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Athebody® DARPin Platform

**Precision Targeting
for Next-generation
Therapeutics**

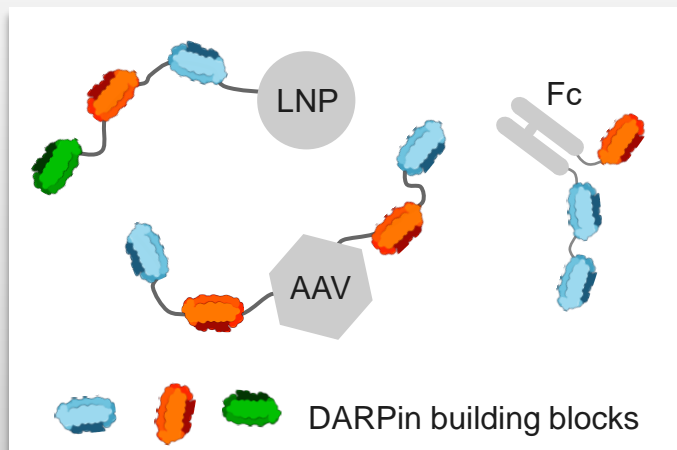
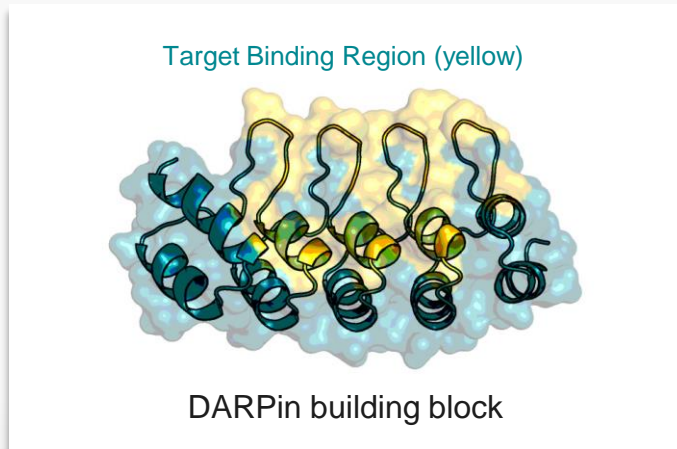
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Precision targeting **Disruptive innovation** **Customer-centered partnering**

We enable drug developers to create superior targeted therapeutics of advanced efficacy and safety by harnessing our proprietary “plug & play” Athebody® DARPin technology platform.

“Plug & play” DARPin (Designed Ankyrin Repeat Proteins) are clinically validated

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“Plug & play”

- The plug & play versatility of the DARPin domains (about 15 kDa in size) surpasses that of immunoglobulins by far (e.g., [Stumpp M.T. et al. 2020](#))

Clinical validation

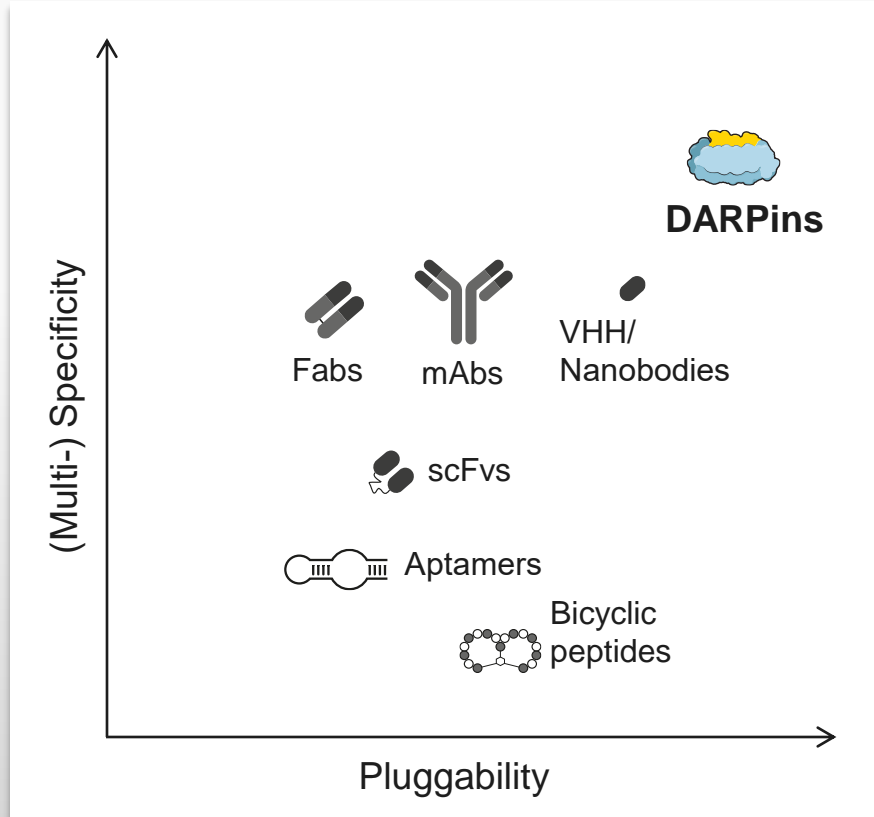
- DARPins are clinically validated (efficacy & safety) by [Molecular Partners](#) and their collaborators (6 clinical programs, >2'500 patients dosed; e.g., ensovibep)

Athebody® DARPins

- Exceptionally high target **specificity** and **affinity** (down to single digit pM) support drug safety and efficacy
- **Ease of generating multi-specificity** far beyond bi-specifics
- **Plug & play:** Easily pluggable into immunoglobulins, AAVs or other formats. DARPins are straight forward to adapt/format because of their extreme stability.
- **Superb developability** with no aggregation tendency due to exceptionally high thermal stability (increased by more than 25°C as compared to state-of-the-art DARPins) ([Schilling J. et al. 2021](#))

Athebody® DARPins surpass other platforms re. specificity and pluggability. Athebio makes them broadly accessible

Binding technologies



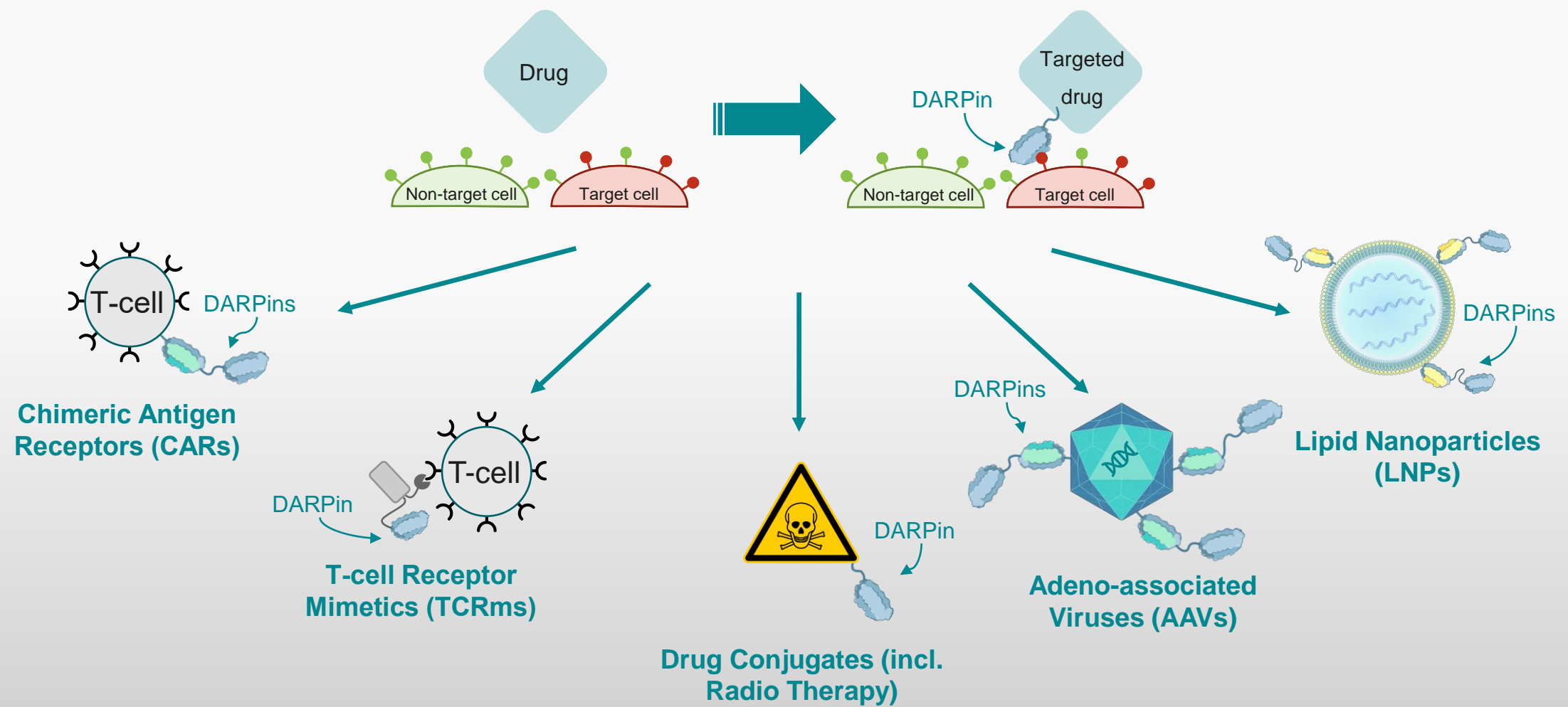
DARPins

- **Unparalleled binding specificity** through innate scaffold characteristics (rigid-body binding); easy to generate multi-specificity allowing, e.g., conditional activation
- **Exceptional pluggability** into broad spectrum of modalities

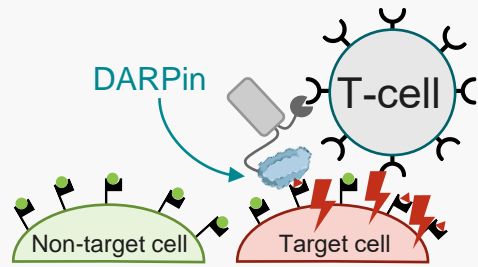
Athebio

- **Enabler model**: Preclinical access for drug developers to proprietary 3rd generation DARPIn technology (no own drug pipeline) -> **customer-centric partnering**
- **A team of DARPIn experts** with together over 40 years of respective know-how; incl., the initiator and co-inventor of the DARPIn technology
- Good FTO prospects through development of best-in-class Athebody® DARPins
- We are driven by **disruptive innovation**: Five patent families filed with one US patent already granted (US11242369); ([Schilling J. et al. 2021](#))

DARPin can be plugged into a broad spectrum of modalities for precise and efficient targeting



Athebio is currently active in four dynamic fields

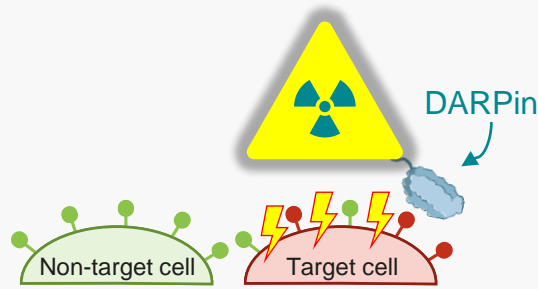


1. T-cell Receptor Mimetics (TCRMs)

Therapeutic area: Immunoncology

Approach: Directing immune cells precisely to kill tumor cells that display specific pHLA-markers

Partner: 3T Biosciences

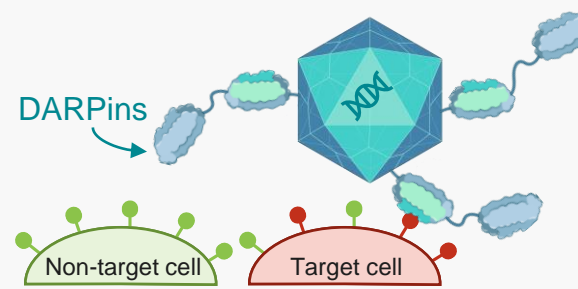


2. Targeted Radio Therapy (tRT)

Therapeutic area: Radiooncology

Approach: Directing therapeutic radio-nuclides precisely to kill tumor cells that display specific markers

Partner: POINT Biopharma

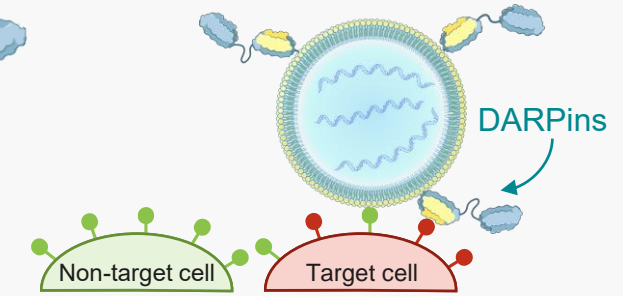


3. Adeno-associated Viruses (AAVs)

Therapeutic area: Viral gene therapy, e.g., applied in neurology and ophthalmology

Approach: Directing AAVs to tissue of interest to deliver therapeutic DNA

Partner: REGENXBIO



4. Lipid Nanoparticles (LNPs)

Therapeutic area: Non-viral gene therapy, e.g., applied in oncology or infectious diseases (cf. COVID19)

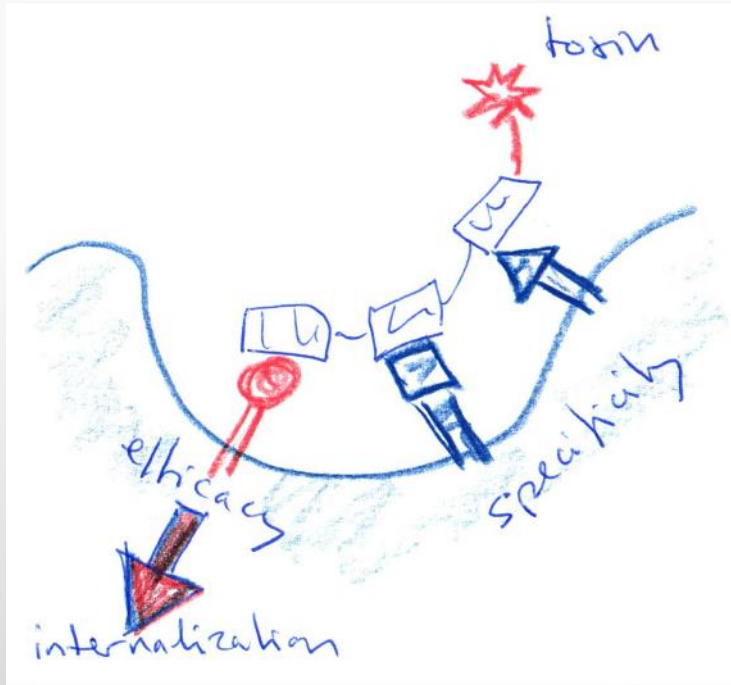
Approach: Directing LNPs to any tissue of interest to deliver therapeutic mRNA

Partner: Acuitas Therapeutics

How can we enable you to develop next-generation targeted therapeutics, e.g., in the ADC field?

ADC-field: What we can offer by using Athebody[®] DDCs

Athebody[®] DARPin Drug Conjugates (DDCs)



Disruptive Innovation

- **Solve unmet medical needs** by making more targets accessible for drug conjugates (“increased target space”), e.g.,
 - Low-, non-internalizing tumor markers
 - Tumor markers present at low copy numbers (e.g., pHLA targets)

Precision Targeting

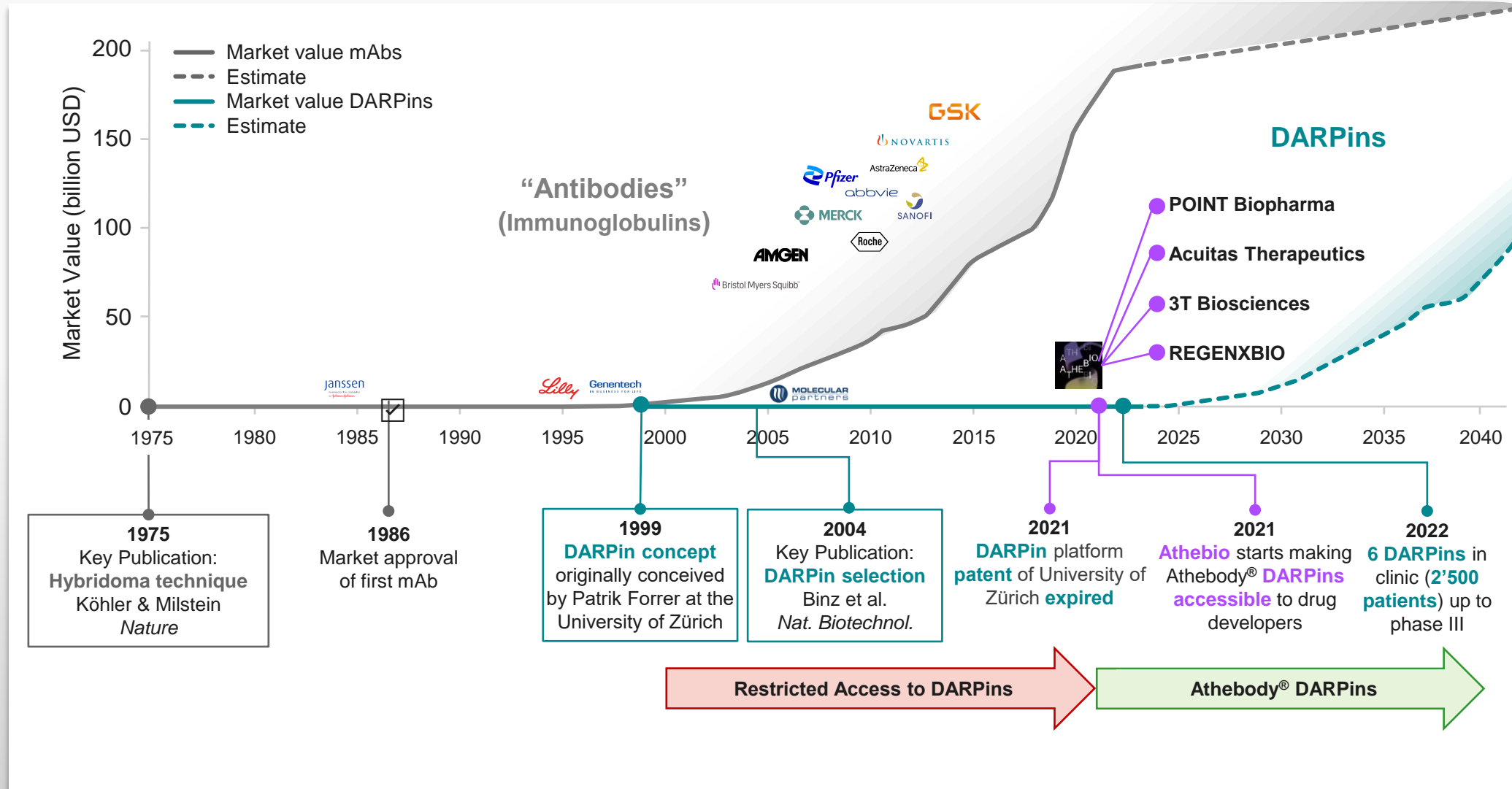
- **Increase the therapeutic index** based on high target-specific binding, multi-specificity and format tuning

Customer-centric Partnering

- Get access to **world-leading DARPin experts** and know-how (incl. engineering, conjugation, developability and CMC know-how)
- Athebio focuses solely on preclinical-work to be able to provide the best possible Athebody[®] DARPin technology and innovation support to our partners

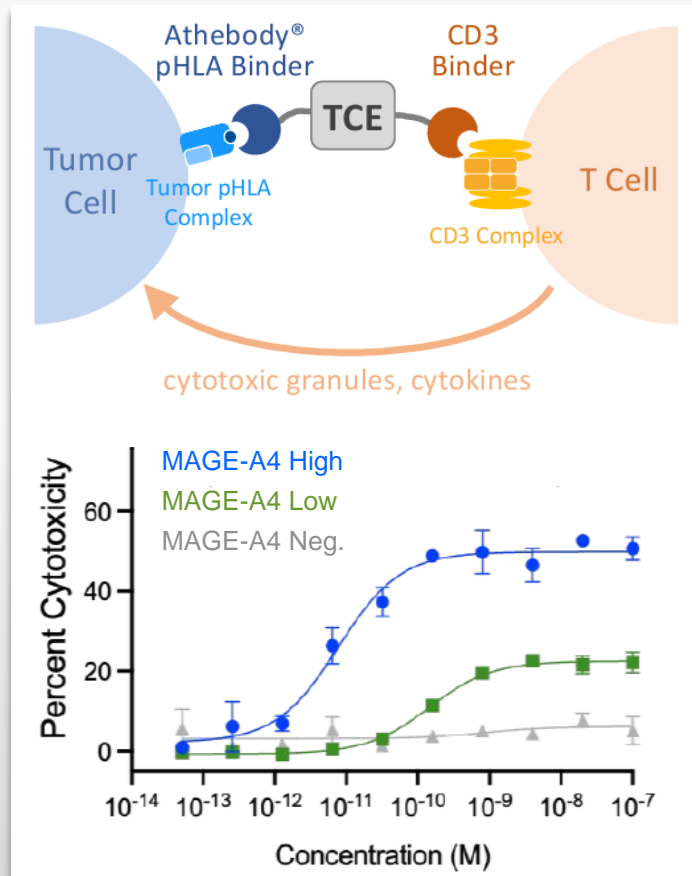
DARPinS have a huge yet untapped market potential

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Case study T-cell engagers (TCEs): Precision Targeting by Athebody[®] DARPin improves Safety

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DARPin-TCE and LDH release assay figures adapted from [Ramirez A. et al. 2022](#)

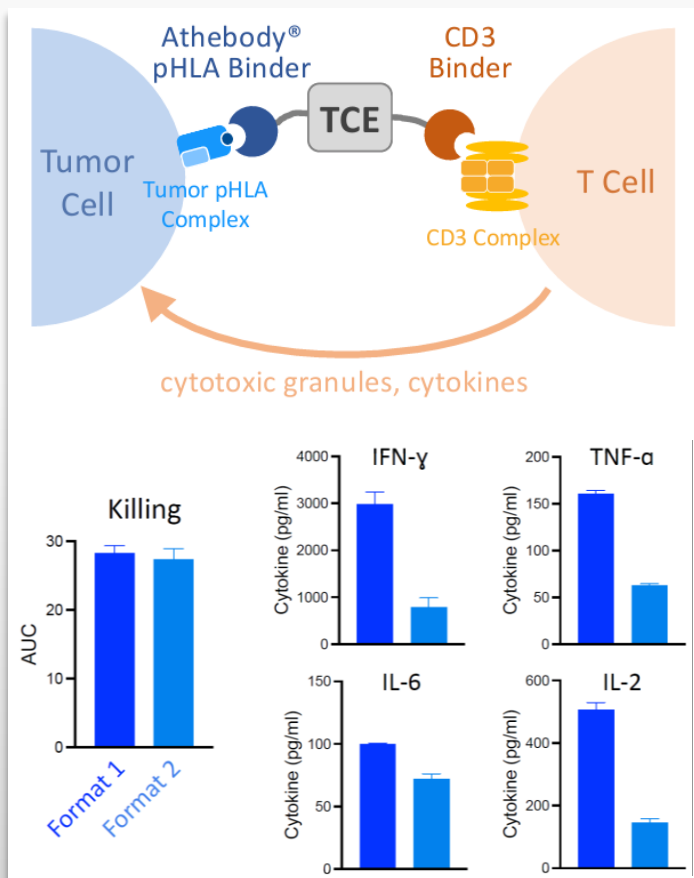
Generation of Athebody[®] DARPin TCEs

- 3T-Biosciences teamed up with us to generate next-generation of pHLA therapeutics using our Athebody[®] DARPin building blocks
- We selected highly specific Athebody[®] binders against an epitope from the cancer-germline antigen MAGE-A4 bound to HLA-A2
- 3T-Biosciences easily plugged these Athebody[®] building blocks into their TCE formats comprising CD3 binding functionality

Exceptional therapeutic index

- The resulting DARPin-TCEs induce high potency killing of MAGE-A4-expressing cancer cell lines (MAGE-A4 Low: ~30 pHLA molecules/cell) with no detectable killing of corresponding antigen-negative cells (CRISPR/Cas9 k-o)

Further improved Efficacy through Format Tuning with Athebody® DARPin



DARPin-TCE and cytokine release assay figures adapted from Ramirez A. et al. 2022

Killing Activity is Decoupled from Cytokine Release

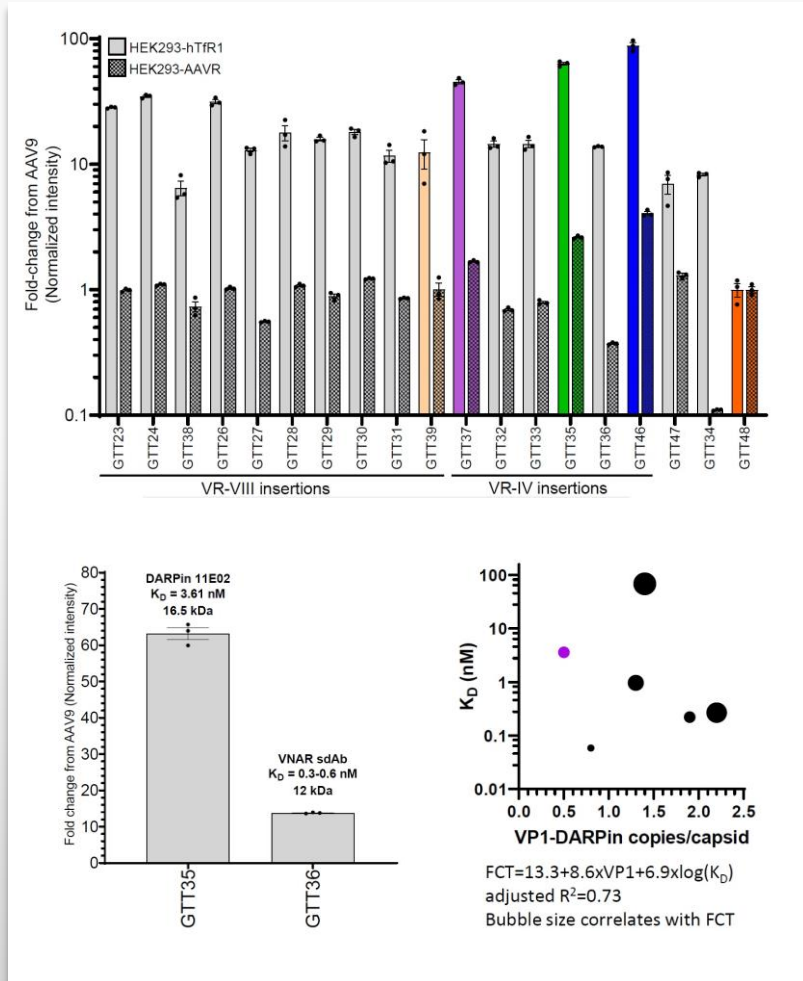
- Whereas two Athebody® DARPin-TCE designs (Format 1 & 2) show equivalent killing activity, Format 2 induces significantly lower levels of cytokine release, which may reduce the risk of cytokine release syndrome and T-cell exhaustion in the clinic.

TCE Case Study: Conclusions

- Tailored Athebody® binder selection followed by simply plugging them into various TCE formats allowed 3T-Biosciences to identify DARPin-TCE leads of **unparalleled efficacy** and **safety** profiles.
- These DARPin-TCEs also exhibit **favorable developability** profiles (Ramirez A. et al. 2022).
- Low cytokine release likely translates into less severe T-cell exhaustion and thus **long-lasting responses** (Yi J.S. et al. 2010).

DARPin-AAV: Athebody[®] DARPin Case Study

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Athebody[®] DARPin AAV particles

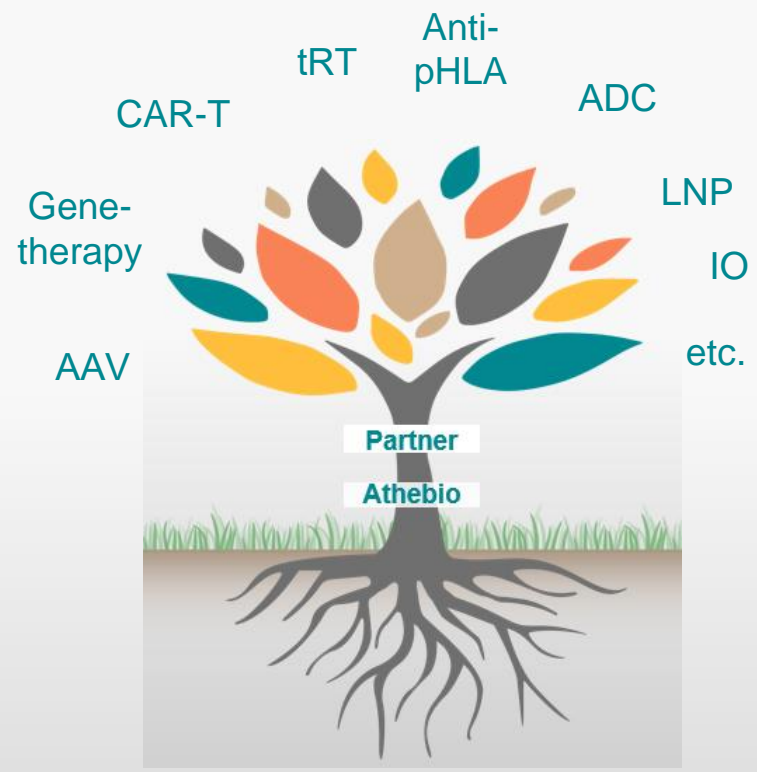
- REGENXBIO teamed up with us to generate AAV therapeutics of tailored tropism using our Athebody[®] DARPin building blocks
- We selected highly specific Athebody[®] binders against human transferrin receptor 1 (hTfR1), cross-reactive to mouse and cyno
- REGENXBIO “decorated” the AAV capsids with these DARPins via genetic fusion, easily constructing different AAV9 formats to assess transduction efficiency and production titer

Successful redirection of AAV capsid tropism

- Up to 90-fold increased transduction of hTfR1-expressing cells
- AAV-DARPin production w/o significant drop in production titer
- Up to 2.2 VP1-DARPin copies per capsid on average

DARPin-AAV transduction data adapted from
 Firnberg E. et al. 2023

Athebody® DARPinS as building blocks for next-generation therapeutics



Knowhow, Patents
 Athebody® DARPinS &
 libraries

Precision Targeting

- We are here to enable drug developers to create superior targeted therapeutics of **advanced efficacy and safety** and thereby increased probability of clinical success

Disruptive innovation

- We revolutionize drug development by bringing the design and selection of DARPinS to perfection and establish them as **state-of-the-art** building blocks of targeted therapeutics. We aim for **high return on investment** for our partners and us through **collaborative breakthrough innovation**

Customer-centric partnership

- We **enable** innovative drug developers to create superior targeted therapeutics by providing them with **tailor-made** “plug and play” DARPinS, working together in a co-creative space, and supporting them with **in-depth expertise** and superb service

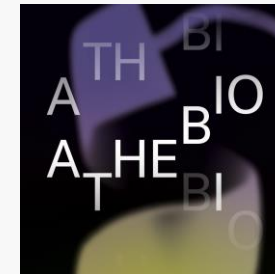
Let's co-create the **next generation** of targeted therapeutics!

You

- Your product ideas and expertise to develop targeted therapeutics
- Your commitment to innovation in drug development



**DARPin-targeted therapeutics
with improved
Safety and Efficacy**



- Our proprietary Athebody[®] platform & expertise
- Our innovation power and out-of-the-box thinking

Team Athebio: *We empower drug developers*



www.athebio.com/about-us

Athebio AG

Grabenstrasse 11a

8952 Zurich-Schlieren

Switzerland

www.athebio.com

E-Mail: hello@athebio.com

Phone: +41 44 508 08 28



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