THE TECHNOLOGY PLATFORM FOR EFFECTIVE DEVELOPMENT OF MONOCLONAL ANTIBODY DRUGS

9 STEPS TO EFFECTIVE DESIGN OF MOLECULE
WHAT IS BONMAB TECHNOLOGY®?

BONMAB TECHNOLOGY

- Universal platform to develop original medicinal products.
- Module intelligent system. Full-integrated high-tech equipment and software.
- BONMAB TECHNOLOGY and MEGAN Lib give effective and safe molecules for any target.
STATE-OF-ART TECHNOLOGIES TO IMPROVE HUMAN LIFE EXPECTANCY AND QUALITY OF LIFE

- Advanced analytical procedures.
- Quality by Design principles. Comprehensive planning of target quality profiles.
- Automation of research activities using integrated high-performance equipment.
- Common information space to plan projects and experiments, process and store data.
- Unlimited search potential (more than 40,000 candidate molecules can be screened for every project).
- High speed of development (not more than 1 year from an idea to a molecule).
- In-house platform for gene synthesis.
UNIQUENESS OF BONMAB TECHNOLOGY®

CREATE PANELS OF FUNCTIONAL ANTIBODIES FOR ANY MOLECULAR TARGETS

Work for result: future experiments are designed based on critical quality parameters of a future molecule.

High speed: 3-5 months from an idea to a pool of candidate antibodies.

Reliability: a minimum number of subjective factors that can influence the outcome of a process.

Flexibility: you can work on several projects in the same time thanks to an intelligent feedback system.

Modularity: you can select the best combination of modules for a project.

Safety: with MEGAN lib, you will get antibodies with minimum immunogenicity.

Versatility: you can get functional antibodies to any targets.
UNIQUENESS OF BONMAB TECHNOLOGY®

WE BUILD THE FUTURE TODAY
INFORMATION CLOUD

Bioinformatic support, in silico methods, statistical analysis

THE TECHNOLOGY PLATFORM FOR EFFECTIVE DEVELOPMENT OF MONOCLONAL ANTIBODY DRUGS.

CHOOSING THE TARGET
preparation of the target profile of the molecule

PHAGE DISPLAY
enrichment of the library with potentially functional molecules

HIGH-THROUGHPUT SCREENING
screening and optimization of candidate molecules

FUNCTIONAL CHARACTERISTICS
selection of the final candidate

CLINICAL STUDIES

PRECLINICAL STUDIES

PHARMACEUTICAL DEVELOPMENT

DEVELOPMENT UPSTREAM & DOWNSTREAM PROCESSES

PRODUCTION OF MONOCLONAL CELL LINE

Anti-IL-6R

Anti-IL-17
THE TECHNOLOGY PLATFORM FOR EFFECTIVE DEVELOPMENT OF MONOCLONAL ANTIBODY DRUGS

**Ingredients**

- **MEGAN LIB** - gene library for human antibodies
- **MBEASY** - platform high-throughput screening of antibody libraries
- **QbD**
- **Cloud information**
- **MABSINT** - platform synthesis libraries of antibody genes

1. **Choosing the Target**
   Preparation of the target profile of the molecule
   - 1 month

2. **Phage Display**
   Enrichment of the library with potentially functional molecules
   - 2 weeks

3. **High-throughput Screening**
   Screening and optimization of a pool of candidate molecules
   - 3 months

4. **Functional Characteristics**
   Selection of the final candidate
   - 1 month

5. **Production of Monoclonal Cell Line**
   - 2 months

6. **Development Upstream & Downstream Processes**
   - 2 months

7. **Pharmaceutical Development**
   - 6 months

8. **Preclinical Studies**
   - 6 months

9. **Clinical Trials**
   - 2 years
CHOOSING THE TARGET

- Clinically validated targets and novel modes of action.
- Target product profile is created according to QbD principles.
HOW DOES IT WORK?

CHOOSING THE TARGET

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1 month

preparation of the target profile of the molecule
MEGAN LIB® (Mega_Naive_Library) – is the largest gene library for human antibodies, an ideal source to search for novel antibody molecules.

Universal and convenient format of a phage display library from a unique collection of cDNA from donors’ cells.

Diversity and quality of sequences have been confirmed by molecular biology methods, including high-throughput sequencing.

- with billions of antibody molecules from 1000 donors in one test tube, you will obtain original molecules of therapeutic antibodies.

Using MEGAN LIB during Stage 1 of MONMAB Technology, you will promptly obtain original therapeutic antibodies conforming to worldwide quality and safety standards.
Megan Lib offers you the largest collection of antibody genes from 1000 donors in one test tube. Unique diversity guarantees success.
Megan Lib® Advantages

Choose the future today

Unique diversity guarantees success.

Only native sequences.

Convenient format for efficient search for candidates.

Efficacy

Safety

High Speed
PHAGE DISPLAY

With a display method used to select phage particles, in vitro selection is similar to natural selection. Hundreds of thousands of antibodies with the best affinity to a target molecule are selected from billions of antibodies contained in the libraries.

Therefore, the phage display will give you high-affinity variants of antibodies. Their genes can be isolated from phage particles for re-cloning and screening in E.coli cultures.
HOW DOES IT WORK?

PHAGE DISPLAY

enrichment of the library with potentially functional molecules

2 weeks
HIGH-THROUGHPUT SCREENING

High-throughput ELISA-screening is based on the interaction of an antigen (molecular target of therapy) and Fab-fragments (from post-selection libraries) expressed by bacterial cells. The complex is detected using enzyme-labeled antibodies against a specified site on the Fab-fragment. Selection of tens of thousands of *E.coli* isolated colonies, ELISA, processing and analysis of results, selection of the best candidates, assessment of their specificity and functionality are carried out using high-performance equipment, information cloud, and universal processing platform.

With MαBSynt, a technology for the optimization of selected candidates, which combines an innovative system for the computer modeling of molecules and gene synthesis de novo, you will be able to develop the nature potential of antigen molecules.
HOW DOES IT WORK?

HIGH-THROUGHPUT SCREENING

screening and optimization of a pool of candidate molecules

3 months
HOW DOES IT WORK?

**MαBSynt** (Monoclonal_Antibody_Synthesis_Technology) – Platform synthesis libraries of antibody genes.

**MαBEasy** (Monoclonal_Antibody_ELISA-based_Screening_Assay) – Platform high-throughput screening of antibody libraries.
FUNCTIONAL CHARACTERIZATION

- Exploration of functional characteristics (specific activity) is critical when selecting the final candidate.
- To ensure the efficacy and safety of investigational products, studies in vitro are used to simulate in vivo effects of candidates.
- Bioassays used for functional characterization should be reliable and standardized; they should adequately reflect the mode of action of the product.
- Several bioassays are used for the functional characterization of candidates, for example, proliferative cell tests, MoA (mode of action) tests [ADCC (antibody-dependent cytotoxicity), CDC (complement-dependent cytotoxicity), apoptosis]; cell-based ELISA (ex. receptor phosphorylation assessment) etc.
- With DoE, robotized technologies, and biostatistics, you can select the final candidate with ideal functional characteristics in the shortest time possible.
HOW DOES IT WORK?

FUNCTIONAL CHARACTERIZATION

selection of the final candidate 1 month
One of key objectives of the production of recombinant antibodies is to create producing cell lines. Producers of medicinal products should be stable, completely characterized, and validated according to Russian and international guidelines. Monoclonal cell lines are obtained using several stages: transfection, selection, cloning, and clone screening.

Monoclonal lines are obtained using a high-efficiency algorithm to rapidly obtain and test stable cell lines. ClonePix and robotized multifactor DoEs significantly reduce the duration of clone screening, selection of highly productive cell lines and incubation regimens.
HOW DOES IT WORK?

PRODUCTION OF MONOCLONAL CELL LINE

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\[ \text{Cell} + \text{C} = \text{Cell line} \]

2 months
Incubation regimens are developed using the Quality by Design concept, which is applied during all stages of development, from the determination of product quality parameters related to its safety and efficacy to the full-scale production of the drug product. The processing platform uses novel serum-free media with specified composition. The producer’s culture condition, its metabolism and productivity, critical quality parameters of the target protein are assessed during development. Primary selection of basal media, nutritive supplements, and cultivation regimens for every producer is carried out in laboratory scale (plates, flasks, minibioreactors) using multifactorial design of experiment (DoE). With this approach, a large number of media and supplement combinations can be used in one experiment, which significantly reduces the duration of development. Incubation parameters of appropriate regimens are improved using desktop bioreactors. An incubation regimen with the best quality and amount of the obtained protein is transferred for scaling up in disposable 250 and 1000 mL bioreactors. With this strategy, a reliable and scalable incubation regimen can be developed in the shortest time possible.
The target protein is isolated and purified by immunoaffinity, ion-exchange, and multimodal chromatography. To find optimal parameters of chromatographic purification, laboratory-scale screening of sorbents and chromatographic conditions is performed using multifactorial experiments (DoE). Control points and analysis methods for protein quality are determined for every stage. Viral safety is confirmed by the validation of all stages using a group of model viruses. Stages with approved ranges of process parameters are reproduced in pilot-scale manufacturing (250 L). Afterwards, the technology is transferred to full-scale manufacturing.
HOW DOES IT WORK?

DEVELOPMENT UPSTREAM & DOWNSTREAM PROCESSES

2 months
PHARMACEUTICAL DEVELOPMENT

- Development of drug product composition
- Development and validation of quality control methods
- Development and validation of manufacturing processes
- Stability studies

* Based on Quality by Design principles

* Development in compliance with ICH recommendations
OUR RESULTS

PRODUCTS WE HAVE CREATED USING BONMAB TECHNOLOGY:

1. CLINICAL TRAILS
15. DEVELOPMENT
THANK YOU FOR BEING WITH US!

www.biocad.ru