

## **Building next generation TCR-T cell therapies for solid cancers**

**Medigene Half-Year Report 2022**

**3 August 2022**

# Forward looking statements disclaimer



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# Investment highlights

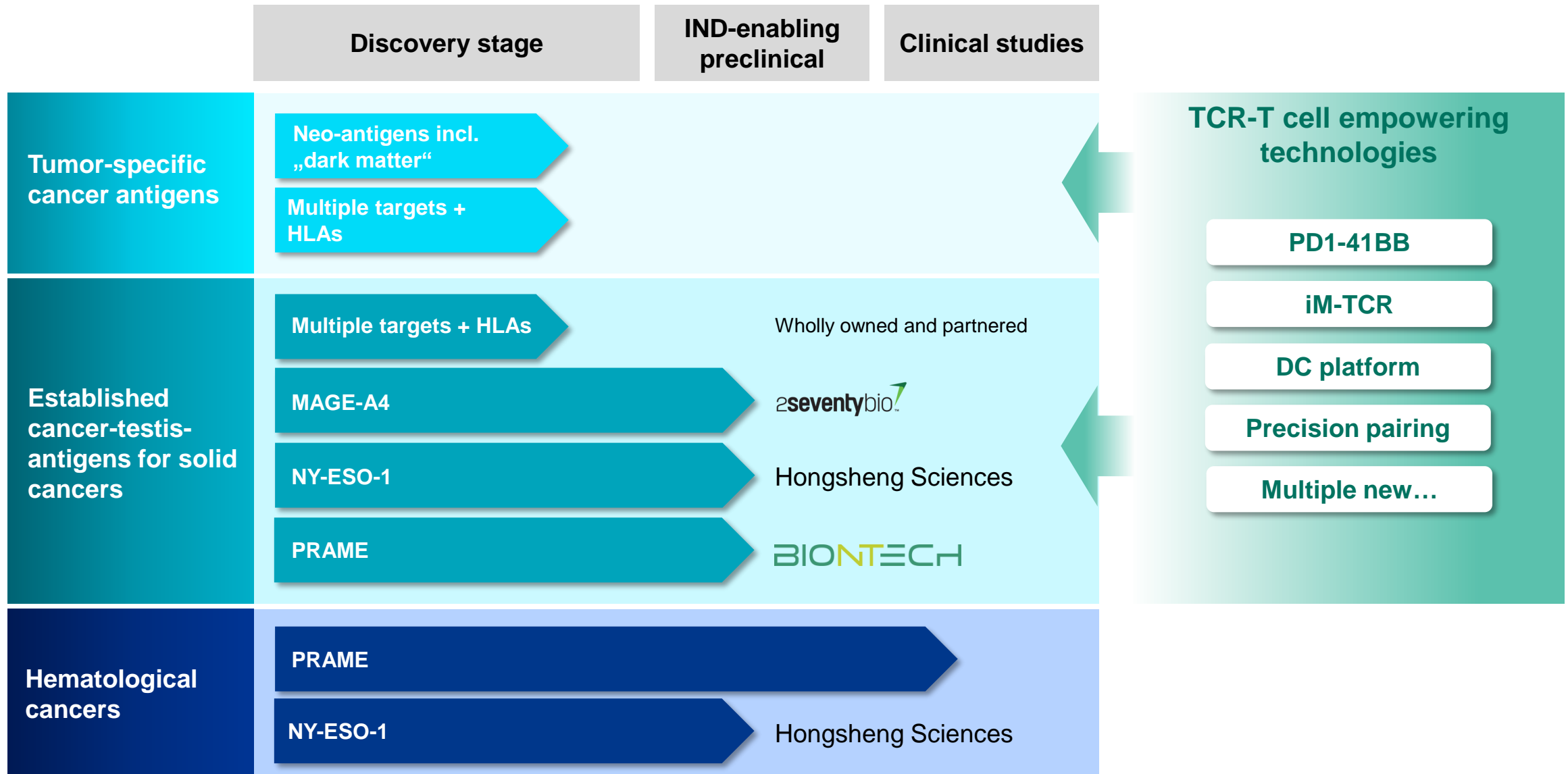
<p>Focus on solid cancers</p>	<ul style="list-style-type: none"> <li>▪ Pipeline developed for multiple cancer indications</li> <li>▪ Exclusive rights to novel solid cancer signature antigens from non-coding genome regions (cancer’s “dark matter”)</li> <li>▪ Tools to empower improved TCR-T immunotherapy of cancer → Persistence of function, safety switch, better expression and efficacy</li> </ul>
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<p>TCR platform + Innovative tools and technologies</p>	<p>Clinically validated and revenue-generating platform to identify optimal TCRs</p> <ul style="list-style-type: none"> <li>▪ Targeting diverse antigen-HLA combinations</li> <li>▪ Showing high specificity, sensitivity and multi-functionality</li> <li>▪ Improved safety by screening TCR repertoires from healthy blood donors</li> <li>▪ Exhibiting signs of biological and/or clinical activity in first Phase I study</li> </ul>
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<p>Validated by partnerships</p>	<div style="display: flex; justify-content: space-around; align-items: center;">   <p>Hongsheng Sciences</p> </div>
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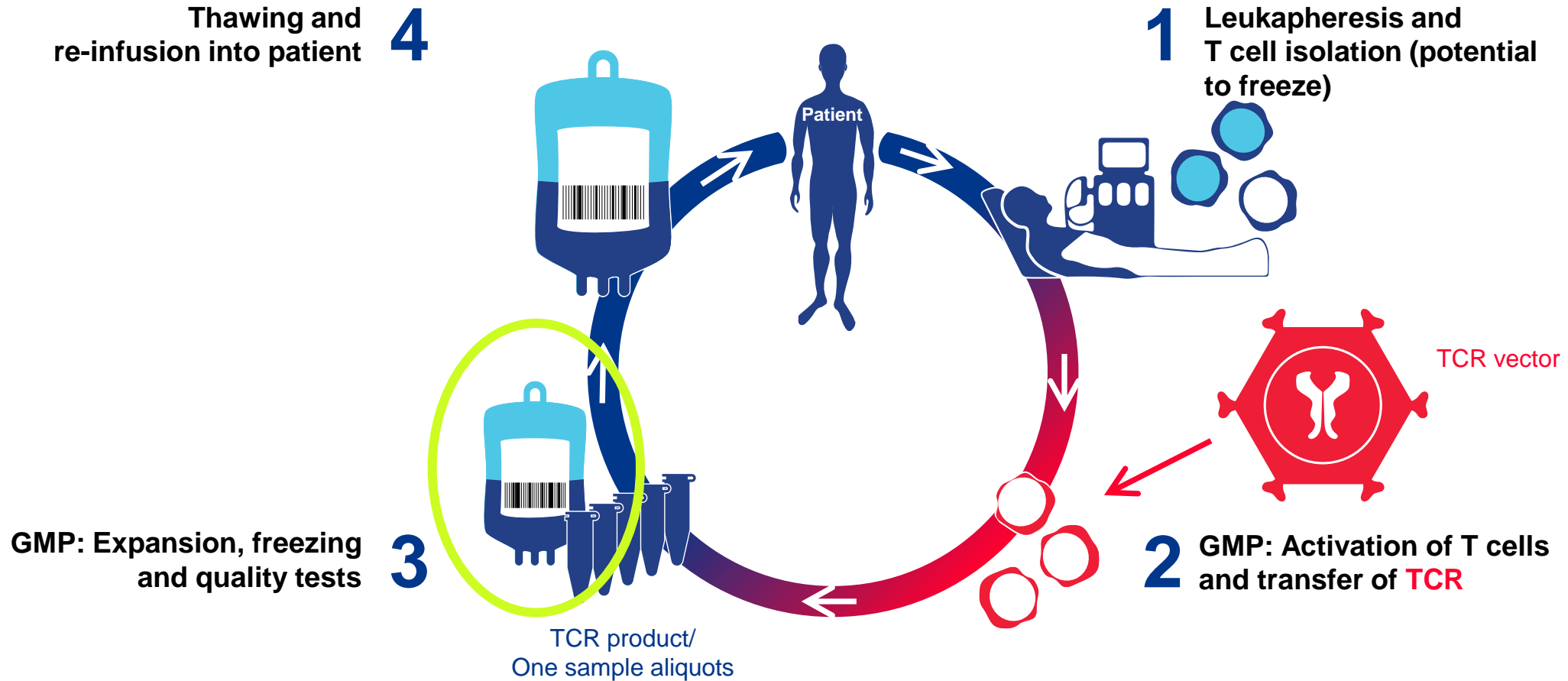
<p>Robust financials</p>	<ul style="list-style-type: none"> <li>▪ Public Company (MDG1 Frankfurt SE); ~70 employees; Martinsried, Germany</li> <li>▪ Revenue streams from out-licensing, milestones</li> <li>▪ Cash runway into Q4 2024</li> </ul>
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# A broad TCR pipeline for immunotherapy of cancer



DC: Dendritic cell; MAGE-A4, NY-ESO-1, PRAME: Tumor antigens

# Drug Product GMP production: Personalized TCR-Ts against cancer



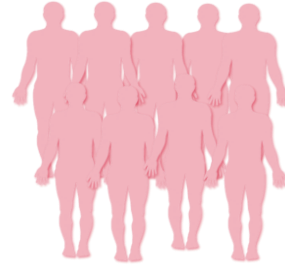
# First proof-of-concept provided by Medigene's MDG1011 Phase I study

## MDG1011: PRAME:HLA-A2-specific TCR-T immunotherapy for blood cancers

- PRAME – well-characterized, broadly expressed cancer-testis antigen
- CD8-enriched TCR-T drug products display multi-functionality

### Phase I part of Phase I/II trial

- Patients with refractory/relapsed
  - Acute myeloid leukemia (AML)
  - Myelodysplastic syndrome (MDS)
  - Multiple Myeloma (MM)
- Three dose levels tested
  - 0.1, 1.0, 5.0 x 10<sup>6</sup> TCR-positive T cells / kg body weight



### Study Outcomes

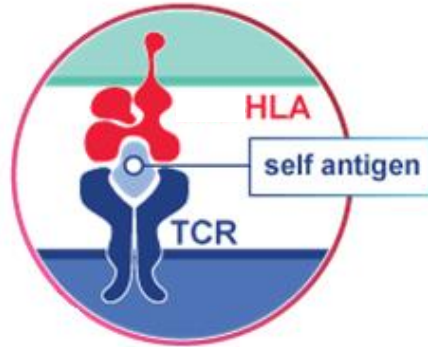
- Well tolerated with no DLT or neurotoxicities
- Successful manufacturing (92%)
- Signs of biological and/or clinical activity
  - 1x CR
  - 2x CRS
  - 1 MDS patient without progression to secondary AML after 12 months → last study visit completed

### Next steps

- Finalize Phase I evaluation
- Based on Phase I, progression into Phase II only with partner

# Discovery platform to potentially isolate “best-in-class” TCRs for solid cancers

**Discovery of optimal affinity TCRs** brings excellence to the development of TCR-T products for solid tumors



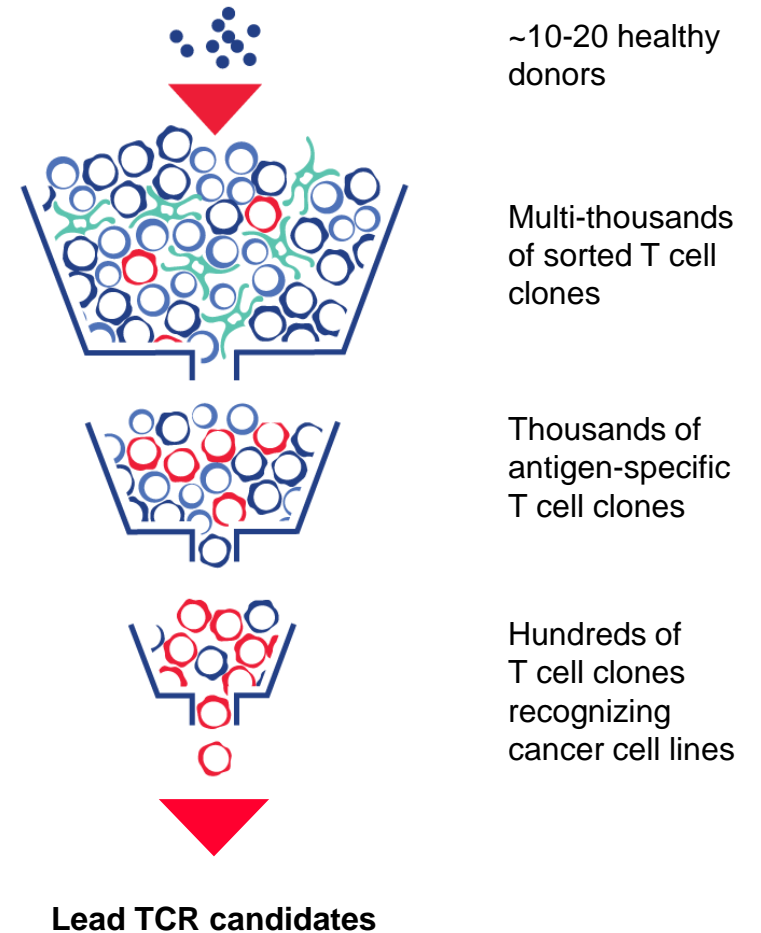
**Non-mutated, safe TCRs** rapidly isolated from healthy donors by automated high-throughput platform



**Different epitopes and HLA allotypes** address population diversity and multiplicity of antigens



Identify TCRs with highest **Specificity, Sensitivity and Safety**



~10-20 healthy donors

Multi-thousands of sorted T cell clones

Thousands of antigen-specific T cell clones

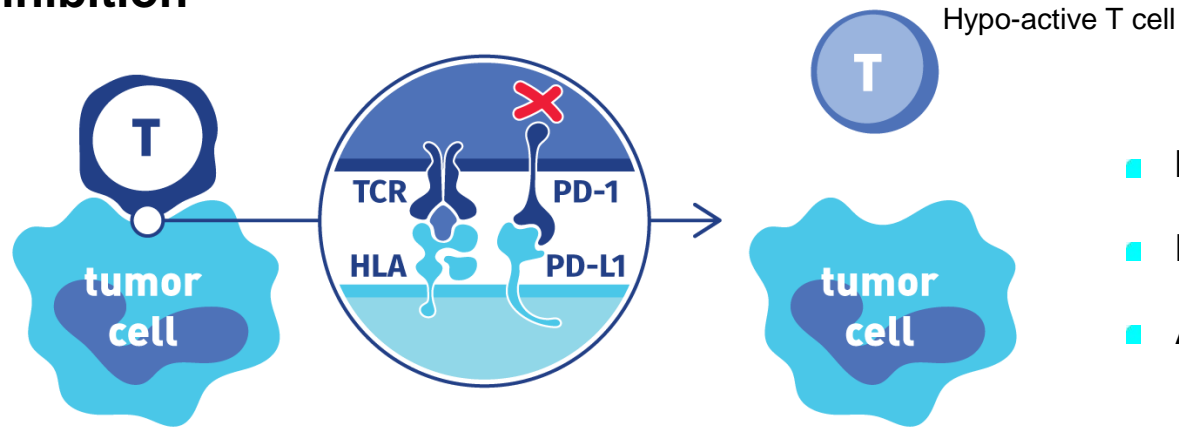
Hundreds of T cell clones recognizing cancer cell lines

Lead TCR candidates



# Empowered T cells for hostile solid tumor microenvironment – Co-stimulatory PD1-41BB switch receptor

## Inhibition

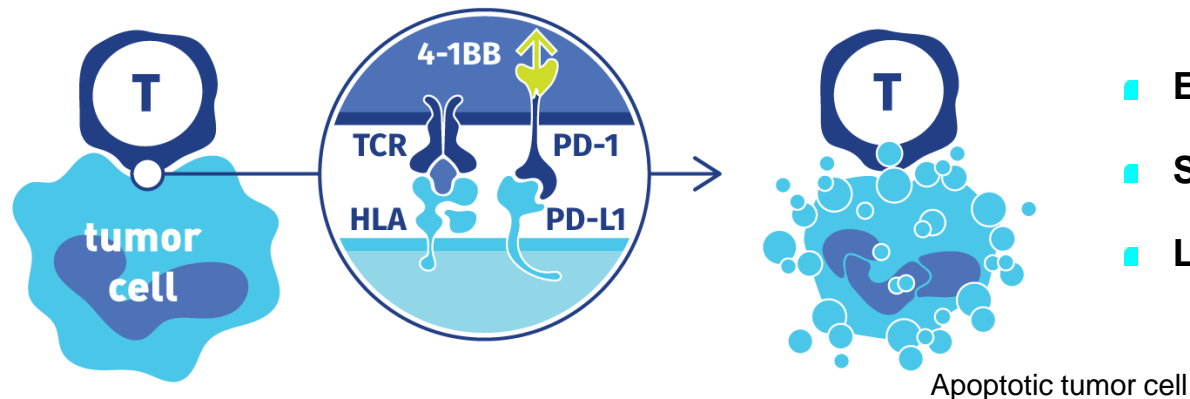


- Inhibition
- Exhaustion
- Apoptosis

## Current therapy options

- TCR-Ts + CI antibodies (anti-PD-(L)1)
- Systemic toxicity from CI therapy
  - Complex pathway for clinical development
  - Dependency on other marketed product(s)
  - Pricing restraints for two costly therapies

## Activation



- Effector functions
- Survival
- Longevity

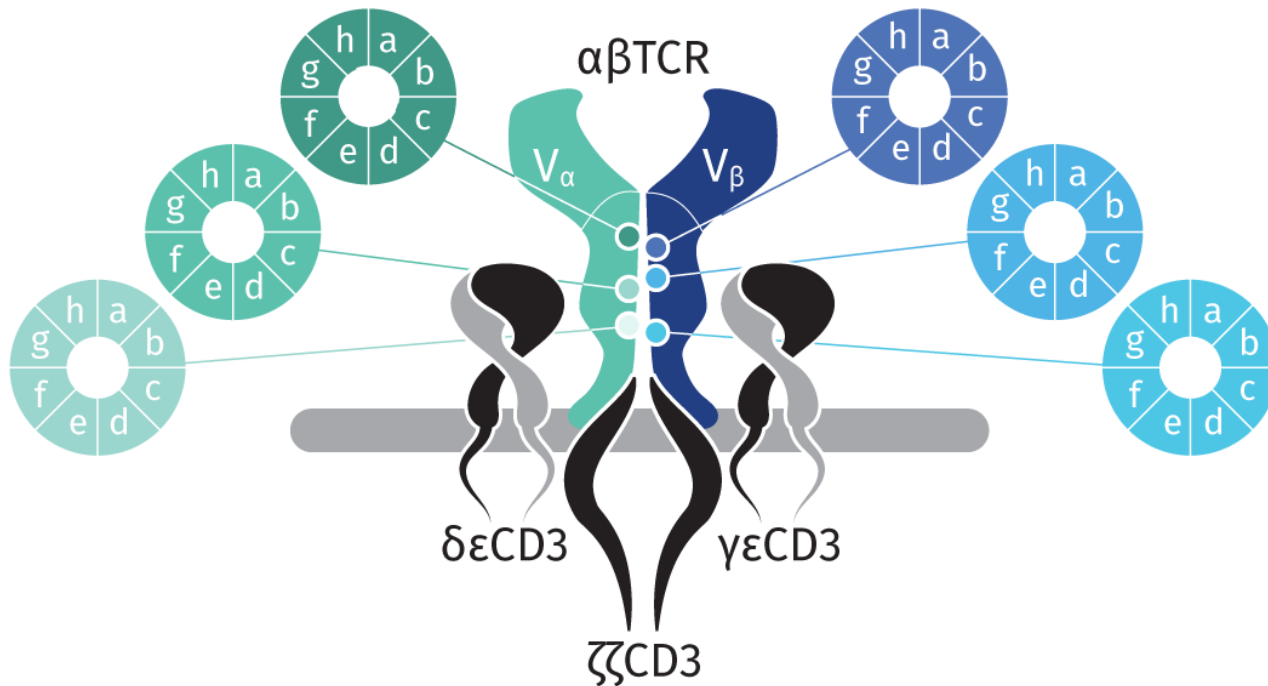
## Medigene’s “two-for-one” approach

- TCR-Ts with integrated PD1-41BB switch receptor
- Single therapy without systemic toxicity
  - Less complex treatment regimens
  - No co-dependence on other companies
  - Lower costs of treatment



# Precision pairing mutational library for enhanced TCR surface expression and function

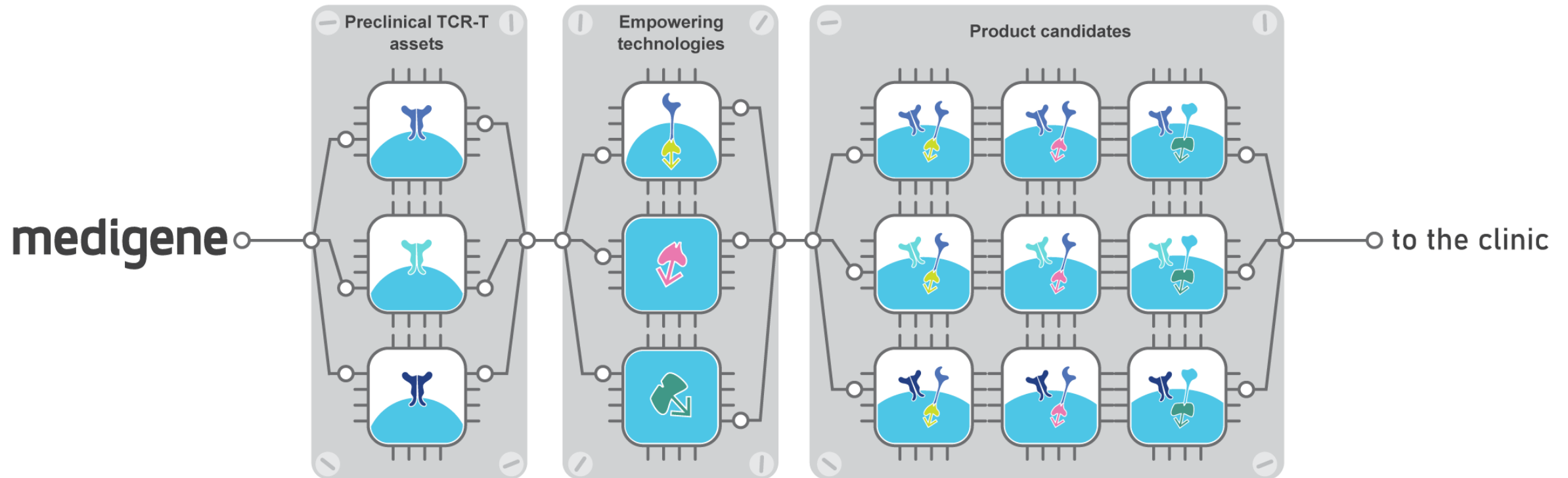
- Precision pairing of transgenic TCRs can increase TCR avidity by increasing cell surface expression
- TCRs with tailored constant regions have reduced capacity to mispair with endogenous TCR chains



- Library of tailored amino acid substitutions in TCR  $\alpha$  and  $\beta$  constant regions to allow selection for improved binding of TCR chains
  - Enhanced TCR surface expression and/or function  
→ potentially **enhanced efficacy**
  - Can reduce mispairing with endogenous TCRs and  
→ potentially **improved safety**
- No impediment of TCR binding with CD3 and zeta

# Value creation is increased through multiplicity of products

- Unique products made by combining different TCRs with different empowering technologies
- Optimal product choice can address unmet medical needs for diverse cancer indications



# Financials and Outlook

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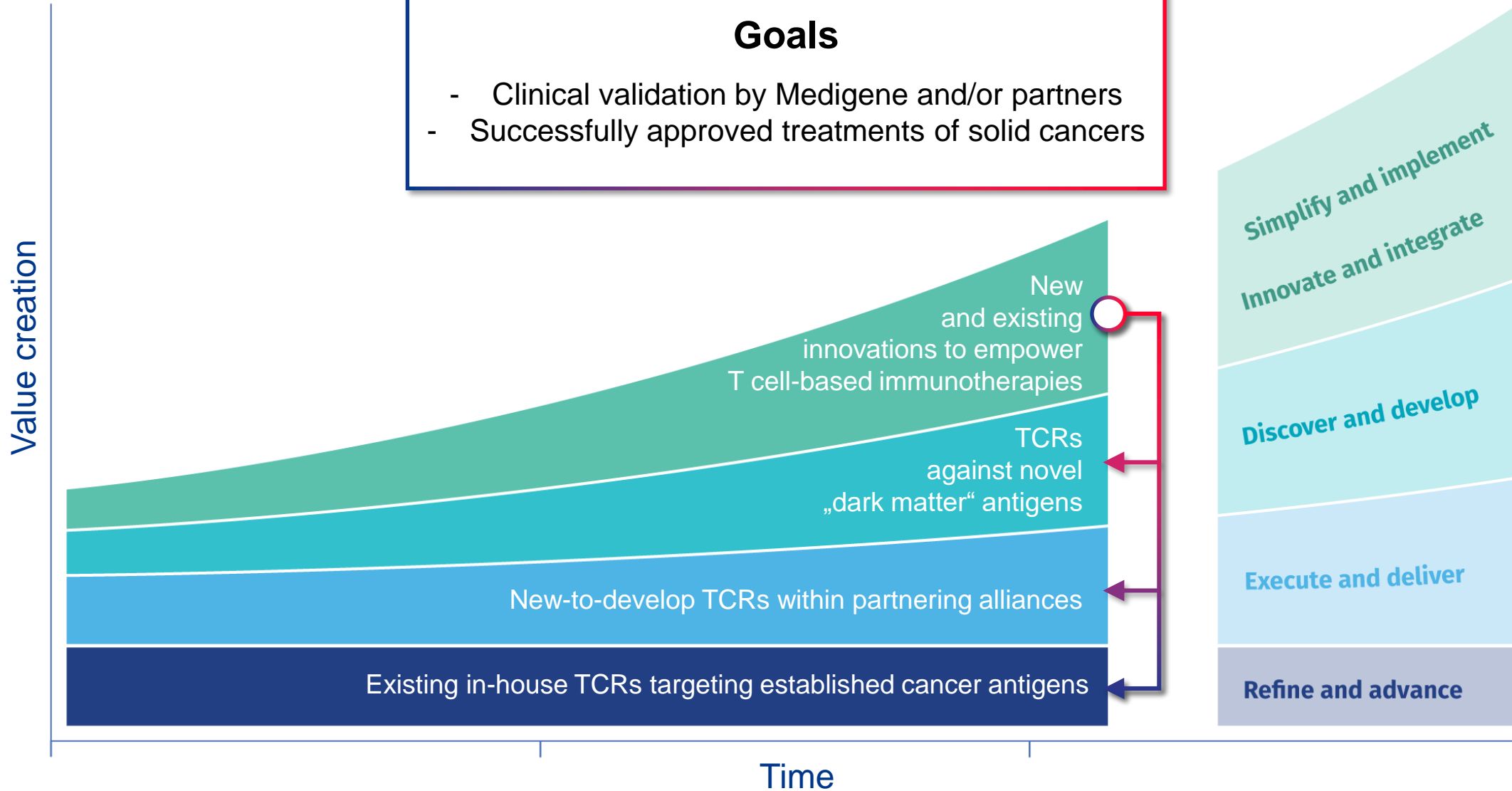
# Financial outlook

	H1 2022	Guidance 2022
Total revenues	€25.3 m	€23 - 28 m
R&D expenses	€3.7 m	€11 - 15 m
EBITDA	€15.4 m	€3 - 5 m

- Cash and cash equivalents as of 30 June 2022: ~€39.4 m
- No milestone payments or cash inflows included from existing or future partnerships or transactions
- Sufficient financial resources to fund business operations into Q4 2024

# Maximize value creation

- Goals**
- Clinical validation by Medigene and/or partners
  - Successfully approved treatments of solid cancers



**Thank you – Q&A**

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# Contact

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