TWIST BIOSCIENCE | BIOPHARMA SOLUTIONS

Writing the future of biologics

Your partner for antibody discovery & development.

Rapidly improving treatment of diseases with therapeutic antibodies

Antibody therapeutics are an important class of drugs that have changed the medical landscape and the treatment of autoimmune disease and cancer. Discovery and optimization efforts in this space are expanding rapidly, and there is significant potential for treating diseases for which no current therapies exist.

Make the impossible possible with Twist Biopharma Solutions' integrated antibody development services

Technological advances over the past five decades have improved our ability to identify and optimize lead antibody candidates for pre-clinical and clinical testing. Yet many targets, especially multi-pass, integral membrane proteins such as G-coupled protein receptors (GPCRs), have been difficult to drug. Discovery research in these fields has proven to be technically challenging, time-consuming, and expensive.

When promising lead antibodies are identified, new bottlenecks emerge. Optimizing these drug candidates for enhanced potency or developability often relies on mutagenesis methods that focus on undesirable sequence space and may lead to downstream manufacturing liabilities.

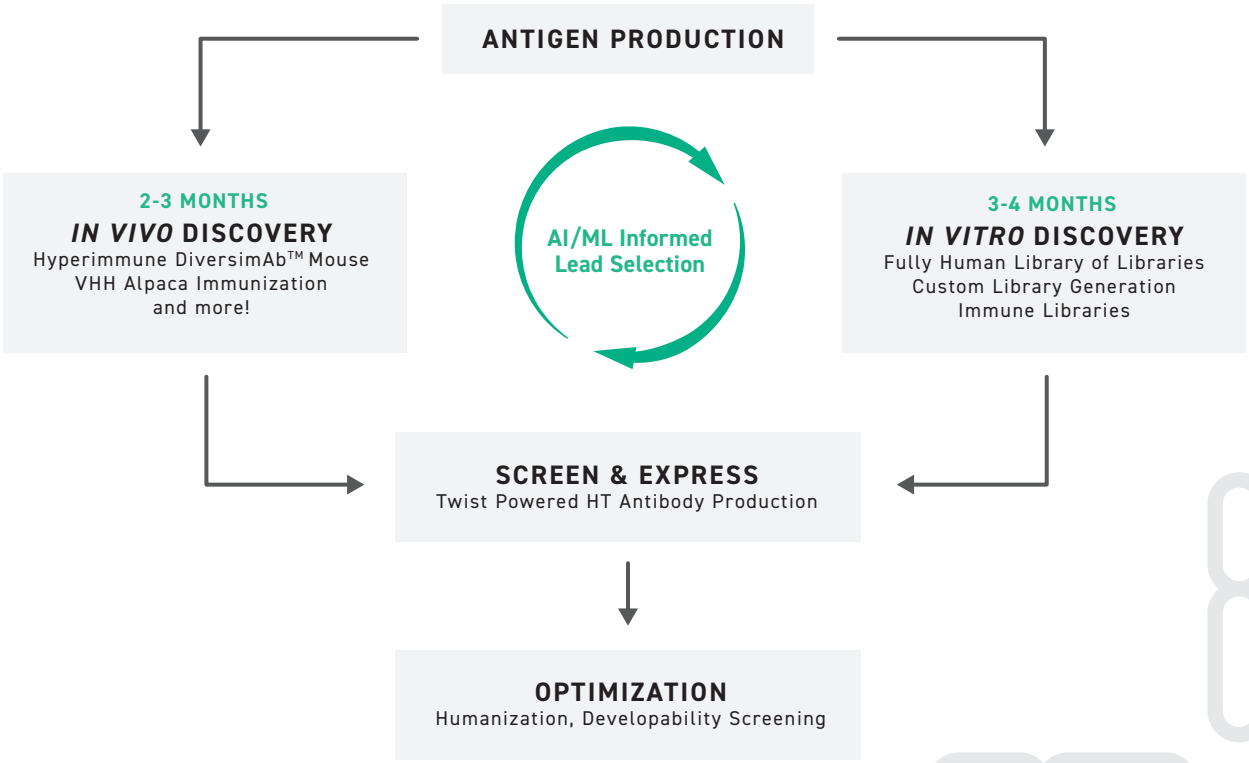
Ultimately, these challenges stand in the way of rapid, streamlined development of transformative biologics. At Twist Biopharma Solutions, a division of Twist Bioscience established by the integration of Abveris Antibody and Twist Biopharma, we are "writing" the solutions to these problems.

Our unique DNA writing technology enables delivery of precise DNA pool with unparalleled diversity, throughput, and quality. With that as our foundation, Twist Biopharma Solutions can create unprecedented synthetic antibody libraries, accelerating the way you discover, optimize, and develop lead antibody candidates.

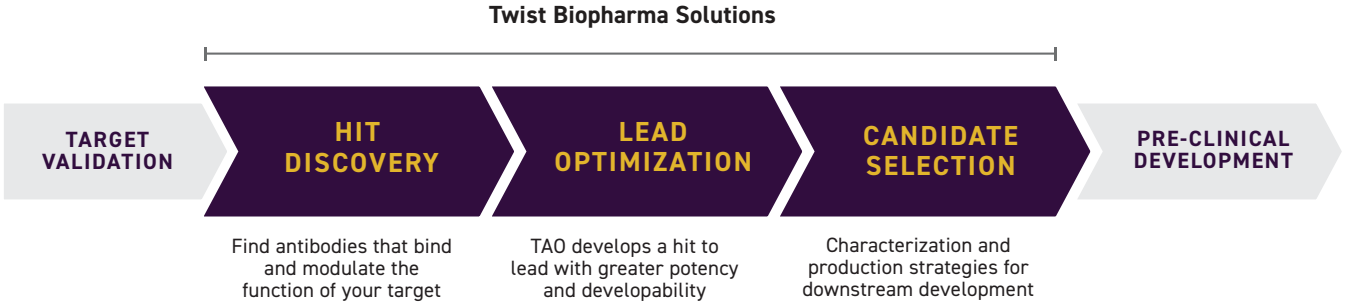
With Abveris' proprietary hyperimmune mouse model, DiversimAb™, an exceptional *in vivo* antibody discovery platform, Twist Biopharma Solutions also provides access to superior epitopic coverage. These best-in-class *in vitro* and *in vivo* technologies, combined with advanced screening methods, and cutting-edge engineering platforms, allow us to offer a comprehensive antibody development solution from concept to clinic, all under one roof.

Streamlined antibody development

Twist Biopharma Solutions' comprehensive end-to-end antibody discovery services translates to unrivaled, industry-leading platforms to address the specific challenges in your program. One-size does not fit all, and at Twist Biopharma Solutions, you don't have to make this decision alone. Our biologics experts will collaborate with you to design and deliver high-quality antibodies that fit your criteria.



Faster, more cost-effective discovery and optimization of functional lead antibodies.



Save time with our "Library of Libraries"

Twist's library of libraries is a collection of proprietary antibody libraries, precisely designed to match sequences that occur in the human body. They are ready-to-use and validated, so you can get started quickly. We can perform panning using multiple phage libraries in parallel against your target-of-interest to save time and identify multiple leads based on different variant pools.

Once your libraries are chosen we perform selections using biotinylated antigens or cells, followed by clone identification and IgG reformatting. In addition, our team can perform downstream IgG protein expression, purification on small or large scales, and biochemical, biophysical, and/or functional assays.

Library of Libraries (2-5 months to sequence)

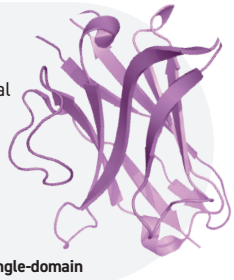
3-5 WEEKS (OPTIONAL)	3-4 WEEKS	2-4 WEEKS	5-8 WEEKS
Antigen and Screening Tool Production	Phage Display Panning: Bread or Cell Based	Screening and Sanger or NGS Sequencing	Recombinant Antibody Expression (+Downstream Engineering/Humanization)

Synthetic DNA libraries enable more shots on goal with sequences ready in as soon as a couple months.

VHH LIBRARIES

Our libraries of small, modular antibodies offer several advantages over human IgG with natural llama CDR sequences and framework.

1. VHH Ratio
2. VHH Shuffle
3. VHH hShuffle
4. VHH hShuffle HI
5. VHH hShuffle GPCR
6. hCamel Bactrain
7. hCamel Zero



Learn more at twistbiopharma.com/library-of-libraries/single-domain

GPCR ANTIBODY LIBRARIES

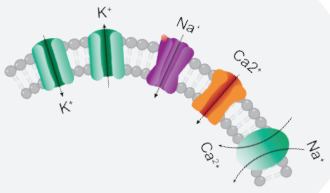
GPCRs have traditionally been difficult to drug. Our libraries offer greater than 100,000 different GPCR binding motifs and helps discover antibodies against this difficult-to-target class.

1. GPCR 2.0
2. VHH hShuffle GPCR

Learn more at twistbiopharma.com/library-of-libraries/gpcr

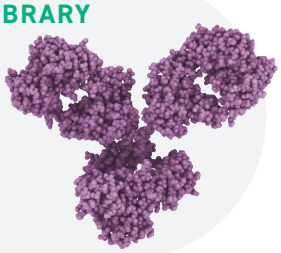
ION CHANNEL LIBRARY

Loop sequences from natural peptide toxins that target ion channels were used to construct our ion channel library. It's available as a library that contains paired cysteines or is cysteineless.



STRUCTURAL ANTIBODY LIBRARY

6 CDRs were selected from 3,700 antibodies with crystal structures in Protein Data Bank to create an scFv antibody library with a size >10^{10}.



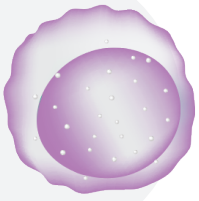
CARBOHYDRATE ANTIBODY LIBRARY

Our library was designed through shuffling unique CDRs from 130 carbohydrate antibodies for CDR1 and CDR2. The diversity of CDR3 at the interface was restricted to observed interface variants at those positions and for CDR3 positions not at the interface, the lot of 130 antibody sequences was incorporated.

HYPERIMMUNE LIBRARIES

Our hyperimmune library is constructed in an Fab scaffold, with a diversity of >10^{10}. Proof-of-concept selections have identified antibodies with nanomolar affinities for TIGIT, CD3e, and more.

1. Original Fab
2. scFv
3. VHH hShuffle



Choose your own antibody adventure

In vivo antibody discovery capitalizes on the natural immune repertoire of host animals to provide diverse, high affinity, and developable lead candidates suitable for downstream development. However, the new wave of challenging therapeutic target classes are becoming too difficult for conventional hybridoma-based methods using wild-type mice.

To address the rising discovery challenges, Twist Biopharma Solutions has built a multi-faceted, accelerated discovery approach based on proprietary hyperimmune DiversimAb™ mice. We are continuously adding to our suite of platforms technologies that hasten conventional hybridoma screening. Our Beacon-based single B-cell screening platform offers several benefits across various applications.

Accelerated antibody discovery with expanded repertoires

ADVANTAGES OF BEACON PLATFORM

HIGH THROUGHPUT
- Up to 30,000 B-cells screened in one day
- 1,000+ specific hits assayed in many cases

RESOLUTION
- Multiple sequential screens, including cell binding, ligand blocking, and multiplexed assays
- Industry-leading resolution among all single B-cell platforms

CUSTOMIZATION
- Highly flexible assay setups with assay development services

SPEED
- Project start to paired HC/LC sequence delivery in as few as 29 days

ADVANTAGES OF HYBRIDOMA SCREEN

THROUGHPUT
- High-throughput flow cytometry screening in primary and secondary screens

OPTIMIZATION
- Function-forward program design
- Proprietary adjuvants

SPEED
- Up to 25% quicker with Twist platform and DiversimAb™ mice compared to traditional hybridoma workflows
- Fast and efficient subcloning process

TRUSTED
- Tried and true technology validated over 100+ campaigns

Small animals

DIVERSIMAB™ MICE ● ●

Our proprietary, milestone-free mouse is engineered to express a high-diversity, high-affinity repertoire of antibodies that overcome tolerance to self-antigens through use of proprietary adjuvants. The DiversimAb mouse also has a heightened immune response, making it useful for high-homology targets and mouse surrogate campaigns, accelerating timeline to the sequencing of selected antibodies.

HUMANIZED TRANSGENIC MICE ● ●

This humanized mouse model is invaluable for antibody discovery because it can replicate human immune responses and express human immunoglobulins. This facilitates accelerated discovery processes and reduces downstream immunogenicity hurdles.

RABBITS ●

With their unique immune system, rabbits are a reliable source of diverse, high-affinity, antibodies. These antibodies can recognize multiple epitopes on an antigen, making them an excellent choice for tool or reagent antibodies in various research applications.

Camelids

ALPACAS ●

Alpacas are advantageous for producing single-domain VHH antibodies, or nanobodies. These smaller fragments exhibit high specificity and stability, making them ideal for therapeutic and diagnostic applications.

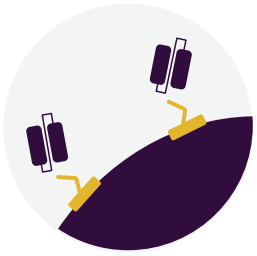
AVAILABLE ON:

● Beacon ● Hybridoma

An antibody for any application

THERAPEUTIC ANTIBODIES (IGG, BSAB, ADC)

- Human and murine antibody discovery
- VHH and scFv discovery for bispecific antibody development
- Proven expertise for targeting cell surface receptors, GPCRs, and ion channels
- Function-forward, high-throughput workflows that deliver rare, functional antibodies
- Integrated characterization and developability assessment options
- Ultra-fast, high-resolution single B-cell workflow that enables the identification of mAb sequences from start of immunization in as few as 29 days



CHIMERIC ANTIGEN RECEPTOR (CAR)

- *In vivo* discovery of the ectodomain in CAR constructs for cell-based therapeutics
- Function-forward workflows to validate on-cell binding
- A diverse range of affinities warranted by the DiversimAb™ technology
- Flexible project deliverables: sequences and/or purified, validated scFv or VHH
- Optimization of transmembrane domain and endodomain by Twist library approach

REAGENT/ANTI-IDIOTYPIC ANTIBODY DISCOVERY

- *In vivo* discovery of the ectodomain in CAR constructs for cell-based therapeutics
- Function-forward workflows to validate on-cell binding
- A diverse range of affinities warranted by the DiversimAb™ technology
- Flexible project deliverables: sequences and/or purified, validated scFv or VHH
- Optimization of transmembrane domain and ectodomain by Twist library approach

Customizable discovery workflows with advanced hybridoma and single B-cell screening.

Hybridoma Workflow (3-5 months to sequence)

3-5 WEEKS (OPTIONAL)	3-8 WEEKS	5-6 WEEKS	1-4 WEEKS	3-4 WEEKS	5-8 WEEKS
Antigen and Screening Tool Production	Mouse Immunization	Hybridoma Generation and High-Throughput Screening	Advanced Screening	Hybridoma Sequencing	Recombinant Antibody Expression (+Downstream Engineering/Humanization)

B Cell Screening (2-5 months to sequence)

3-5 WEEKS (OPTIONAL)	3-12 WEEKS	1 DAY	2 WEEKS	5-8 WEEKS
Antigen and Screening Tool Production	Mouse, Rabbit, or Alpaca Immunization	Beacon-Based B Cell Screening	B Cell Sequencing	Recombinant Antibody Expression (+Downstream Engineering/Humanization)

Hybrid approaches using *in vivo* and *in vitro* antibody discovery technologies

Every foundational antibody discovery project requires a unique approach. That's why we tailor our services and workflows to your individual needs. Immune libraries harness the diversity of the immune system, offering a focused repertoire of antibody candidates for various applications. However, achieving optimal results demands expertise at every stage of the process.

At Twist Biopharma Solutions our campaigns are specialized at every step starting with immunization strategies through library design, ensuring strategic representation of diverse antibody fragments. The proficiency of our team guides the meticulous screening and selection processes, producing antibodies with exceptional specificity and affinity due to the uniformity and precision of our technology. We ensure the delivery of reliable and customized solutions for your specific research needs. Partnering with our experts will make your journey from concept to high-quality antibody discovery seamless and successful.

Immune Libraries (2-5 months to sequence)					
3-5 WEEKS (OPTIONAL)	3-12 WEEKS	2-3 WEEKS	3-4 WEEKS	2-4 WEEKS	5-8 WEEKS
Antigen and Screening Tool Production	Mouse or Alpaca Immunization	Immune Library Generation	Phage Display Panning: Bead or Cell Based	Screening and Sanger or NGS Sequencing	Recombinant Antibody Expression (+Downstream Engineering/Humanization)

Faster iterations to optimized antibodies with Twist Biopharma Solutions' comprehensive capabilities.

Antibody optimization with a Twist

The dynamic process of optimizing antibodies relies on the iterative design-make-test-analyze cycle. This systematic approach involves generating a diverse library of antibodies, followed by thorough testing to identify those with the desired binding, specificity, and functionality. Benefits to your antibody discovery campaign include:

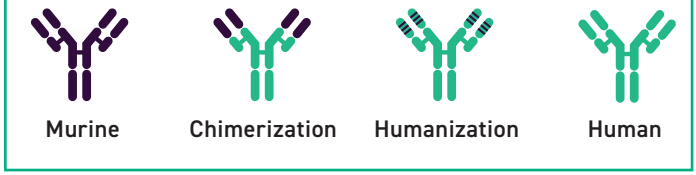
- Rapid and flexible response for real-time adjustments and optimizations
- Speed and agility that puts you on the critical path to the clinic
- Reproducibility and reliability in the generated antibodies
- Centralized data management to ensure precision and quality
- More effective and targeted therapeutic candidates

Antibody engineering to deliver fully human optimized leads

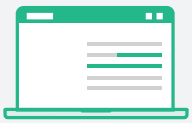
Twist Antibody Optimization (TAO) uses bioinformatics and our proprietary software platform to create an optimization library with natural human heavy and light chain CDR sequences. Simply input your murine, chimeric, humanized, or fully human antibody sequence into our software and our algorithm will determine which natural variants you should focus on. This "human repertoire inspired" phage library is selected for multiple rounds, enriching for high-affinity binding clones using bead- or cell-based assays.

The identity of unique, high-affinity clones can then be converted to full-length IgG and screened using biochemical, biophysical, and functional assays. This is all part of Twist Biopharma Solutions' comprehensive TAO service.

INPUT

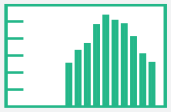


4 MONTHS



1
Input antibody sequence into software

2
Order oligo pools and template DNA



3
Twist Bioscience creates library and screens against target

OUTPUT

Fully human optimized leads

NEED YOUR ANTIBODIES HUMANIZED?

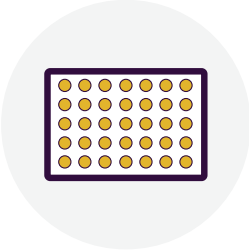
Regardless of what platform you used to discover your antibodies, Twist Biopharma Solutions provides services to ensure your antibodies have the desired safety and efficacy profile and avoid downstream roadblocks such as human anti-mouse antibody (HAMA) responses.

For IgG and VHH, our humanization services include:

- Sequence liability ID
- Structural modeling
- % humanness analysis
- Immunogenicity scoring
- Generation of up to 64 humanized variant sequences (HC/LC)
- Expression and purification
- Full binding kinetics analysis

Supporting capabilities and downstream characterization

Every discovery campaign, regardless of whether it comes from an *in vivo*, *in vitro*, or *in silico* platform is best complemented with experimental characterization data to ensure the best antibody candidates are selected to progress. Twist Biopharma Solutions offers additional development and production services to complement your discovery program.



ANTIBODY REFORMATTING, EXPRESSION, AND PURIFICATION

Antibody production can be costly and time-consuming. As a result, many research programs are forced to pick a subset of candidates to focus their downstream efforts.

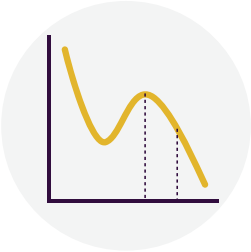
Our gene synthesis capabilities quickly and easily convert 10s to 1000s of antibody candidates into full-length, codon-optimized IgG genes cloned into our high-copy, custom expression vectors. We use a high-throughput automated workflow to express and purify IgG antibodies on small or medium scales – in as little as two weeks.

ANTIBODY CHARACTERIZATION

Downstream antibody characterization can be challenging, particularly if the internal capabilities and expertise are limited.

Our scientists can assess the yield and purity of IgG proteins and do rapid biophysical characterization, including thermostability (Tm and Tagg). We can also evaluate binding affinities and polyspecificity in a high-throughput way using the Carterra LSA system and BVP binding ELISA, respectively.

Contact an expert to learn more about our full suite of developability assays to ensure downstream manufacturability.



FUNCTIONAL ASSAYS

Determining the mode of action (MOA) for lead antibodies without internal expertise or validated assays can be a bottleneck for many research groups.

Our scientific experts use off-the-shelf or develop custom assays to readily assess the antagonist, agonist, or allosteric effects of your purified antibodies.

Ask us about internalization, cytotoxicity, or other functional assays that can be performed on Beacon or more traditional methods like ELISA and Flow Cytometry.

WHAT CAN WE HELP YOU DISCOVER?

Twist Biopharma Solutions is committed to helping you realize the potential of your biggest biologic development programs. Wherever you are in the development pipeline we have a solution that will elevate you to the next level of discovery

LEARN MORE

www.twistbioscience.com/twist-biopharma-solutions

For Research Use Only (RUO). Not for use in diagnostic procedures.

Success in Numbers

218+ PARTNERS

112+ ACTIVE PROGRAMS

4+ ANTIBODIES IN CLINICAL STUDIES

465+ COMPLETED PROGRAMS

59+ MILESTONE ROYALTIES