

ADC

DISCOVERY

BIOCHEMISTRY

Well established ADC preparation and characterization procedures

- Antibody-drug conjugation with different chemistries.
- Validated ADC production and purification process.
- Dedicated ADC conjugation labs and In-process QC equipments.
- Complete ADC quality control and characterization methods
 - » ELISA, FACS and Biacore for antigen binding activity
 - » Cell based assays for *in vitro* efficacy and bioactivity of antibody and ADC
 - » Quality control in each production step for drug to antibody ratio (DAR), purity, aggregation, endotoxin, residues of free drug and solvent
 - » Advanced analytical tools and technologies, LC-MS, HPLC-HIC/SEC, iCIEF, peptide mapping, conjugation site mapping
 - » ADC scale-up process development and formulation development
 - » GMP-like ADC production up to 40 grams

PHARMACOLOGY

- Efficacy Studies
 - » 160+ Cell Line Derived Xenografts (CDX)
 - » 270+ Patient Derived Xenograft (PDX)
- Biodistribution
 - » Imaging with labeled mAb
 - » Ex vivo tissue concentration analysis

PHARMACOKINETICS

- Mouse, rat, monkey
- Bioanalytical development PK/PD modeling and simulation
- *In vitro* stability in biological matrices

EXPLORATORY TOXICITY

- Single dose
- Repeated dose
- Dose range finding

CHEMISTRY

- High potency lab facility to limit toxin exposure (OEL<1ug/m3)
- 35 chemists with experience in payloads and linkers
- Resynthesis of Kadcyca and Adcetris from Mertansine and Auristatin
- Identification, synthesis and modification of toxins
- Linker design, synthesis and evaluation
- Optimize payload-linker for overall profile

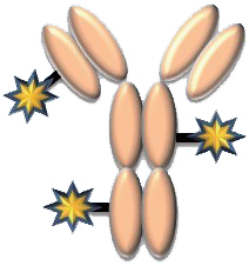
RELEVANT SERVICES

Chemistry Synthesis
Hybridoma Development
Analysis Method Development
PK/PD/TK
In vivo efficacy

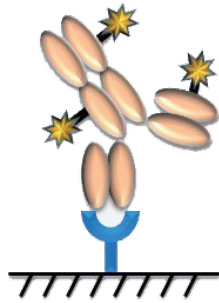


FROM *IN VITRO* TO *IN VIVO*

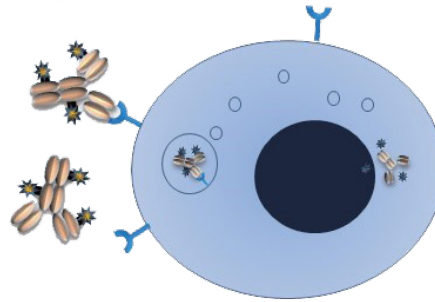
CONJUGATION AND BIO-ANALYTICS



ANTIGEN BINDING ACTIVITY



IN VITRO POTENCY TEST



IN VIVO POTENCY TEST AND PK/PD STUDY

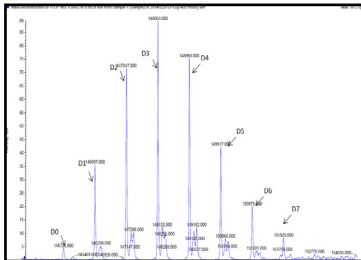


2-3 WEEKS

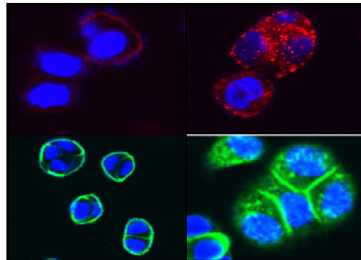
3-4 WEEKS

3-4 WEEKS

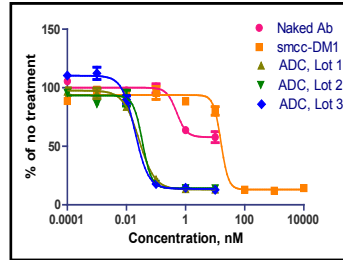
2-3 MONTHS



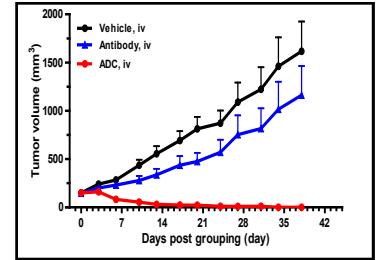
DAR BY LC/MS



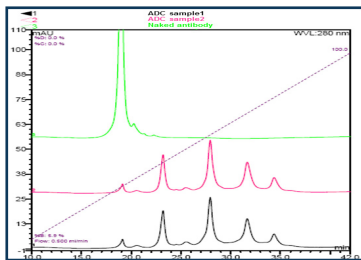
INTERNALIZATION ASSAY



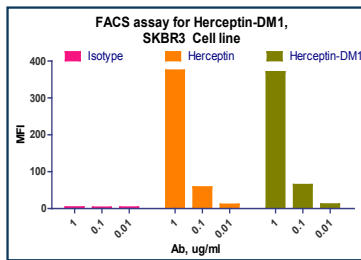
CYTOTOXICITY ASSAY
(TARGET POSITIVE CELL LINE)



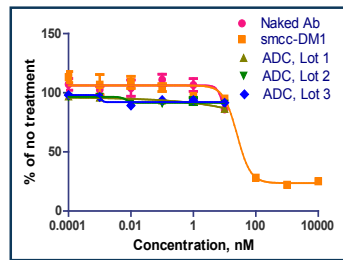
IN VIVO EFFICACY STUDY



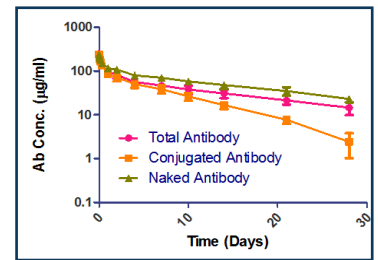
DAR BY HPLC-HIC



FACS BINDING ASSAY



CYTOTOXICITY ASSAY
(TARGET NEGATIVE CELL LINE)



IN VIVO PK STUDY

DELIVERABLES

- A final report and all the product will be delivered at the end of the study
- Full set of QC data (optional)
- Protocol and Notebook for conjugation optimization project

mAbs

- Variable target
- Variable species
- Variable isotype
- Variable epitope

LINKER

- Cleavable linker
- Non-cleavable linker

DRUG

- DM1
- MMAE
- MMAF
- Other potency drug