Disruptive biological approaches in immunotherapy, based on next generation BiXAb® bi- and multi-specific antibody platform for cancer treatment

Corporate deck for Galien start-up prize:
Deck3: Development, preclinical & clinical evidences
May 2023

A robust pipeline of disruptive proprietary BiXAb® programs in oncology

Programs	Mechanism of Action / Indication	Discovery	Candidate nomination	Preclinical (CMC, Tox)	Clinical Phase 1 & 2
DEVELOPMENT PROGRAMS					
BMX-00X BiXAb bispecific Ab (out-licensed; codevelopment)	Dual immune checkpoints Clinical development planned in hemato-logical malignancies and solid tumors				*Should start first in man clinical Phase 1 soon in 2023*
BMX-003 BiXAb bispecific Ab	RTK (EGFR) family of receptors Potential in colon and pancreatic cancers				*Ready for CMC and regulatory preclinical*
CURRENT DISCOVERY PROGRAMS					
BMX-501 MAIT engagers BiXAb (MAIT x HER2)	1st program (HER2, considered as an anchor for MAIT redirection) => solid tumors (ie. CRC, lung, pancr., etc				*CMC and regulatory preclinical*
BMX-50X MAIT engagers BiXAb (MAIT x TAA2)	2nd program (TAA2) => solid tumors				*Ready for CMC and regulatory preclinical in early Q4 2023*
Early-stage discovery programs	Other BiXAb bispecifics Ab • MAIT engagers • Anti-CPI-PD1 • Immune cell redirection				
BMX-900 TriXAb trispecific antibody	Different programs with MAIT cell redirection				

TAA: Tumor Associated Antigen; CPI: (immune) CheckPoint inhibitor; MAIT engagers (MAIT cell redirection): Mucosal Associated Invariant T cell redirection

Our first BiXAb program (BMX-00X) is ready to start clinical trial, with a great potential in immuno-oncology, confirming the validation of BiXAb platform

- **Novel approach for the treatment of hematological malignancies and solid tumors (dual Immune checkpoints)**
- **Excellent Efficacy and Pharmacokinetic profile in mice**
  - No steric hindrance, potent ADCC, Exhibit PK profile similar to the parental antibody
  - **In vivo superior activity** vs parental mAbs and combination
- **Optimal Manufacturability**
  - **Cognate HC/LC pairing**; High purity
  - Titre of the **GMP batch much superior to any other BsAb platforms**

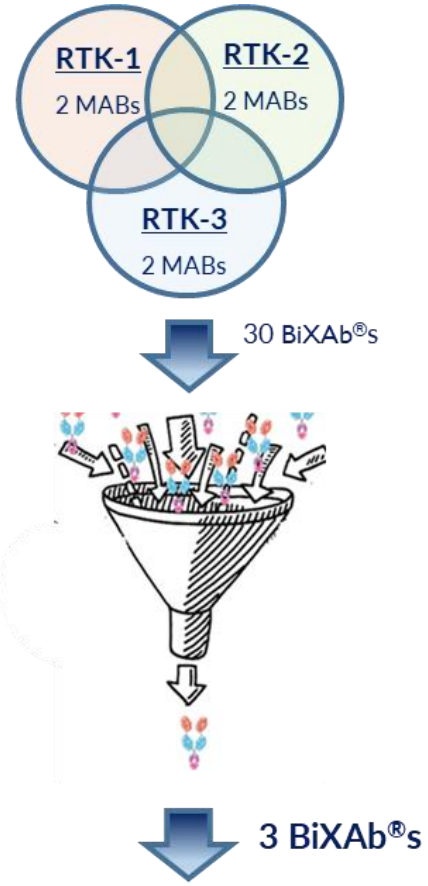
- **Finalized regulatory preclinical development / IND-enabling studies**

  => should start **Phase 1 clinical trial soon in 2023**
- Potential to be a **cutting-edge immunotherapeutic in hematological malignancy & solid tumors**
- **First in man Phase 1 clinical study will confirm the validation of the BiXAb platform (+ deals with pharma)**

=> **Biomunex will become a clinical-stage company in a few months**

BMX-003 program: a BiXAb® targeting two RTKs (EGFR family of receptors) with superior activity in several *in vivo* models of pancreatic cancer

- Rapidly generated 30 BiXAb®s from 6 mAbs against 3 RTKs (EGFR family of receptors)
- In collaboration with Univ. of Montpellier / IRCM (FR; Inserm)
- Tested in screening funnel
- Significant anti-tumoral activity in several *in vivo* models of pancreatic cancer (i.e., PDX), demonstrating the potential superiority vs the standard of care
- Lead candidate ready to start CMC development in early 4Q23 (humanized development candidate)
- Program available for internal development (ie. ready to start CMC) and or partnering / out-licensing



Institut de Recherche en Cancérologie I R C Montpellier

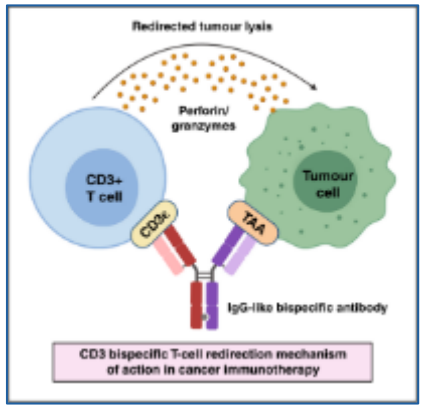
Inserm
Institut national de la santé et de la recherche médicale

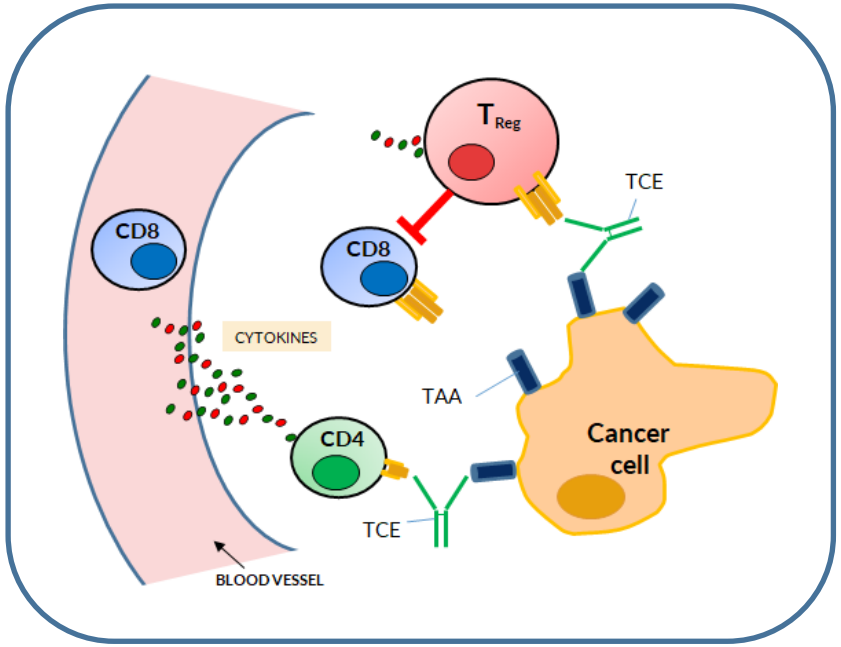
Thanks to its unique BiXAb-MAIT engager platform, the problem Biomunex is trying to solve is to overcome the main weakness of traditional CD3+ TCE

- T-cell redirection is a successful clinical modality in Hematological tumors
  - Blincyto (CD3xCd19) is a billion dollar drug.

- To date, **T-cell redirection has failed in solid tumors**
  - All 6 CD3xPSMA TCEs in clinic were reviewed at ESMO 2022:
  - Conclusion, **none of them had clinically meaningful results**

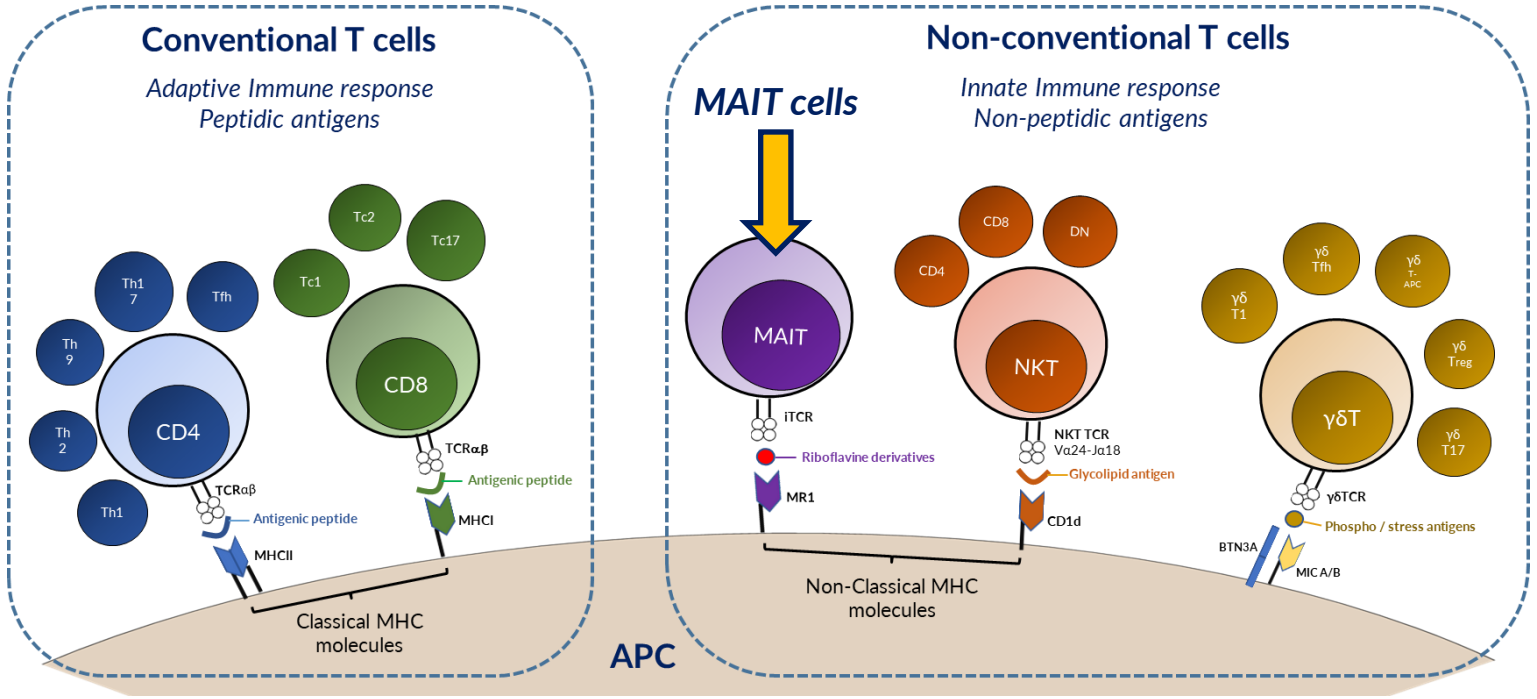
- **Classical TCEs activate all T-cell subsets** leading to:
  - **Cytokine release syndrome (CRS) that can be fatal and limits higher dosing**
  - **Activation of Tregs in the tumor microenvironment increases immunosuppression of cytotoxic T-cells**





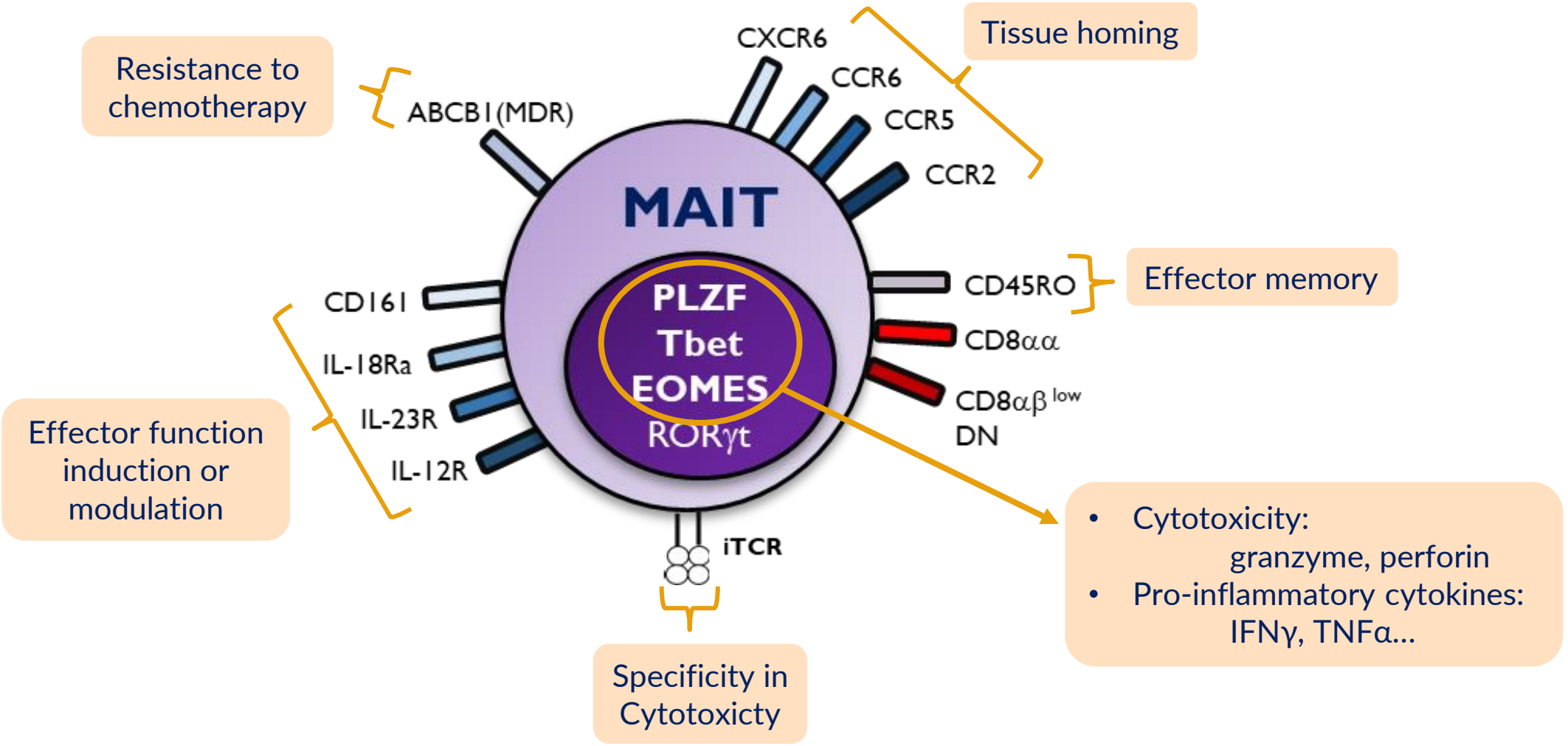
Redirection of MAIT-cells => BiXAb-MAIT engager platform (MAIT cell: *Mucosal Associated Invariant T Cell*)

- MAIT cells are a subset of CD8+ T-cells; residing especially in barrier/mucosal tissues
- Institut Curie with Biomunex => identified the potential role of redirecting MAIT cells in cancer therapy
- Strong IP position for BiXAb®-MAIT engagers
- BiXAb® will bind and redirect MAIT cells to kill cancer cells



TAA: Tumor Associated Antigen; MAIT engagers (MAIT cell redirection): Mucosal Associated Invariant T cell redirection

The Characteristics of MAIT-cells to kill cancer cells will enable cancer control, notably solid tumors

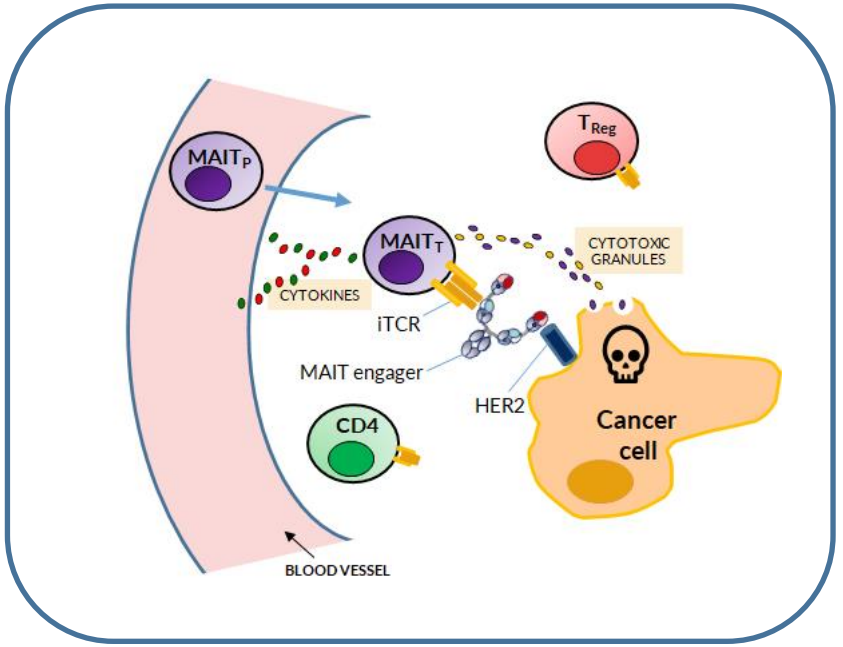


The Biomunex solution: MAIT engagers
Simple, elegant and universal

- **MAIT cells have all the characteristics to solve these problems in solid tumors**

- MAITs are **potent cytotoxic T-cells**
- **Abundant in tumor** (> 25% of TILs) and in the **blood** (> 15% of CD8s)
- **Naturally reside in tissue and tumors**, and readily infiltrate inflamed tissues.
- Memory phenotype (**primed to kill**)
- **Resistant to** many **chemotherapies**

- Differentiation of MAIT engagers
  - **Safety: No CRS** (no CD4 activation) and so **can be dosed higher**
  - Efficacy in solid tumors: No increased immunosuppression from Tregs
  - **More abundant** than γ/δT cells and **not switched to regulatory cells** by TME (like γ/δT cells)



In the right place, at the right time, with the right capability

BiXAb-MAIT engager BMX-501 is nominated and ready to start regulatory preclinical development (incl. CMC and IND-enabling studies)

Efficacy
(BiXAb/TAA dependent)

- Activation
- Proliferation
- Degranulation (granzyme B and perforin)
- Cytokine release (local, proinflammatory)
- Potent cytotoxicity over wide range of HER2 expression

Ex vivo human patient data

- Cytotoxicity of tumor resident MAITs in patent samples
- Migration into Patient derived 3D organoids (PDO)
- Cytotoxicity of PDOs

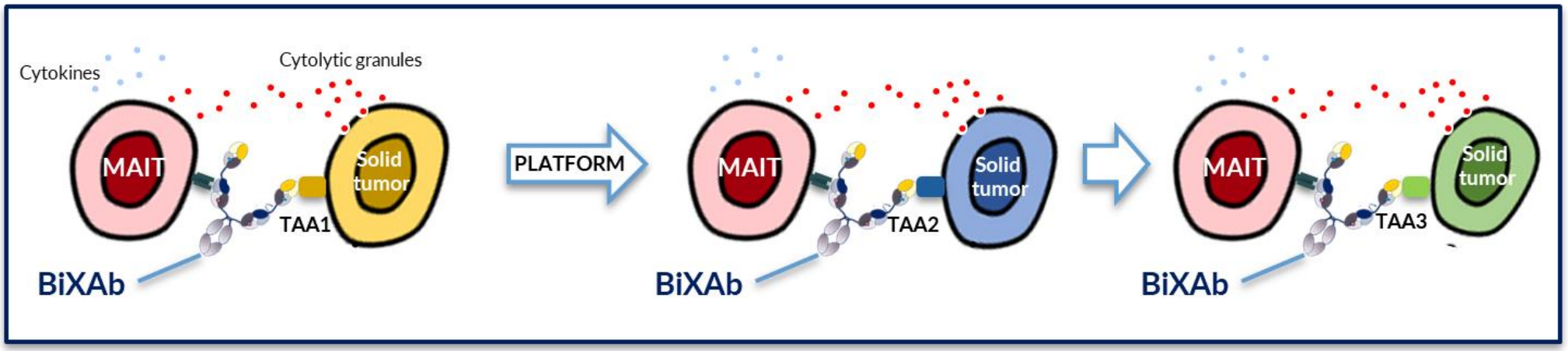
Safety

- Limited cytokine release from whole blood
- No activation of T-regs
- No activation of other T-cell subsets
- No discernable toxicity in NHP study
- No significant toxicity in Phase I with Ertumaxomab and GBR-1302 (that would activate MAITs)

The unique and proprietary BiXAb®-MAIT platform currently with 2 programs (BMX-501 and BMX-50X)

- **Potential first candidate is nominated to start regulatory preclinical development**
  - BMX-501: Evaluating **HER2 (as an anchor for MAIT redirection)** as a potential candidate **for initial indication in solid tumors** (i.e. for HER2+ lung or colorectal or pancreatic or bladder or small intestine cancers, etc)

- **Platform approach development**
  - Generating a **large proprietary panel of antibodies** (diverse epitopes and affinities) **towards the MAIT iTCR**
  - BMX-50X: **3 different TAAs evaluated** to define the best BiXAb MAIT engager as a potential other candidate (starting Phase 1 at the same time)
  - **Additional TAAs in the pipeline** being evaluated
  - **Potential for several programs in solid tumors**



Preliminary conclusions: MAIT cells can become a game-changer in cancer immunotherapy

Taking all the in vitro, ex vivo and safety data together strongly supports the contention that:

MAIT cells are potent cytotoxic cells that can be redirected to efficiently kill cancer cells and that "MAIT engagers" have great promise for the treatment of solid tumors.

Many impressive data are available, showing that **BiXAb-MAIT engagers can become a true game-changer in cancer immunotherapy**