JANVIER GROUP
BIOSCIENCES

mAbs
ANTIBODIES
FOR MEDICINE

THE ANTIBODY DISCOVERY PARTNER

HIGHLIGHTS FROM DEVELOPMENT TRACK RECORD

MImAbs antibody packages reaching the clinics after transfer to Biotech/Pharma

2013
creation as academic platform

2017

Naked mAb: CD73
Transferred to clinical development (Innate Pharma)

2018

Naked mAb: CD39
Transferred to clinical development (AstraZeneca)

2019

Bispecific mAb NK engager,
Pharmacological package (*in vitro* / *in vivo*) transferred to clinical development (Sanofi)

2020

Academic period achievements
20 target validation programs (16 naked mAbs, 3 ADCs, 1 bispecific)
100 immunization programs

2021

MImAbs Privatization

2022

mAb or ADC packages for biotechs
- **GPCRs**
- **Ion channels**

ADC: Nectin 4
Data package led to 87 million $ fundraising (Emergence-Tx)
Clinics started in 2024 (acquired by Eli Lilly in 2023)

2023

Acquisition by Janvier Group Biosciences

2024

***New* service on PDX-DC**

Dedicated BD Team

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Scientific and Technical Expertise
Full Program Overview

MISSION: GENERATION AND SELECTION OF ANTIBODY LEADS COMPATIBLE WITH GMP & IVD REQUIREMENTS

A modular expert platform for antibody selection and characterization

Project analysis

Scientific advice

Development Plan

mAb Generation

Antigen or mRNA immunization

Single B cell screen on Beacon® platform

Hit validation

mAb Engineering

Humanization

Conjugation (ADC, …)

Multispecific formats

Fc modifications

Bioproduction

Biophysical characterization

Formulation

Up to 400 mg production

Pharmacolgy

In vitro Pharmacology

- Cytotoxicity test on cell lines, PDX-DC
- Functional tests

In vivo Pharmacology

- Efficacy in syngeneic & xenogeneic models
- Immunophenotyping

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Business model

BUSINESS MODEL

MImAbs is seeking collaborations with biotechs / pharmas / academia

Fee-for-service collaboration

- Antibody campaign
- Antibody production, reformatting
- In vitro tests (ADCC, CDC, Immunopharmacology tests, custom tests…)
- In vivo tests, PK/PD, efficacy, immune profiling.

- **Reserved and dedicated prioritized resources**
- Definition **of early target validation workplan** (immunogen design, specifications of mAbs (naked, ADC, bispecifics), in vitro and in vivo POC design (KI models))
- **Scientific advice** on antibody generation and characterization strategies

In both scenarios MImAbs does not retain any IP rights

- **All IP** generated during the collaboration **belongs to Client**
- MImAbs has **no proprietary drug-discovery program**

BUSINESS MODEL

MImAbs is seeking collaborations with biotechs / pharmas / academia

- **Antibody expertise and know-how**
- **Flexibility - personalized support**
- **Operational capabilities**
- **Integrated or specific projects**

MImAbs

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Technical slides

Step 1 – Project analysis

Design of a comprehensive development plan

- **Generation of mAbs**
  - Design and production of immunogen (soluble proteins, transfectants, peptides…)
  - mRNA for difficult-to-express targets (proprietary immunization protocols with several track records of success with GPCR)
  - Generation of screening tools (transfectant human / mice / cyno for cross-reactivity)
  - Choice of animal strains: mice, KO mice for target if available to diversify epitope and allow mouse cross-reactivity, genetically engineered mice for direct fully human mAb obtention (Alloy Tx GK mice), rabbit
- **Format of antibodies**
  - Full range of mice and human isotypes
  - Blocking, ADCC, ADCC enhanced Fc mutations
  - Compare advanced formats (ADC, bispecifics, nanobodies…)
- **Design of preclinical models**
  - KI mice (18 months to generate mice colonies for pharmacology evaluation, via JCD)
  - Surrogate strategy (necessitates both human and mice immunization campaigns)
- **Generate comprehensive work program (Gantt and associated resources)**
  - Definition of go-no-go and milestones
  - Definition of reporting schedules
  - Resources are followed and adjusted depending on results/priorities

Step 2 – Beacon workflow

Immunization

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ATX-Gx Certified Service Provider

- Rec-protein - Transfectant - mRNA
- BALB/c model - KO model - C57Bl/6
- ATX-Gx Humanized mice (Alloy Tx)

Serum tested by ELISA or FACS

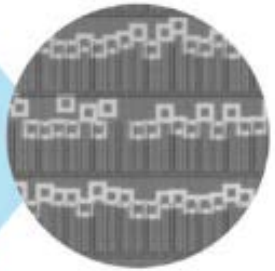
8 weeks

On chip single cell screening, amplification, sequencing, *in silico* analysis, selection of hits to produce

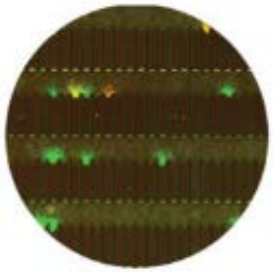
Beacon® screen, export and sequencing

Bioinformatic hit selection step

Beacon® system and OptoSelect™ chip



Clone 10K single B cells /chip into NanoPen™



Cell characterization within minutes

***In silico* analysis**
CDR liabilities / CDR patches

2 – 3 weeks

Cloning

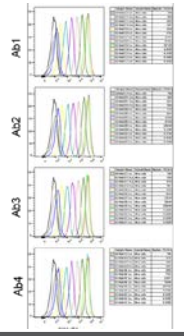
Production • Purification

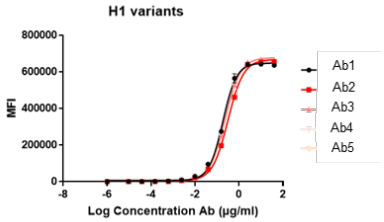
EC_{50} • Affinity • Functional

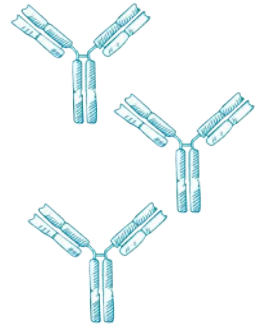
Selected hits

Robotized production of hits 100 µg level (up to 100 hits), or mg level if lower numbers (< 50 hits)

Selected Hits



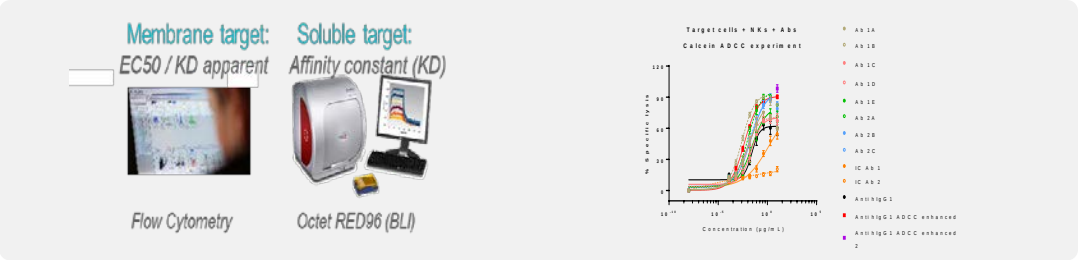




6 – 8 weeks

Step 2 – Lead Selection / pre-CMC

- **Functional characterization (affinity, in vitro pharmacological profiling ADCC, blocking direct lysis, see pharmaco test)**



- **Humanization of rodent mAbs; In silico analysis of mAb behaviour and sequence liabilities.**
  - Antibody modelling, CDR grafting
  - In silico analysis of sequence liabilities on fully human or along humanization process : propose variants to decrease identified liabilities
- **Biochemical characterization**
  - Purity, integrity, aggregate content (SDS, SEC HPLC)
  - Identity (Mass spectrometry)
  - Endotoxin (LAL test)
- **Pre-CMC behaviour as naked and ADC formats**
  - Pre-formulation (buffer, polysorbate, sucrose)
  - HIC (ADC)
  - NanoDSF studies
  - Stress tests (pH, freeze thaw cycles)
  - Accelerated stability studies of different variants

Modelization and analysis of sequence liabilities (N and W) of a lead candidate (MOE software)

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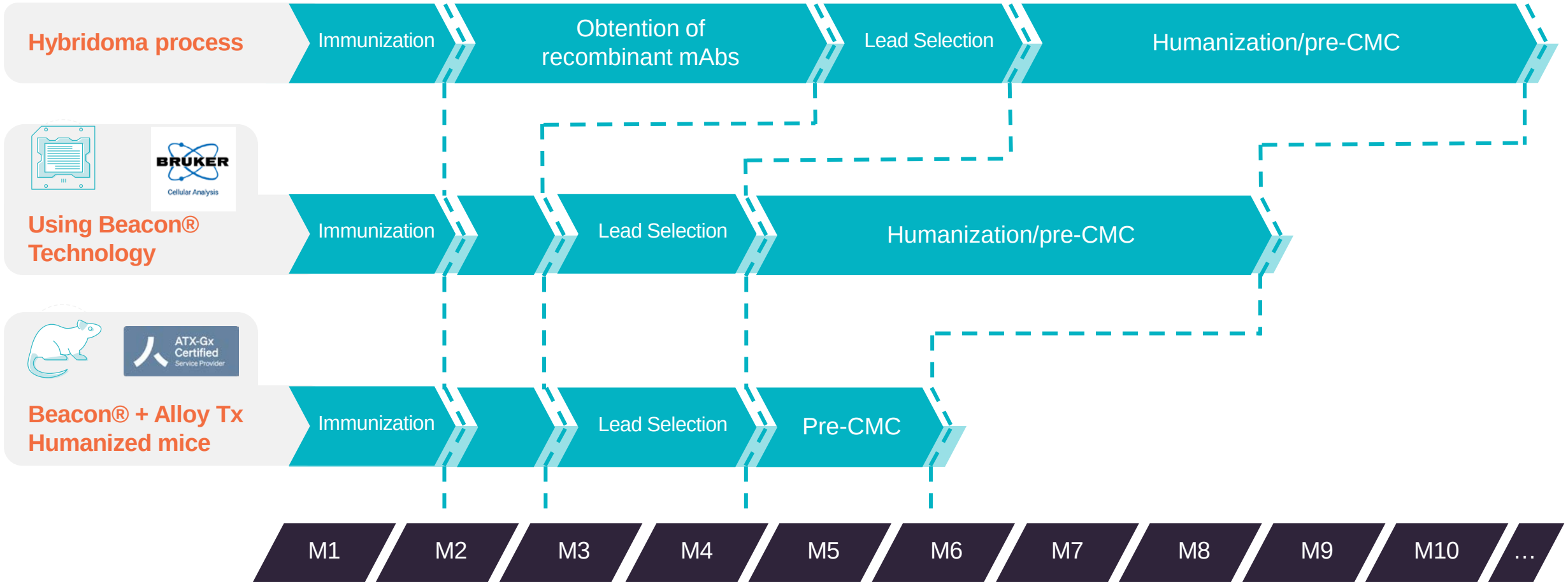
Step 2 – Lead Selection Time



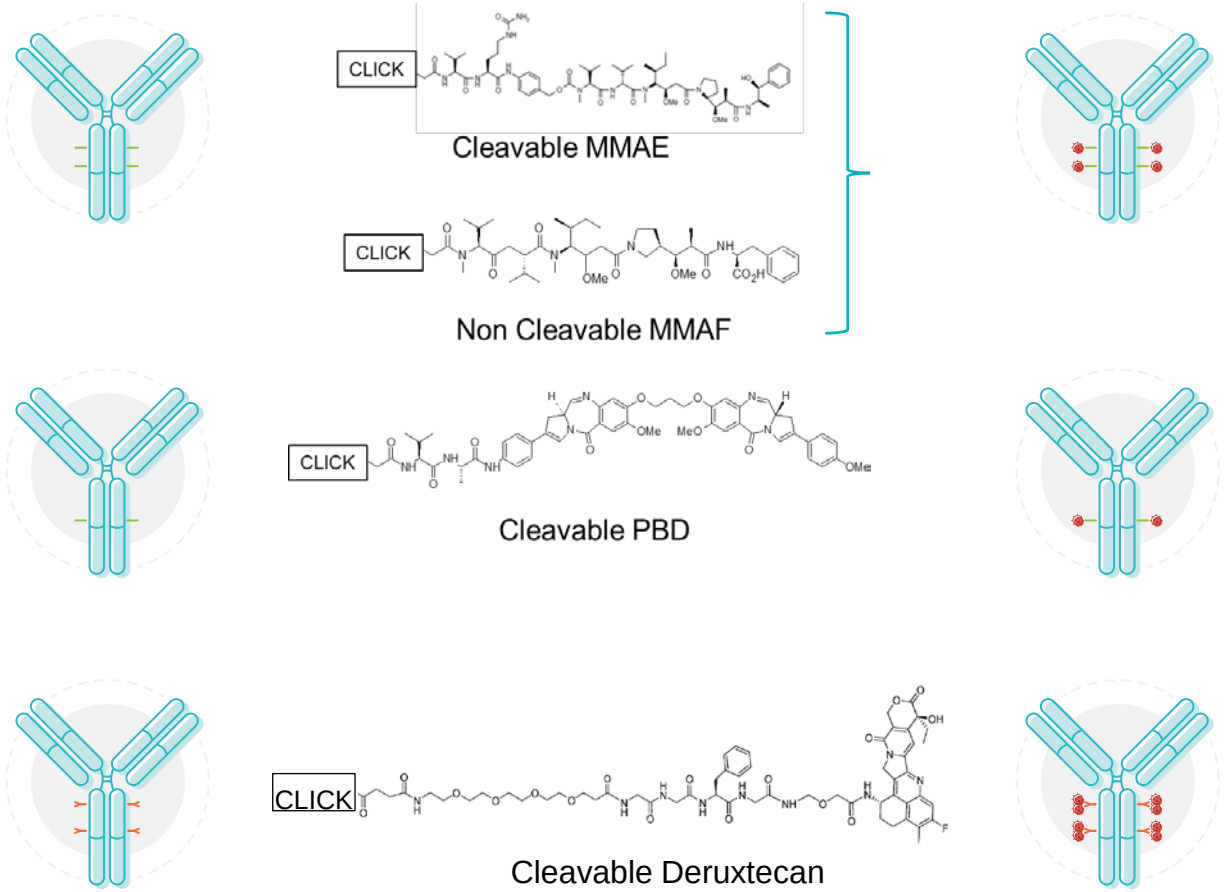
Step 3 – mAb Engineering / ADC

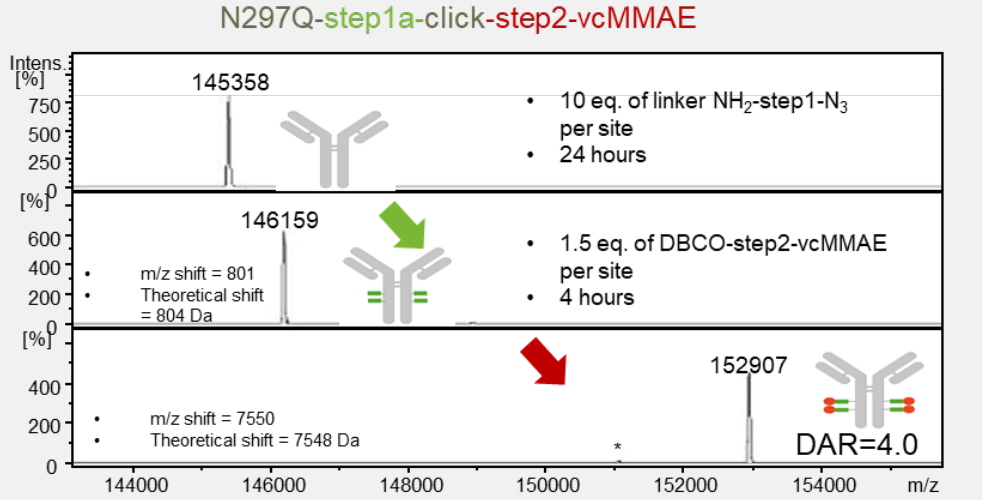
Generation of several validation packages for different candidate/toxin leading to pharma development

- **Generation of ADC: technology agnostic**
  - Various technologies of coupling (random Cys-coupling, site directed (engineered Cys-coupling, enzymatic coupling))
  - Varous Toxins and linker validated in the clinics
  - Goal is to select best options (coupling, linker payload) adapted to a given target
- **Back and forth dialog between biochemistry characterization and pharmacological evaluation**
  - Selected mAbs coupled with different toxins evaluated for in vitro pharmacological activity
  - Xenogeneic or syngeneic (human target transfected murine cancer cell lines) models to evaluate efficacy
  - MTD evaluation in mice
- **Pre-CMC package: production to different scales (mg to hundreds of mg scale)**
  - Biochemical characterization (high level quality controls)
  - Accelerated stabilty studies
  - Ex-vivo and in vivo stability : Extraction from sera, followed by LC-MS analysis
- **To date, up to 300 mg scale compatible with MTD determination (mice, rat) or acute toxicology in monkeys**
  - High level quality controls, stability studies, pre-CMC packages
- **Possibility to generate KI mouse models (JC Discovery) to evaluate therapeutic window**

Step 3 – mAb Engineering / ADC

Examples of Toxins and DAR ratio commonly used at MImAbs





Mass spectrometry control of a DAR 4, 2 steps, site directed MMAE ADC

Step 3 – mAb Engineering / ADC (cont'd)

List of toxin available at MImAbs

Toxin Class	conjugation chemistry	payload reference
Auristatin	Click Reactive	DBCO-PEG4-vc-PAB-MMAE
Auristatin	Click Reactive	Undisclosed
Auristatin	Click Reactive	Azido-MMAE
Auristatin	Click Reactive	DBCO-PEG4-MMAF
Auristatin	Click Reactive	DBCO-PEG4-vc-PAB-MMAF
Exatecan & derivatives	Click Reactive	DBCO-PEG4-GGFG-DX8951 (Deruxtecan)
Exatecan & derivatives	Click Reactive	BCN-PEG4-GGFG-DX8951 (Deruxtecan)
Pyrolobenzodiazepine (PBD)	Click Reactive	DBCO-PEG4-VA-PBD (Talirine)
Pyrolobenzodiazepine (PBD)	Click Reactive	azido-Tesirine
Pyrolobenzodiazepine (PBD)	Click Reactive	Undisclosed
SN38	Click Reactive	Undisclosed
Amanitin	Thiol Reactive	MC-cleavable-linker-α-amanitin
Auristatin	Thiol Reactive	MC-vc-PAB-MMAE
Auristatin	Thiol Reactive	MC-vc-PAB-MMAF
Exatecan & derivatives	Thiol Reactive	MC-GGFG-DX8951 (Deruxtecan)
Exatecan & derivatives	Thiol Reactive	Mal-bGLU-Exatecan-PSAR (Mablink Biosciences)
Pyrolobenzodiazepine (PBD)	Thiol Reactive	MA-PEG8-VA-PAB-SG3199 (Talirine)
SN38	Thiol Reactive	CL2A-SN 38
Exatecan & derivatives	Thiol Reactive	MC-VA-PAB-Exatecan
Exatecan & derivatives	Thiol Reactive	Mal-PEG8-VA-PAB-Exatecan
Exatecan & derivatives	Thiol Reactive	Mal-bGLU-PAB-Exatecan
Exatecan & derivatives	Thiol Reactive	Mal-spacer-bGLU-Exatecan
Exatecan & derivatives	Thiol Reactive	MC-PEG-GGFG-Exatecan
Exatecan & derivatives	Thiol Reactive	undisclosed
Exatecan & derivatives	Thiol Reactive	undisclosed
Exatecan & derivatives	Thiol Reactive	undisclosed

Step 3 – mAb Engineering / bispecific mAb

Generation of several validation packages for different bispecific leading to pharma development

- **Knob in the hole format (off patent)**
  - Knob in the hole mutations combined with crossmab
  - Set up of purification protocol to isolate bispecific from byproducts
- **Arm exchange format (Genmab technology)**
  - Genmab mutations and production of separated mAbs
  - Arm exchange protocol
  - Set up of purification protocol to isolate bispecific from byproducts
- **Production scale and QC compatible with pharmacology in mice (KI models) or acute toxicology in monkeys**
  - High level quality controls, determination of true bispecific format over parent antibodies or byproducts
- **Possibility to generate KI mouse models (JC Discovery) to evaluate therapeutic window**
  - HCD3ε KI mice available at MImAbs (validated with blinatumomab)

Step 4 – Bioproduction

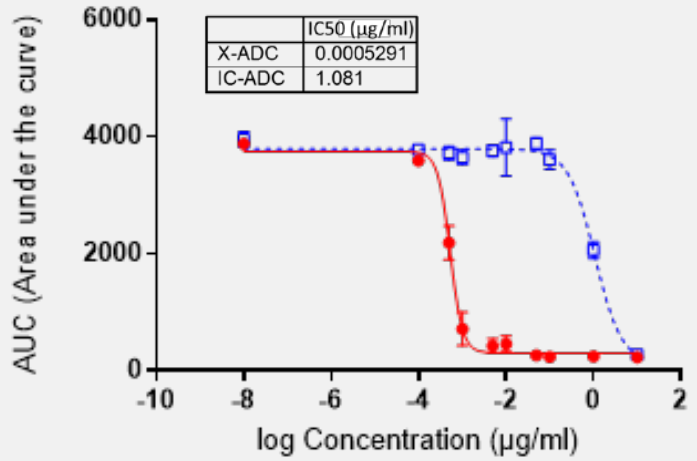
Naked , Antibody drug conjugates, bispecifics routinely produced to hundreds of mg

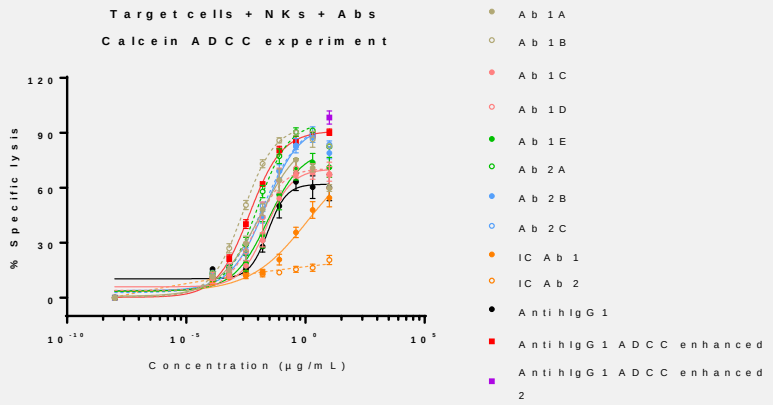
- **Mg to hundreds of mg level in transient transfection production in HEK and CHO**
  - High titer expression vectors for HEK and CHO
  - Production level compatible with in vitro and most in vivo experiments in mice
- **Purification and Quality controls**
  - Standard protein A purification
  - Second purification step and polishing step if needed (IEX, SEC, HIC)
  - Quality controls at pharma standards for all formats (SDS, SEC, MS …)
- **Batches of hundreds of mg of naked mAbs, Antibody Drug Conjugates are routinely produced at MImAbs**
  - Although not GMP, quality fulfill industry requirements
  - Size of batches compatible with MTD determination in mice and rats, or preliminary tox studies in NHP

- **Cytotoxicity: Direct, ADCC, ADCP, CDC**
  - Direct (IncuCyte, ATP, to test ADCs), (on CDX and PDX-derived in vitro models transferred from Xentech)
  - Mediated by effector cells (luciferase or calcein for ADCC, T- or NK-DCC with naked or bispecific Abs)
  - Indirect flow cytometry (CD107) on effectors

- **Immune Modulation (mice and human)**
  - T cell functional assay, NK functional assay
  - Primary or secondary MLR
  - In vitro DC differentiation
  - Cytometry read-outs (surface/intra cellular stainings, cell sorting)
  - (ELISA, Luminex) read outs for cytokine production

Direct cytotoxicy analysis of ADC





Step 5 – Immunopharmacology / in vivo (mice)

Naked , Antibody drug conjugates, bispecifics in syngenic, KI or xenogenic models

- **Antibody bioanalysis**
  - PK parameters (including DAR follow up for ADC by MS)
  - Pharmacodynamy parameters (receptor saturation by flow)
- **Safety parameters**
  - Weight
  - Health status
  - Blood counts
- **Efficacy readouts**
  - Survival
  - Tumor load (caliper or bioluminescence),
  - Inflammatory response, immuno-profiling (advanced with JC Discovery)
- **In vivo models**
  - Syngeneic models (surrogate, crossreactive mAbs): MC38, CT26, B16F10, EMT6…
  - Xenogeneic models (large panel of different cell lines from different histologies)
  - KI models (can be newly generated with JC Discovery)
  - Large panel of additional CDX and PDX with Xentech & Urosphere
  - Efficacy in Humanized mice with PBMC or CD34 with JC Discovery and/or Xentech