Twist Bioscience
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Therapeutic antibody discovery and optimization with a twist

By coupling Twist Bioscience's DNA-writing technology with expertise in antibody engineering, Twist Biopharma is helping companies accelerate the development of new biologics.

The number of approved biologic drugs has risen steeply in the past decade[1]. Of the 50 novel drugs approved by the US Food and Drug Administration (FDA) in 2021, 14 were biologics licence applications[2]. Biologics are typically manufactured through engineered biological processes in living cells. They include recombinant proteins and antibody-based drugs that are used to treat a wide range of diseases, from cancer and rheumatoid arthritis to diabetes and infectious diseases.

Compared with chemically synthesized medicines, such as aspirin and statins, biologics are large and complex drugs that are typically much more difficult and costly to develop. However, biologics offer major benefits to patients as they are able to specifically reach targets often previously considered 'undruggable', and have fewer side effects.

As pharmaceutical companies shift their pipelines towards biologics, many are looking for specialist support in their discovery and development efforts. A recent survey of more than 200 biopharma executives conducted by Fierce Biotech revealed that monoclonal antibodies are by far the most common type of biologic being developed in their drug discovery programs, and that to reduce the time-to-market for new drug candidates, they plan to engage with external partners with expertise in discovery and optimization processes[3].

"On average it takes 10 years for a biologic drug to complete the journey from initial discovery to the marketplace," said Aaron Sato, CSO of Twist Bioscience, who has a background in protein engineering and antibody discovery. "At Twist, we help companies realize the potential of their biologic development programs by accelerating the discovery, optimization and development of lead antibody candidates."

Twist Biopharma, a division of the leading silicon-based DNA manufacturing company Twist Bioscience, supports end-to-end biologics discovery (Fig. 1). Companies can partner at any stage of their antibody development journey.

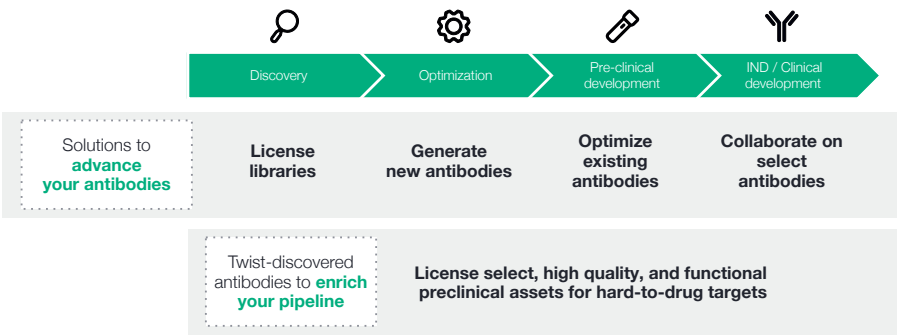

Fig. 1 | Flexible partnering. Twist Bioscience can partner with companies throughout the drug development process.

Explore more antibody space in less time

With Twist Bioscience's unique DNA technology, which enables the writing of oligonucleotide pools with game-changing throughput and quality, Twist Biopharma has created a suite of synthetic antibody libraries designed to tackle hard-to-drug targets.

Companies can license Twist Biopharma's 'library of libraries', currently comprising 15 phage display libraries, each containing up to 10^{10} antibodies in proven and highly developable human antibody frameworks, to find high-affinity antibodies that bind and modulate the function of their target. Alternatively, companies may wish to partner with Twist Biopharma to build a custom library in a vector and scaffold of their choice.

A discovery cycle with Twist Biopharma's proprietary processes can take as little as 8 weeks, even if the target class is notoriously hard to drug, such as G-protein-coupled receptors (GPCRs), ion channels or carbohydrates.

As well as helping companies overcome the bottlenecks that stem from the DNA synthesis process in antibody discovery, Twist antibody optimization (TAO) services facilitate the identification of therapeutic antibodies with the desired properties against emerging or established targets. TAO uses bioinformatics and custom software to generate high-quality molecules inspired by the human repertoire.

"With our precision DNA-writing platform and software, we can remove frame shifts, stop codons and potential downstream manufacturing liabilities, and focus on those with the highest probability of downstream preclinical success," Sato explained.

Alongside antibody discovery and TAO, Twist Bioscience offers additional development services, including high-throughput, full-length IgG conversion, expression, purification, and biochemical, biophysical and functional characterization.

Streamlining antibody development

By using the library of libraries, Twist Biopharma has discovered several development-ready antibody candidates. These include antibodies that reduce tumor growth in an in vivo mouse model of human colon cancer by binding specifically and with high efficacy to the GPCR and immuno-oncology target ADORA2A[4], and antibodies that show strong in vitro neutralization activity against new SARS-CoV-2 variants[5].

Twist has licensed the anti-SARS-CoV-2 bispecific antibody candidate RBT-0813 to Revelar Biotherapeutics, which will continue to advance the preclinical development of RBT-0813 and intends to submit an investigational new drug (IND) application to start human clinical trials later this year. "Our vetted array of lead antibodies against high-value targets are engineered for developability so companies can quickly tap into first-in-class or next-generation therapeutics," said Sato.

With 42 partners and 52 active programs at the end of 2021, Twist Biopharma is supporting the development of biologics across a broad range of indications. "By lowering failure rates, our partners can bring therapies that address some of the most difficult-to-treat diseases to market much faster," Sato concluded.

1. Batta, A. et al. *J. Family Med. Prim. Care* **9**, 105–114 (2020).
2. Mullard, A. *Nat. Rev. Drug Discov.* **21**, 83–88 (2022).
3. Optimizing drug discovery in a fast-moving market (Fierce Biotech, 2022). https://www.phamed.com/optimizing-drug-discovery-in-a-fast-moving-market-pharmalive/
4. Taking aim at hard-to-drug GPCRs with therapeutic antibodies (Twist Bioscience, 2021). https://www.twistbioscience.com/blog/science/Therapeutic-Antibodies-Target-GCPRs
5. Yuan, T. Z. et al. bioRxiv 2022.01.04.474803; https://doi.org/10.1101/2022.01.04.474803

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