

DISCOVERY

## SuperHuman Antibody Discovery Platform

### A revolutionary approach to engineer tomorrow's medicines

For more information visit  
[www.criver.com/antibody](http://www.criver.com/antibody)

#### Advantages

- Unprecedented speed
- More hits to any target
- Superior developability
- Rapid multi-parameter optimization
- Support through IND

A combination of Distributed Bio's antibody discovery platform and Charles River's extensive drug development expertise creates an elite end-to-end solution for therapeutic antibody discovery and development. With access to the Distributed Bio's SuperHuman, AbGenesis, and Tumbler technologies, clients can quickly discover, analyze, and engineer therapeutic antibodies with unprecedented speed.

The SuperHuman discovery platform provides a new paradigm for antibody discovery. Guided by machine learning and computational optimization, the library of incomparable diversity consists of antibodies carefully selected from humanity's natural immune repertoire and engineered to perform optimally as therapeutics. With hits against even the most challenging targets, the platform dramatically reduces therapeutic hit discovery time to as little as 4 weeks.

#### SuperHuman

- Achieve higher numbers of quality hits
- Ensure more and better hits through diversity
- Reduce downstream time and costs with pre-optimized hits
- Connect seamlessly into an end-to-end platform for antibody therapeutic development

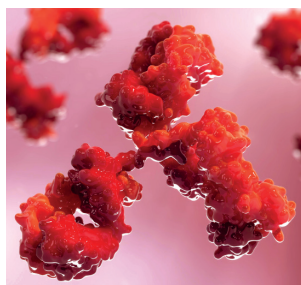
#### Tumbler

- Create billions of variants of your starting antibody to find improvements and remarkable therapeutic properties
- Optimize your molecule's affinity, thermostability, immunogenicity, biochemical liabilities and species cross reactivity in a single pass
- Access bio-superiors with remarkable new characteristics

#### AbGenesis

- Identify candidate clones
- Analyze CDR diversity
- Analyze human antibody library selections
- Assess hybridoma and immunization data
- Monitor population immune responses

EVERY STEP OF THE WAY



### Parameters for SuperHuman Design

- Safe scaffolds as defined as Phase1 +
- Low immunogenicity
- Aggregation resistance
- Display fitness
- Thermostability
- Structural diversity
- Scaffolds with longer half-lives and known stability

### Unparalleled Diversity

The SuperHuman library contains 76 billion antibodies, the vast majority of which are sequence-unique. This exceptionally low sequence redundancy renders the library in excess of 100 times more diverse than previous human antibody libraries. As a result, the platform elicits 5,000-9,000 enriched, specific clones against any target based on deep-sequencing, with an average of 100-300 sequence-unique clones confirmed to bind the target from screening 500-1,000 clones. The immense library size and functional fitness allows for rapid discovery of therapeutic leads that have better affinities, better species cross-reactivity, more epitopes and unique biological functions. The platform readily generates picomolar binders, triple-species cross-reactive binders, cell surface receptor-confirmed binders, functionally active antagonists and agonists, and saturated epitope coverage. Additionally, the platform consistently delivers leads where other antibody discovery technologies have failed, specifically for GPCRs and other multi-pass transmembrane proteins, peptide-MHC and anti-idiotypes (where single amino acid discrimination is essential), low human-mouse sequence homology to eliminate the need for surrogate antibodies, highly specific binding that is irrespective of glycosylation patterns, and engineering dual specificity into a monoclonal.

### Superior Developability

The SuperHuman design is computationally optimized for both sequence diversity and therapeutic fitness through the analysis of thousands of human antibody repertoires and all known monoclonal therapeutics in human clinical trials. 100% natural CDR diversity is pre-screened by human bodies and sourced from blood. Developability and dosing tolerability liabilities are addressed up-front in the library design and construction through careful scaffold selection and thermal tempering steps. Immunogenicity is reduced by only using scaffolds that look the most human. Thermal tempering during both library construction and selections enriches for thermostable antibodies which, among other benefits of high thermostability, renders them less immunogenic in the body.

### Tumbler: Antibody Optimization & Engineering Technology

Tumbler technology provides a solution for optimizing multiple features in a single process. The library-based platform allows for rapid construction of 500+ million versions of an input antibody, then applies rigorous simultaneous selection pressures to affinity mature, thermostabilize, refine specificity or selective activation, minimize immunogenicity, remove biochemical liabilities, humanize, pH sensitize, and otherwise engineer an antibody, whether from a different library, an animal/chimera, or Tumbler. It enables selection across a vast local search space for bio-superiors with remarkable new characteristics (acid resistance, selective binding in tumor environment, pH switch binding, BBB passage, species cross-reactivity engineering, and more), and furthermore clarifies the affinity maturation landscape around a parental antibody for robust IP protection of a therapeutic candidate.

### Integrated Discovery & Development

Together with Distributed Bio, Charles River can now offer a next generation antibody discovery platform seamlessly linked with unmatched biology, PK, pharmacology, biologics and safety services. These services can be accessed individually or collectively and tailored to client requirements under a highly accessible, outcome-focused business model.