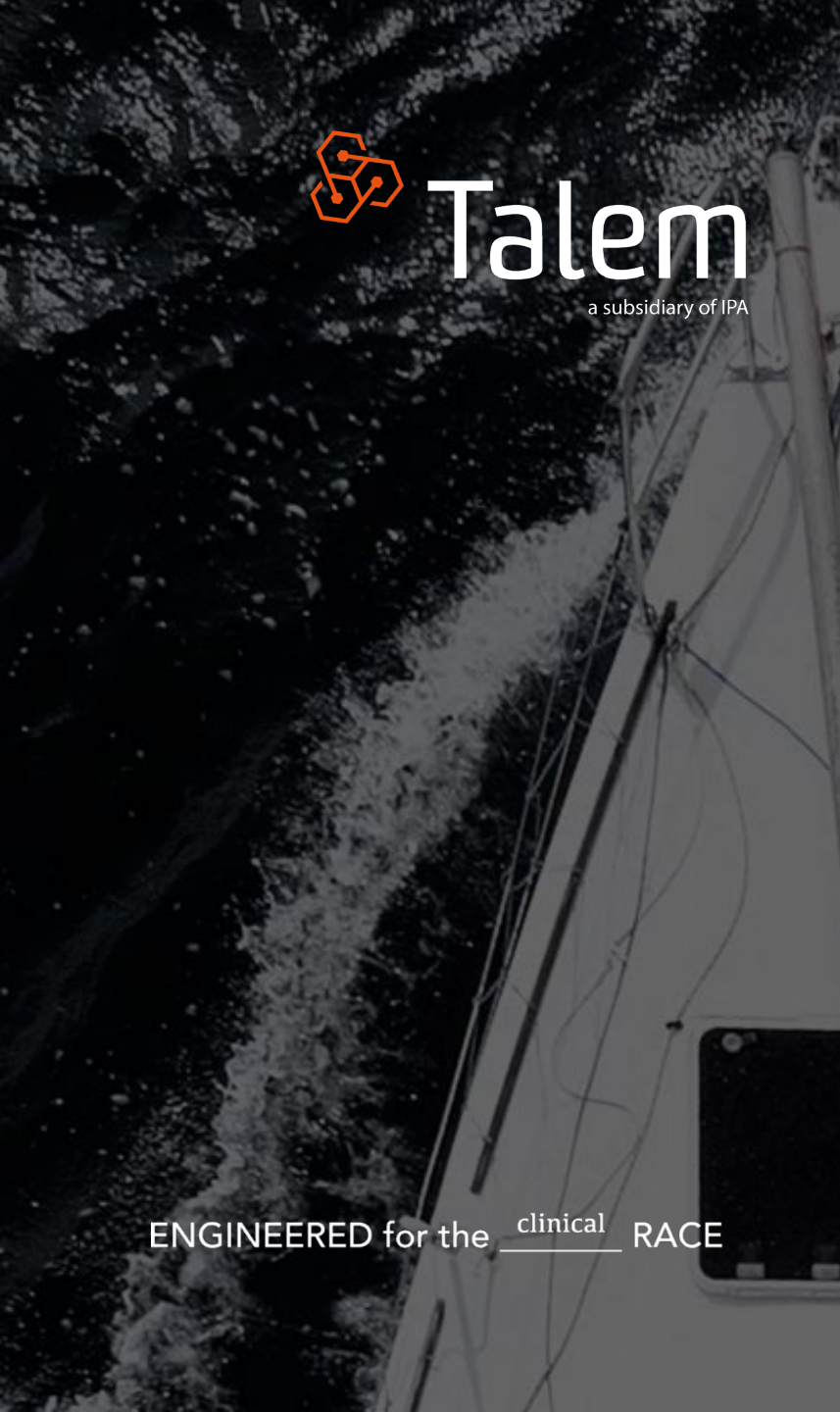




Talem Therapeutics

Antibody Pipeline for Out-Licensing / Partnership



ENGINEERED for the clinical RACE

Talem Therapeutics

- Established in 2019, Talem is an independently operating subsidiary of ImmunoPrecise Antibodies (IPA).
- Leverages IPA's 30 years of experience in innovative antibody discovery and development.
-  Focus on licensing & partnering early-stage assets.



Talem Antibody Therapeutics Pipeline

Program ID	Target	Indication	Format	Target Identification	Target Validation	Discovery	Lead Candidate Selection	Preclinical IND-Enabling
TATX-20	CAXII	IO, ONC	mAb					
TATX-24	CD3	IO	CD3δ ϵ targeting arm for bi- or multi-specific					
TATX-25	Undisclosed	IO, ONC	Undisclosed					
TATX-28	B7-H3	IO	Undisclosed					
TATX-112	TrkB	IO, ONC	mAb for ADC					
TATX-200	TrkBxCD3	IO, ONC	bsAb					
TATX-03	SARS-CoV-2	ID	Multi-antibody combination Tx	PolyTope®				
TATX-21	ALK1	OP/VD	mAb					

INDICATION KEY: ID= Infectious Disease | IO= Immuno-Oncology | ONC = Oncology | OP= Ophthalmology | VD= Vascular Disease

 Available for out-license


Pierre Fabre

Undisclosed partnership





Talem Pipeline: Overview of Prioritized programs

Program (target)	Indication	Differentiator(s)	Status
TATX-020 (CAXII)	Solid tumors, in particular • Ovarian cancer	• Fully human inhibitory mAb • Preservation of chemosensitivity • Reversal of pro-oncogenic phenotype of macrophages in TME	Lead candidate selected • Fully human mAb inhibiting CAXII
TATX-021 (ALK1)	Vascular pathologies, in particular • Diabetic retinopathy • Pulmonary Arterial Hypertension Solid tumors	• Currently no curative treatments for these indications • Agonistic activity • Vascular normalization • Novel avenue for reduction of tumor angiogenesis	Lead candidates selected • 8 potential agonists • 2 potential antagonists
TATX-024 (CD3δε)	Generation of multi-specific molecules in combination with tumor target of prospective partner	• Unique and potentially safer T-cell activation profile	Lead candidates selected • Binding and or activation of reporter T-cells • Provisional patent filed



Talem Pipeline: Overview of Prioritized programs

Program (target)	Indication	Differentiator(s)	Status
TATX-112 (TrkB)	Solid tumors, in particular - Breast cancer - Non-Small Cell Lung Cancer - Ovarian Cancer	8 Internalizing mAbs - No other TrkB immunotherapies in development - Potential for indication agnostic tumor therapy	Lead candidate selection from prioritized potential internalizing antibodies - Confirmation of mode of action - Provisional patent filed
TATX-200 (TrkBxCD3)	Breast Cancer, in particular - Triple-Negative Breast Cancer - HER2 Negative Breast Cancer	- No other TrkB TCEs in development - Unique T-cell activation profile - Potential for indication agnostic tumor therapy	Lead candidates selected (3) - Simultaneous bi-target binding confirmed - Bi-target dependent activation of reporter T-cells, preliminary proof-of-concept - Provisional patent filed

TATX-200

TrkB x CD3 Bispecific (BsAb) for Oncology



The Purpose

Develop a more effective treatment for metastatic and triple negative breast cancers (TNBC) against a target that is widely expressed on various cancers



The Strategy

T cell-mediated tumor cell destruction

- Talem identified TrkB, a tumor associated antigen (TAA), as a target of interest for a first-in-class antibody therapeutic.
- Current Trk-targeting therapies are small molecule-based and lack specificity for TrkB, leading to various adverse effects.
- **Talem generated a novel T cell engager against low immunogenic tumors by combining proprietary anti-TrkB arms with Talem's next-gen anti-CD3 T cell engaging arms**



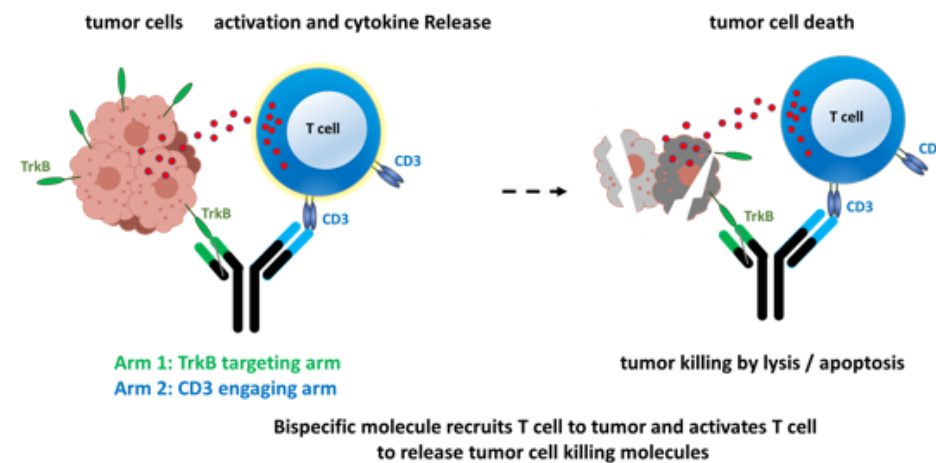
The Potential

Due to TrkB's diverse tumor expression profile, TATX-200 has high repurposing potential. TrkB expression in normal tissues is limited to the immune-privileged CNS.

First-in-class BsAb for metastatic or triple negative breast cancer



Anti-TrkB x CD3 bispecific - mechanism of action



The Product – Lead Candidates

3 Bispecific Combinations (TrkB x CD3)

- Bispecific #1 – TrkB_3XCD3_A
- Bispecific #2 – TrkB_3XCD3_B
- Bispecific #3 – TrkB_40XCD3_A



Targeting TrkB as Tumor Associated Antigen for Solid Tumors

TrkB or Tropomyosin receptor kinase B

- TrkB's main ligands are NT-4/5 and BDNF
- Significant and specific aberrant (over)expression and signaling of TrkB in various solid tumors.
- **Overexpression of TrkB associated with:**
 - Uncontrolled cell proliferation and tumor metastasis
 - Poor prognosis due to role of TrkB in suppression of anoikis and epithelial-mesenchymal transition

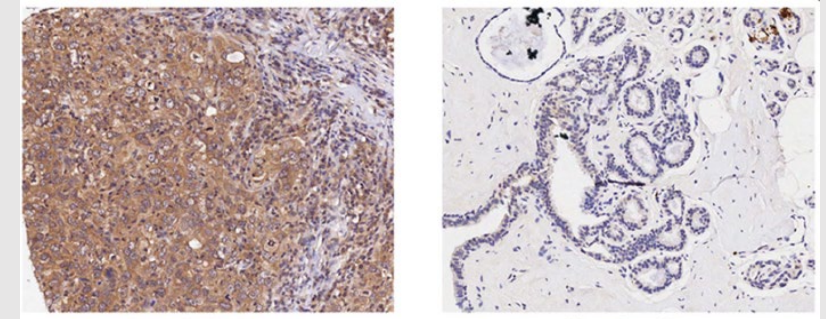
Examples from literature

Tumor	Subtype	% IHC samples positive for TrkB Expression
Breast Cancer	Triple Negative Breast Cancer	84.2% TrkB+ expression of primary TNBC patient tumor samples ¹ 100% TrkB+ expression of recurrent TNBC cases ¹
Lung Cancer	Non Small Cell Lung Cancer	75% TrkB+ expression of patient tumor samples ²
	Small Cell Lung Cancer	56.9% patients have high TrkB expression ³
Gall Bladder Cancer	-	91% TrkB overexpressed ⁴
Gastric Cancer	-	63.8% patient cancer tissue expressed TrkB ⁵
Colon Cancer	-	83% tumors overexpressed TrkB ⁶

¹Yin et al. 2015. ²Okamura et al. 2012. ³Kimura et al. Lung Cancer 2018. ⁴Jia et al. 2015. ⁵Jin et al. 2021. ⁶Yu et al. 2020.
Full list of TrkB associated cancer and expression, including prognosis, available upon request

TrkB tumor specific expression in human tissues

Breast cancer tissue (left) and matched adjacent normal tissue (right)



<https://doi.org/10.1016/j.anndiagpath.2022.152017>

Manageable risk of on-target off-tumor effects expected

- Low expression outside CNS
- Antibodies do not readily cross the blood-brain-barrier
- Pan-TRK inhibitors are on the market as tumor-agnostic treatment with manageable adverse effects
- Contrary to pan-TRK inhibitors, Talem's mAbs are highly specific for TrkB, no activity on TrkA nor TrkC

TATX-200 TrkB x CD3 Bispecific T cell engager for Oncology



Design of TrkBxCD3 BsAb

BsAb platform:

- Bispecifics generated with "knob-into-hole" technology
- Bispecific format **scFv/Fab**

Properties TrkB targeting arm:

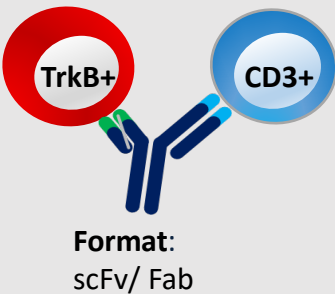
- Low Kdis
- Cross-reactive with mouse and cyno
- Non-internalizers
- Highly specific to TrkB, no pan-TRK activity

Properties CD3δε Fab:

- Unique T-cell activation profile intended to dampen cytokine release
- Potentially safer and potentially more effective immunotherapy

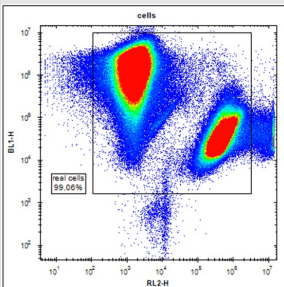
Characteristics TrkB x CD3 BsAb

- Single target binding confirmed using plate- and flow-based assays
- Simultaneous target binding confirmed using flow-based bridging assay
- Activates CD3 in a TrkB-dependent manner in a Jurkat reporter cell assay

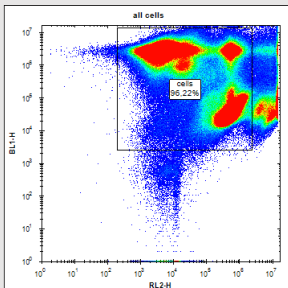


Bridging assay outline

Without BsAb



With BsAb



Characteristics TrkBxCD3	TrkB_3XCD3_A	TrkB_3XCD3_B	TrkB_40XCD3_A
Binding to TrkB	+++++	+++++	+++++
Binding to CD3	+++++	+++	+++++
Simoltaneous binding to TrkB AND CD3	+++++	+++++	+++++
Jurkat activation	+++++	++	+++++

TATX-112

TrkB Antibodies for Oncology (ADC)



The Purpose

Develop a first-in-class receptor internalizing mAb targeting TrkB for ADC-based therapeutics for solid tumor malignancies.



The Strategy

Develop highly specific internalizing anti-TrkB antibodies to combine with various ADC platform or linker/payload technologies to deliver toxic payload to target cells.



The Product

- 8 fully human lead candidates for linker/payload conjugation

First-in-class TrkB targeting for ADC-based therapeutics



TrkB or Tropomyosin receptor kinase B

- Its main ligands are NT-4/5 and BDNF
- Binding of BDNF to TrkB induces endocytosis
- Aberrant (over)expression and signaling in various cancers

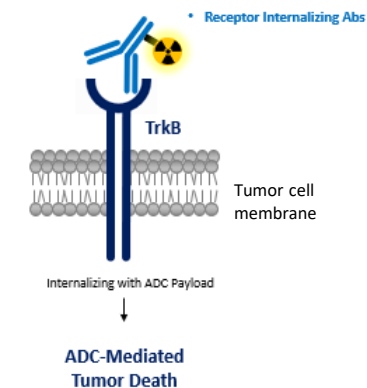
Overexpression of TrkB associated with:

- Uncontrolled cell proliferation and tumor metastasis
- Poor prognosis due to role of TrkB in epithelial-mesenchymal transition and suppression of anoikis

Primary Indications - Oncology:

- Triple-Negative Breast Cancer (TNBC)
- HER2 Negative Breast Cancer
- Non Small Cell Lung Cancer (NSCLC)

Receptor Internalizing with ADC Payload



TATX-112

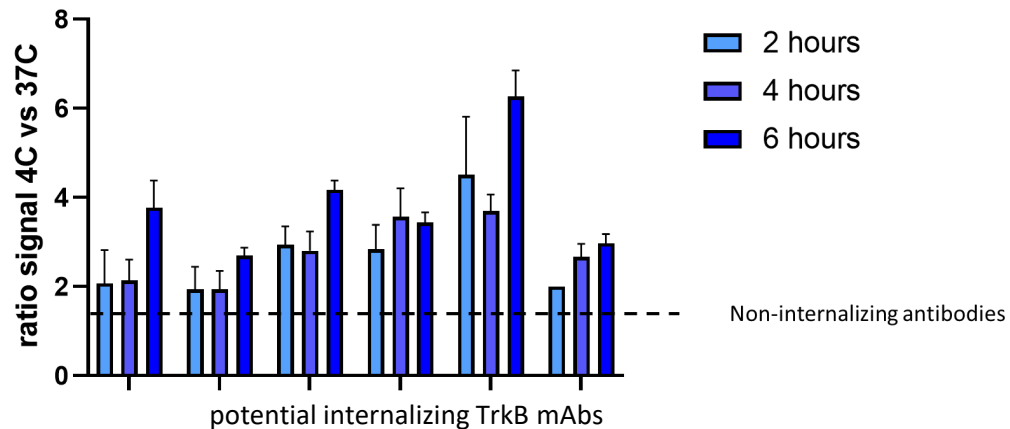
First in class mAbs for ADC therapeutics



All 8 TATX-112 Lead mAbs derived from human phage libraries

- All specific for TrkB , no cross-reactivity with TrkA and TrkC
- All bind to hu-, cyno-, and mo-TrkB
- 3 epitope bins located throughout the TrkB extracellular domain
- Diversity in off-rates (hu-TrkB)
- 3 mAbs partially block BDNF binding to the ECD of TrkB

Examples of potential internalizing TATX-112 mAb



CHO-TrkB cells were incubated for different timepoints with potential internalizing TrkB mAbs (10µg/ml) at 4°C (non internalizing conditions) or 37°C (internalizing conditions) after which remaining membrane-expressed TrkB expression was analyzed using flow cytometry by labeling cells with anti-human-PE antibodies which detect TrkB mAb bound to TrkB. Median fluorescence at 4°C was divided by that at 37°C. Data is the mean plus SD of 1 experiment with 3 technical replicates. Ratios observed with CHO parental cells and isotype controls were used to determine baseline. Baseline indicated with dashed line designated as non-internalizing antibodies.

Eight (8) fully human potential internalizing antibodies

mAbs	Epitope bin (arbitrary)	Blocking of BDNF
IN_01	1b	no
IN_02	1b	no
IN_03	1b	no
IN_04	1b	no
IN_05	3b	partial
IN_06	3b	partial
IN_07	3b	partial
IN_08	5	no

Note: The TATX-112 mAbs are unique for this program, no overlap with the TATX-200 program

TATX-24

CD3 Fabs for T cell engagement



The Purpose

Develop best-in-class CD3 $\delta\epsilon$ targeting arm to be used in bi- and multi-specific antibody therapies to target poorly immunogenic tumors.

MOA → TAA binding to tumor cell, followed by CD3-mediated (local) T cell recruitment and activation for tumor killing.



The Strategy

Develop anti-CD3 Fab with selective affinity to reduce the risk of cytokine release syndrome.

To combine with a variety of tumor antigen targeting arms.



The Product

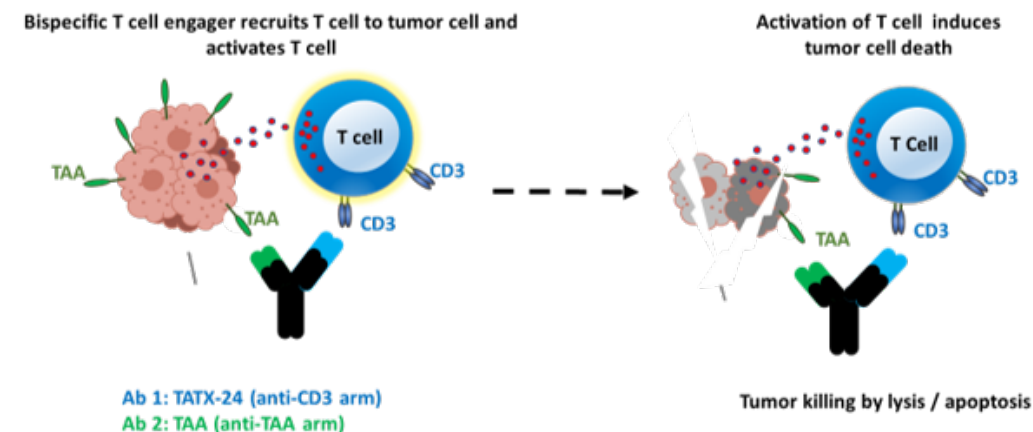
- 5 lead candidates, specifically bind CD3 $\delta\epsilon$
- Jurkat cell binding Fabs
- Off-rates & EC50's in the same range as the OKT-3 benchmark
- Additional candidates under evaluation



Next gen CD3 $\delta\epsilon$ Fabs for T cell engagement

CD3 Targeting Program – T cell engagers

- Specifically selected for reactivity toward CD3 $\delta\epsilon$ heterodimer to reduce probability of cytokine release syndrome
- Stable, bispecific antibodies (bsAbs) with confirmed simultaneous binding to CD3 and tumor-associated antigen (TAA)
- Each molecule has a unique T cell activation profile in bsAb format when compared to the OKT-3-based benchmark (reporter cell assay)



TATX-20

Anti-CAXII for Oncology



The Purpose

Develop first-in-class therapy to target CAXII in solid tumors by inhibiting enzyme activity.



The Strategy

Target CAXII in ovarian cancer due to the high unmet need, high recurrence rate, and resistance to chemotherapy. Potential value to overcome multi-drug resistance.



The Product

Lead antibody candidate

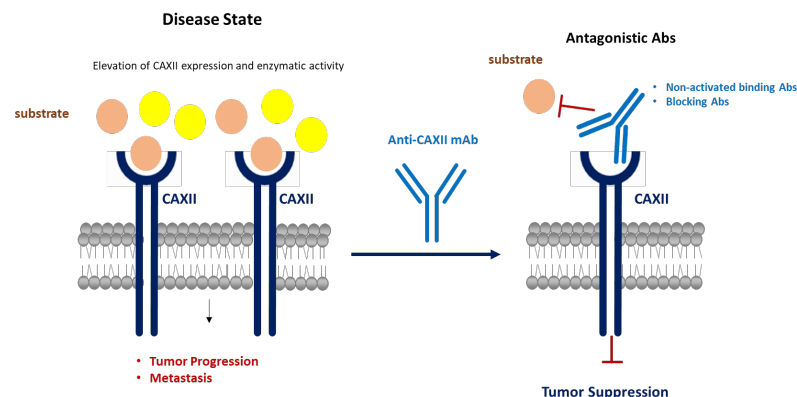
- Fully human, antagonistic mAb
- CAXII-specific, no cross reactivity with CAIV, CAIX and CAXIV
- Confirmed binding to endogenous expressing cell line
- Cross-reactivity to cyno CAXII

First-in-class antagonistic mAb against CAXII, a solid tumor and TME target



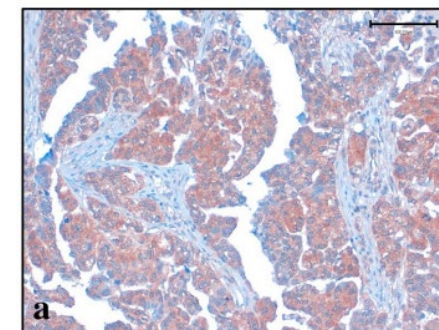
Carbonic anhydrase CAXII

- Membrane protein induced under hypoxic conditions in solid tumors
- CAXII plays a crucial role in the survival and proliferation of cancer cells
- Mediates the survival and pro-metastatic functions of macrophages in TME
- Required for Pgp-mediated resistance to chemotherapy (multi-drug resistance)
- Inhibiting CAXII activity has shown to reduce tumor size, inhibit tumor migration, and restore sensitivity to chemotherapy in preclinical models.



Selectively targeting ovarian cancer via CAXII

- CAXII is significantly overexpressed in ovarian cancer, relation with malignancy grade
- Blocking CAXII impairs tumor cell survival and reverses Pgp-mediated drug resistance
- Ovarian cancer has an uncrowded antibody therapeutic market compared to other cancers



IHC staining for CAXII on ovarian cancer
DOI: [10.1371/journal.pone.0271630](https://doi.org/10.1371/journal.pone.0271630)

TATX-21

ALK1 for vascular disease (DR & PAH)



The Purpose

Develop monoclonal antibodies for a safe and effective therapeutic for vascular pathologies such as DR and PAH.



The Strategy

Improve signaling through the ALK1 pathway to reduce hyperpermeability and restore endothelial function in vascular pathologies.



The Product : Lead Selection Stage

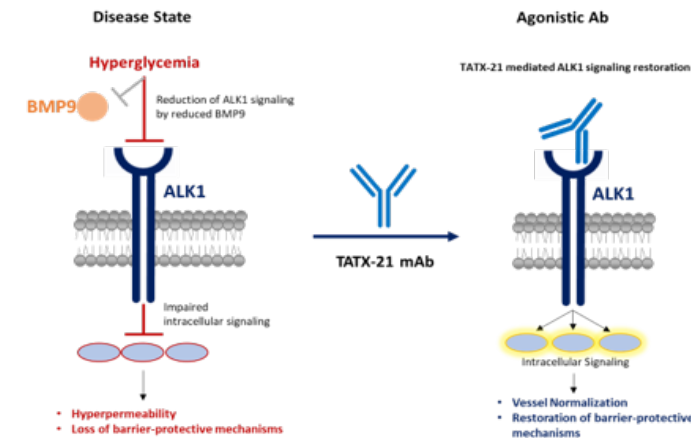
- 8 sequence-unique ALK1 agonists (human-rabbit chimeric antibodies)
- Specific for ALK1
- Binding to and activity on HUVEC confirmed

First-in-class vascular therapeutic



Activin A receptor like type 1 (ALK1)

- A member of TGF- β superfamily of receptors, ligands BMP9 and BMP10
- Preferentially expressed on endothelial cells, regulates normal blood vessel development
- Enhancing signaling reduces symptoms of PAH and prevents hyperglycemia-induced vascular permeability in preclinical models



Diabetic Retinopathy (DR)

- Most common cause of vision loss in diabetic patients
- Hyperglycemia results in reduced ALK1 signaling and subsequent vascular permeability
- DR being used as POC for other diabetic pathologies and ophthalmological diseases

Pulmonary Arterial Hypertension (PAH)

- No curative treatments currently available
- No other ALK1 antibodies for PAH in clinical evaluation nor on the market
- Aim to restore normal vascular integrity and function with agonistic mAbs



Engineered
for the race
and the shared pursuit
of clinical success

Leadership

Dr. Jennifer Bath



Chief Executive Officer and President

Jennifer Bath is the CEO and President of ImmunoPrecise Antibodies. She obtained a Ph.D. in Cellular and Molecular Biology, specializing in immunology and biochemistry, with a focus on discovering and validating biologics for the prevention and treatment of neglected tropical diseases. Dr. Bath held a tenured position as an Associate Professor of Cellular and Molecular Biology, while concurrently serving as the Founder and Executive Director of the Concordia Global Vaccine Institute. She also served many years as a strategic growth and business operations advisor for global pharma, biotech, and government.

Dr. Bath has held executive roles in both biotechnology and contract research organizations, with her most recent post on the executive team at Aldevron, LLC. Here, she headed the global sales and client relations teams, and defined business strategies by applying knowledge based on the science, technology and market. In addition, she served as a key technical specialist, converting challenges for pharmaceutical and biotechnology clients into operational initiatives.



Dr. Ilse Roodink



Chief Scientific Officer

Dr. Ilse Roodink serves as Chief Scientific Officer (CSO) of ImmunoPrecise Antibodies, supporting the company's global research and development teams. Prior to her appointment as CSO, she held different scientific positions at the Company's Dutch facility in Oss from 2013 until 2021. In her last role as Scientific Director of ImmunoPrecise Europe, Dr. Roodink was overseeing contract research project execution and management and actively involved in the integration of innovative technologies supporting antibody characterization and engineering. Following its establishment in 2019, Dr. Roodink has served as Chairwoman of Talem Therapeutics' Scientific Advisory Committee, leading the development of Talem's pipeline assets.

Dr. Roodink graduated from Radboud University of Nijmegen, the Netherlands with a Master's degree in Biomedical Health Sciences and a Ph.D. in Medical Sciences. Her work, resulting in several peer-reviewed publications, focused on platform development to facilitate the discovery of antibodies specifically recognizing native tumor targets.



Dr. Jetta Bijlsma



Senior Director of Product Development

Dr. Jetta Bijlsma serves as Senior Director Product Development of Talem Therapeutics and has overall responsibility for the development of the company's internal programs. Prior to joining Talem, Dr Bijlsma served as Director (pre) Clinical Development at Intravacc, a Dutch vaccine company, where she was responsible for delivery of preclinical data packages for and organisation of clinical trials by the Department. As Associated Principal Scientist at Merck Animal Health, she was a discovery and development specialist, managing her team to execute highly complex projects to deliver proof of concept in animal health vaccines in close collaboration with RA, RD, IP and manufacturing departments. Projects ranged from antigen discovery, immunological characterisation of novel vaccines and assessment of novel platform technologies. As Assistant Professor at the University Medical Centre Groningen she established and managed her own research group on host-pathogen interactions.

Dr. Jetta Bijlsma graduated from the RijksUniversiteit Groningen, the Netherlands with a Master's degree in Molecular Biology and obtained her PhD in Medical Sciences at the Vrije Universiteit Amsterdam, the Netherlands. Her work focused on molecular and immunological facets of host-pathogen interactions.





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