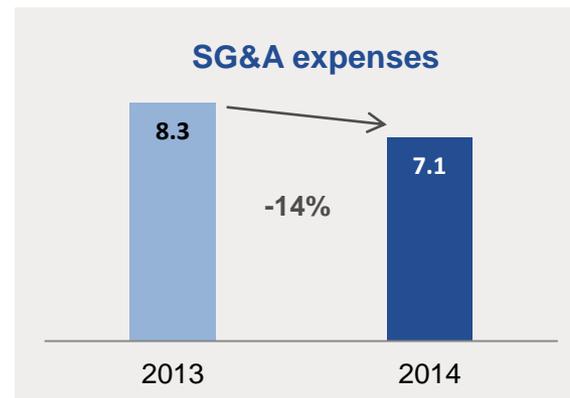
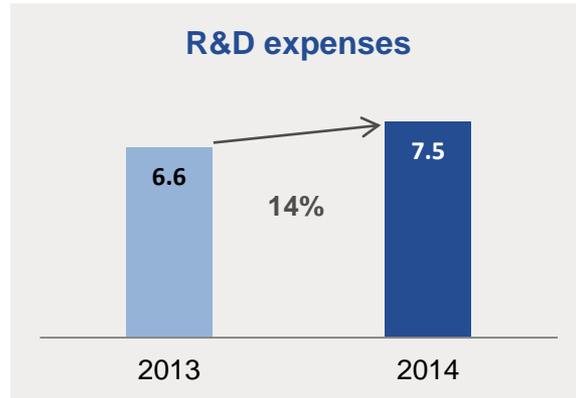
Revenue (in € k)	2013	2014	Change
Eligard license fees (Cowen)	2,493	2,493	0%
EndoTAG <sup>®</sup> milestone (SynCore)	13	2,699	-
EndoTAG <sup>®</sup> research funding (SynCore)	833	1,936	132%
Other operating income (Upfront/API RhuDex <sup>®</sup> , Grants)	44	1,461	-
<b>Total other operating income</b>	<b>3,383</b>	<b>8,589</b>	<b>154%</b>

- EndoTAG<sup>®</sup> Milestone from SynCore
- Income from RhuDex<sup>®</sup> outlicencing

# Operating expenses

## R&D increased, SG&A decreased

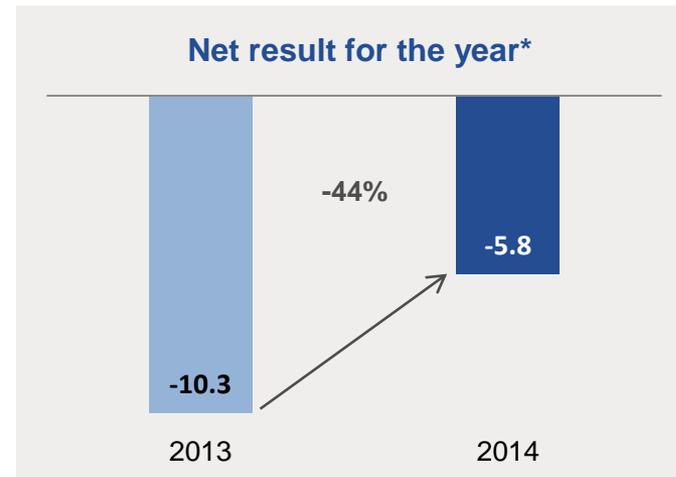
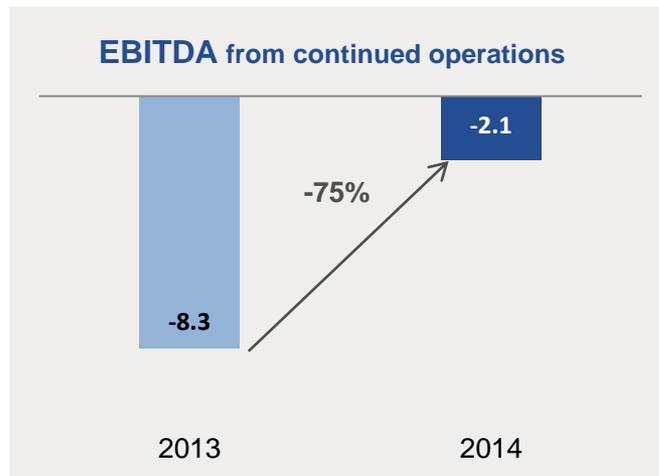
In €m



- Increased expenses for clinical immunotherapy programmes
- Lower RhuDex<sup>®</sup> expenses
- Higher costs in 2013 (Abbott 740K)
- Lower consulting fees

# EBITDA and Net result significantly improved

In €m



- One time events had major impact on EBITDA and net result

## Cash position improved

- Capital increase in July 2014 provided €15.9 m gross proceeds
- Cash position at 31 December 2014 of €15.0 m (31 December 2013: €10.2 m)
- Cash usage from operating activities decreased by 30% to €8.8 m (2013: cash usage of €12.5 m)
- Average monthly cash usage 12M 2014 €0.7 m (2013: €1.0 m)

# Financial guidance 2014 surpassed

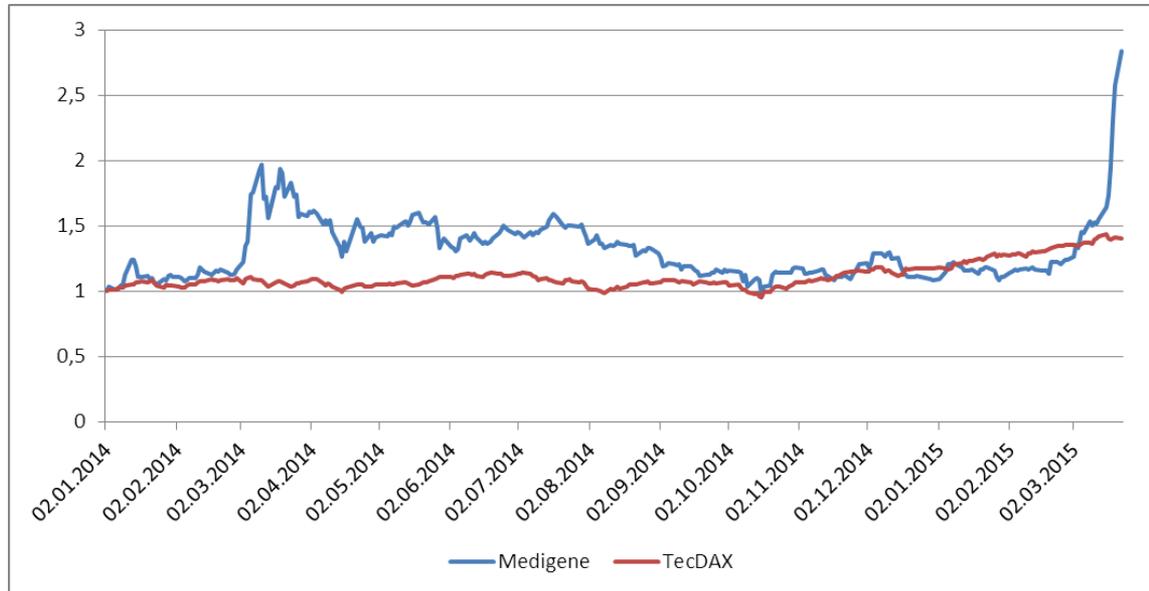
	2013	Guidance 2014	Actual 2014
Total revenue	€7.6 m	+20 - 30%	€13.8 m
Veregen® total	€4.2 m	€5 - 6 m	€5.2 m
EBITDA loss	€8.3 m	€4 - 6 m	€2.1 m

## Financial guidance 2015 - Significant investments in immunotherapy

	Actual 2014	Guidance 2015
Veregen <sup>®</sup> royalties	€2.4 m	Double digit percentage increase
Veregen <sup>®</sup> total revenue	€5.2 m	stable
R&D expenses Immunotherapies	€2.9 m	€7-9 m
EBITDA loss	€2.1 m	€11-13 m

- Cash reach into Q2 2016 without licencing deals or capital measures
- Increase in EBITDA loss mainly due to lower milestone payments from outlicenced products as well as significantly higher investments in the innovative immunotherapy programs

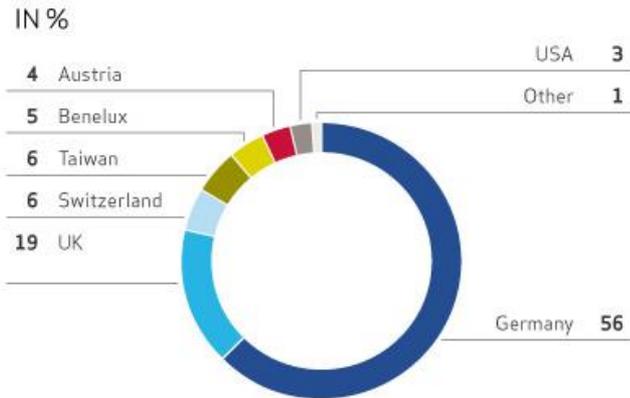
# Share price development 1 Jan 2014 - 23 Mar 2015



- Share price up 5.4% in 2014 (from €3.53 to €3.72)
- Market capitalisation increased from € 37m to € 52m (currently ~ €170m)
- Shares issued increased from 9.9m to 13.9m (currently 13.9m)
- Average daily trading volume 44,273 shares (2013: 14,155) (currently 942,290)

# Shareholdings of institutional and international investors increased in 2014

## OWNERSHIP INFORMATION BY COUNTRY



As at 31 December 2014, figures rounded, based on Medigene AG assessment

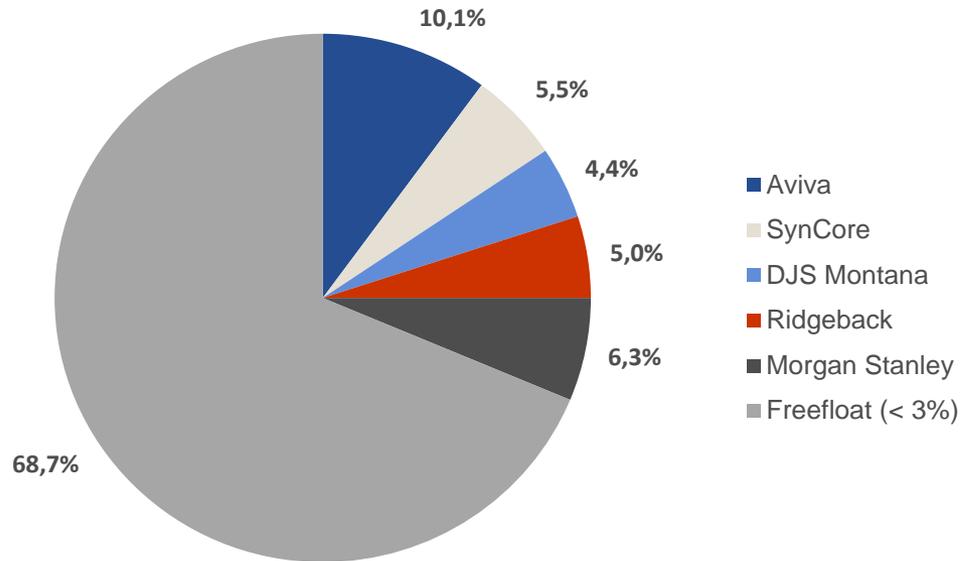
## OWNERSHIP INFORMATION BY TYPE OF INVESTOR



As at 31 December 2014, figures rounded, based on Medigene AG assessment

- Free float reduced from 84% to 77% (2012 >90%)
- Institutional and international investors increased to 46% (2013: 41%)
- New key investors: DJS Montana, Ridgeback, Aviva, SynCore (2013)
- Germany: reduced to 56% (2013: 74%), UK: Increased to 19% (2013: 7%)
- USA: 3,3% (2013: 0.3%)

# Current shareholder structure\*



## Key share information

- Listed on the FSE (Prime Standard)
- Number of shares: 13,9 m
- Current market cap of approx. ~ €170 m

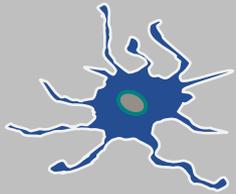
\* based on last voting right notifications

# **Focus immunotherapies**

## **- Highlights and outlook**

# T cell oriented immunotherapy with three complementary platforms

## *DC vaccines*



### **Dendritic cell (DCs) vaccines**

**for low tumour burden and combination therapies:**

induce the maturation of own, cancer-specific dendritic cells and trigger both T cells and natural killer (NK) cells to attack the tumour

## *TCR-modified T cells*

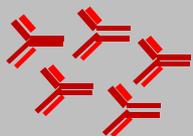


### **Adoptive T cell therapy with T cell receptors (TCRs)**

**for high tumour burden:**

arms patient-derived T cells ex vivo with suitable TCRs that enable them to detect and efficiently kill cancer cells in vivo

## *T cell-specific antibodies*

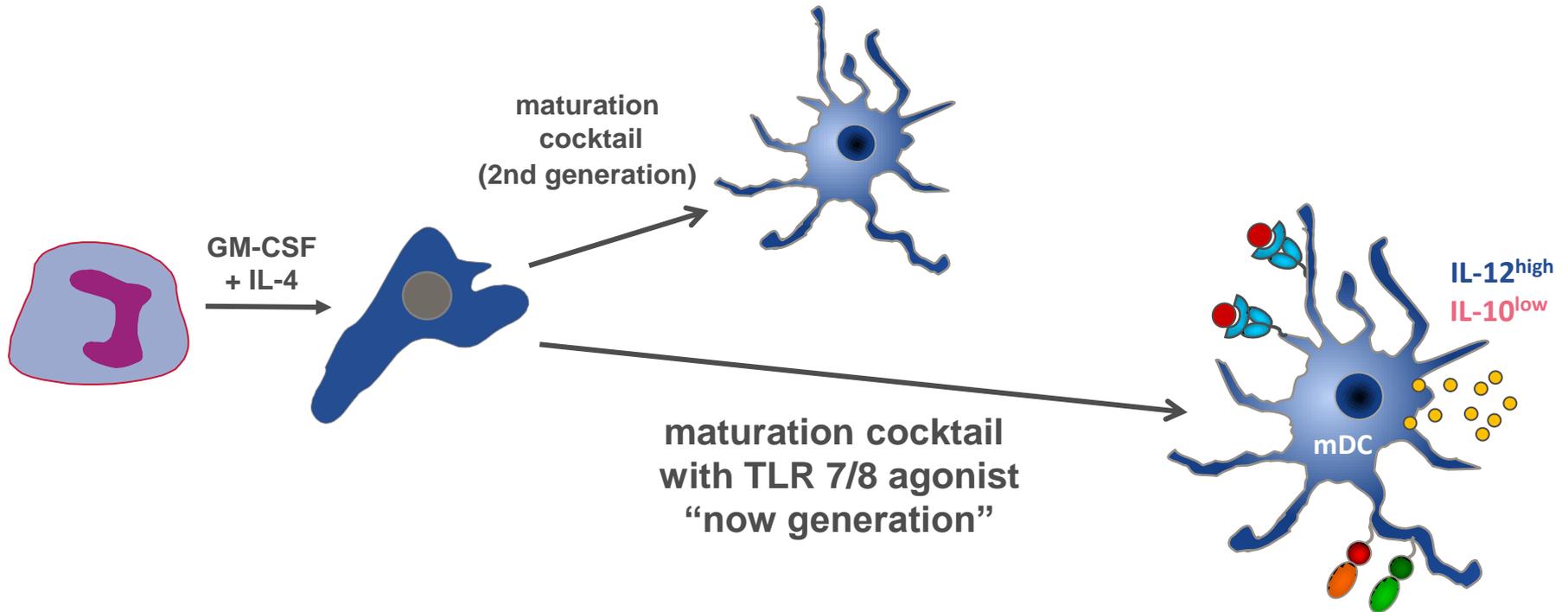


### **T cell-specific antibodies (TABs)**

**for T cell leukaemia and autoimmune diseases:**

deplete unwanted T cells

# Medigene's "now generation" DC vaccines



monocytes

1st generation  
immature DCs

2nd generation  
7-9-day mature DCs

"Now generation"  
3-day polarized mDCs

**for optimal innate and adaptive immunotherapy**

## DC vaccines – Clinical advances since the integration

- Ongoing investigator-initiated trials (phase II prostate cancer, phase I/II AML) and compassionate use programme
- Publication of preclinical and initial clinical data at scientific conferences (PIVAC and DC 2014 Conferences, Europe; ASH and SITC Conference 2014, US) and in “Cancer Immunology, Immunotherapy”
- US and EU patent relating to the manufacturing of mature dendritic cells granted
- Phase I/II Study with DC vaccine for the treatment of AML started (March 2015)

# First results from compassionate use convince and motivate to advance clinical development

Courtesy of Prof. Dr. G. Kvalheim, Oslo University Hospital  Oslo University Hospital

Cancer Patient	Tumour Type	Stage	Vaccination Time (months)	Status 10/2014
1	Lung cancer	IV	34	SD
2	Prostate cancer	IV	Drop out	
3	Glioblastoma	IV	14	CR
4	Glioblastoma	IV	11	CR
5	Glioblastoma	IV	11	Pseudo-relapse (7 + 9 months)
6	Glioblastoma	IV	10	CR

**SD = stable disease, CR = complete remission**

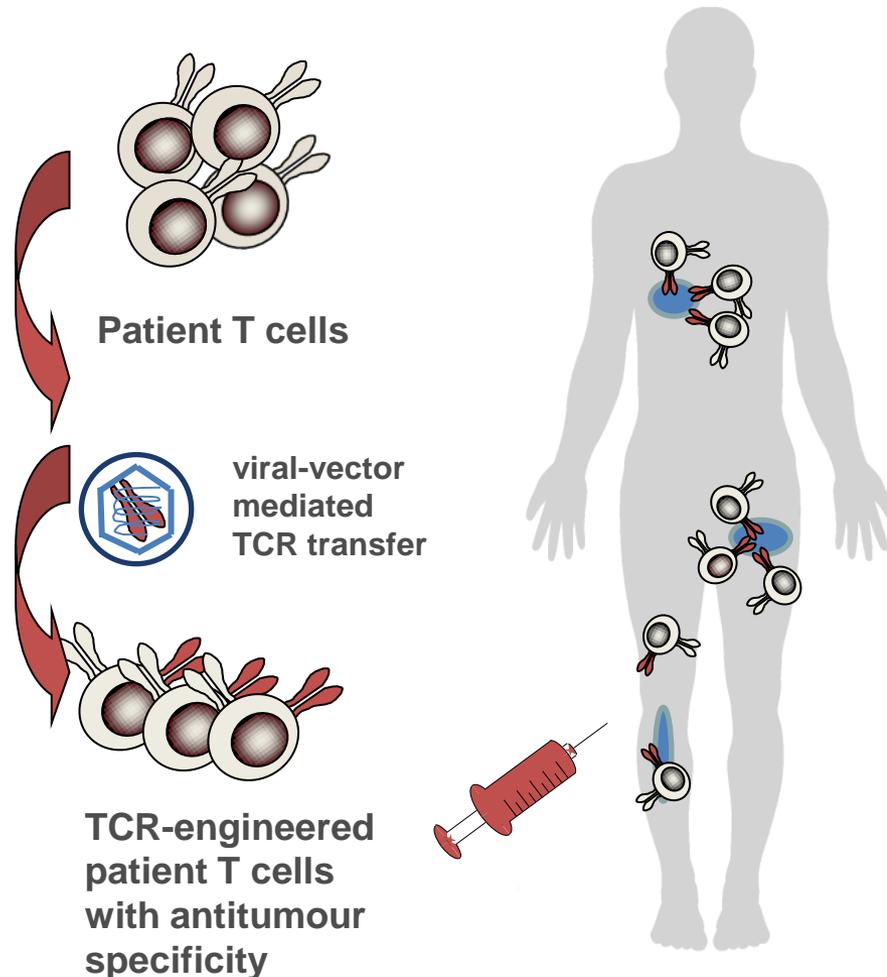
Abstract ASH Annual Meeting, Dec 6-9 2014:

[http://www.medigene.de/sites/default/files/downloads/ash14\\_paper\\_vaccination\\_with\\_a\\_new\\_generation\\_of\\_fast\\_dendritic\\_cells\\_transfected.pdf](http://www.medigene.de/sites/default/files/downloads/ash14_paper_vaccination_with_a_new_generation_of_fast_dendritic_cells_transfected.pdf)

# Medigene's DC vaccine phase I/II trial in AML

- Started on 24 March 2015
- Trial design:
  - phase I/II multi-centre, open-label, prospective, non-randomized trial
  - 20 AML patients (6 phase I + 14 phase II) with complete remission after chemotherapy who are not eligible for allo-transplantation
  - Primary objectives: Feasibility and safety
  - Secondary objectives: Induction of immune responses, Control of minimal residual disease (MRD), Clinical response: time to progression (TTP)
  - vaccinated for 50 weeks and a follow-up period of one year or until progression.

# Medigene's TCRs have natural non-mutated high-affinity structures



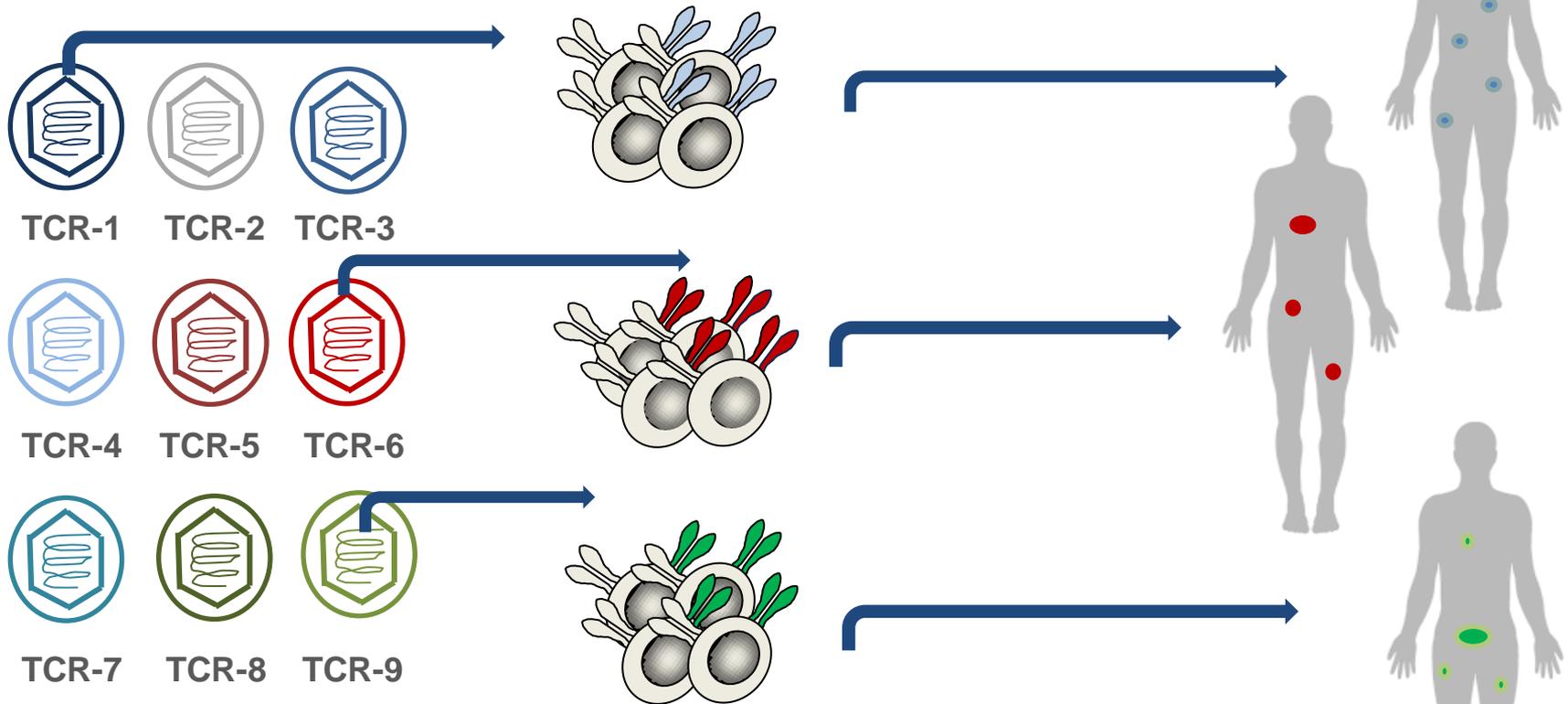
## Competitive Advantages

- High-throughput in vitro platform to rapidly obtain TCRs
- Patient-material is not required to build an extensive library of TCR lead candidates
- TCRs are of human origin - lowering chance of rejection
- TCRs must not be mutated to obtain high-affinity giving less chance for deleterious errors

## TCRs – Progress since integration

- Patent in the USA and Australia for a T-cell receptor which targets the tumour-associated antigen tyrosinase
- Extension of research funding by the German Research Foundation (DFG) for the Collaborative Research Centre for adoptive T-cell therapy
- Presentation of preclinical data at SITC-Conference, USA
- Progressing development of the GMP compliant manufacturing process
- Talks with the regulatory authorities in preparation of first clinical trials
- Publication in “Nature Biotechnology”

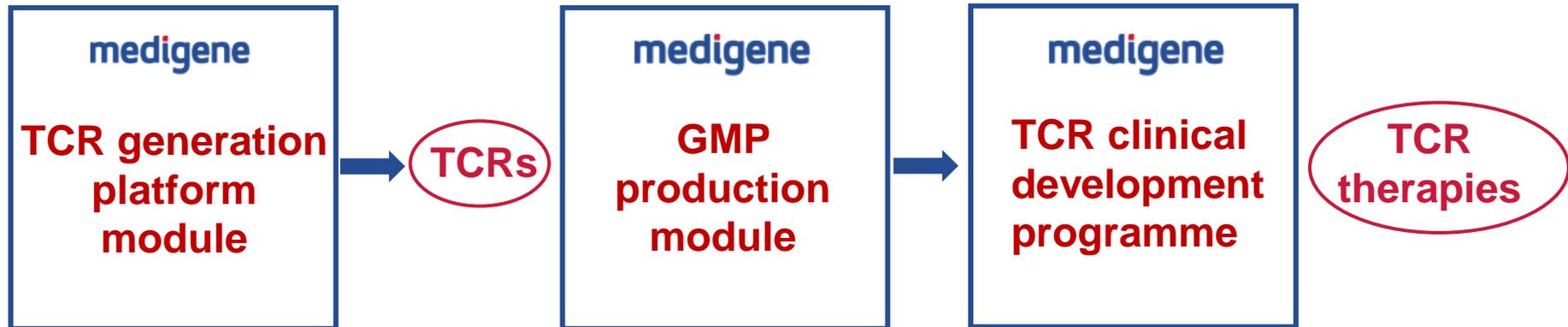
# Patient T cells are tailored to tumour type using library of tumour-specific TCRs



Library of therapeutic TCRs  
(in form of recombinant vectors)

TCR-engineered patient T cells

# Value creation through TCR development chain



- Value creation through:
  - TCR R&D collaborations
  - TCR product development collaborations
  - own TCR product development programmes

# T cell specific monoclonal antibodies (TABs)

- Intended to remove misguided or unwanted T cells
- Full-scope platform is developed to isolate antibodies specific for treatment of T cell leukemia & autoimmunity
- Highly unique animal models are available to assess mechanisms of action and clinical efficacy
- Proof-of-principle is established for the technology
- Studies are ongoing to establish proof-of-concept in pre-clinical animal models



## TABs: Progress since acquisition

- Continuation of preclinical development with the aim of delivering proof of principle
- German Ministry of Education and Research (BMBF) grant received and increased
- New research collaborations with Max Delbrück Centre for Molecular Medicine and Helmholtz Zentrum München entered

# Outlook for immunotherapy platforms

## ■ DC vaccines:

- Continue investigator-initiated trials and compassionate use programme
- Conduct the company-sponsored phase I/II study in AML

## ■ TCR-modified T cells:

- Establish GMP-compliant manufacturing process
- Prepare Clinical Trial Application (CTA) for first product candidate
- Isolate and characterise TCRs with specificities for promising tumour-associated antigens

## ■ TABs:

- Further advance pre-clinical studies

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# Questions & Answers

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