

arana  
therapeutics®

## technology platform

Developing high quality antibody products to meet demand in the international pharmaceutical industry.

Superhumanisation™,  
Synhumanisation®,  
EvoGene™ and  
Domain Antibody  
Technology

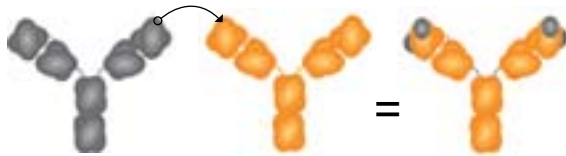


### Arana Therapeutics Technology Platform

Arana Therapeutics has a powerful technology platform, incorporating the company's Superhumanisation™, Synhumanisation®, and EvoGene™. As a suite of technologies, the Arana Therapeutics platform transforms lead proteins or antibody reagents into potent, safe drug candidates.

### Superhumanisation™ & Synhumanisation®

Humanisation is a process applied to non-human (usually mouse) antibodies which demonstrate positive activity against a drug target protein. The goal is to retain the activity of the mouse antibody while replacing as much of it as possible with corresponding regions from a human antibody.



Mouse antibody      Human antibody      "Humanised" mouse antibody

Superhumanisation™ compares the structure of the target-binding region of a mouse and a human antibody, specifically the antigen-binding regions.

Superhumanisation™ converts the mouse antibody, which would otherwise be rejected if administered to humans, into a "humanised" form, which can be given safely to patients. Superhumanisation™ produces antibodies that are specific for the target and have a higher human content – therefore a lower likelihood of rejection.

In addition, Superhumanisation™ delivers a lower median loss of affinity compared to standard humanisation with a 100% success rate to date.

By starting with a rodent antibody and humanising, the Superhumanisation™ technology retains the properties of the starting rodent antibody. Competitor approaches that use immunisation of fully human antibodies often lose the properties of the starting rodent antibody as they generate an entirely new antibody potentially against a different or overlapping epitope.

Synhumanisation® is Arana Therapeutics' related, patent-protected technology that uses a novel method of recombining human and non-human sequences to convert antibodies of non-human origin to antibodies with about 95% human sequence.

Synhumanisation® is a stand-alone technology that can also be used in combination with Arana Therapeutics' other protein engineering technologies, Superhumanisation™, EvoGene™ or Domain Antibody.

A key advantage of Arana's Synhumanisation® technology is that for some existing, validated targets it opens up an approach to generate patentable new antibody products that would be excluded by conventional 'humanisation' or fully human antibody approaches.

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## EvoGene™

Humanisation of an antibody can result in a decreased tightness of its attachment to the target and therefore lower potency. This can be restored, or greatly improved, if required, using Arana's EvoGene™ technology.

The EvoGene™ process involves:

- Production of billions of slightly mutated variations of an original antibody
- Testing of the variations for improved binding activity to the target and selection of the best
- Repeating these two steps to select engineered antibodies with the best properties arising from the fewest mutations.

EvoGene™ uses a unique proprietary mutagenesis that enhances the randomness of the mutations created to give a high level of diversity, which is maintained by directly accessing the mutants using a technique referred to as ribosome display. Competitor approaches such as phage display require a transformation step that is associated with a significant loss in diversity.

Arana Therapeutics' technologies actually reduce any potential immunogenicity of the final antibody in several ways:

- Use of human germ line frameworks that are closest to the human sequence

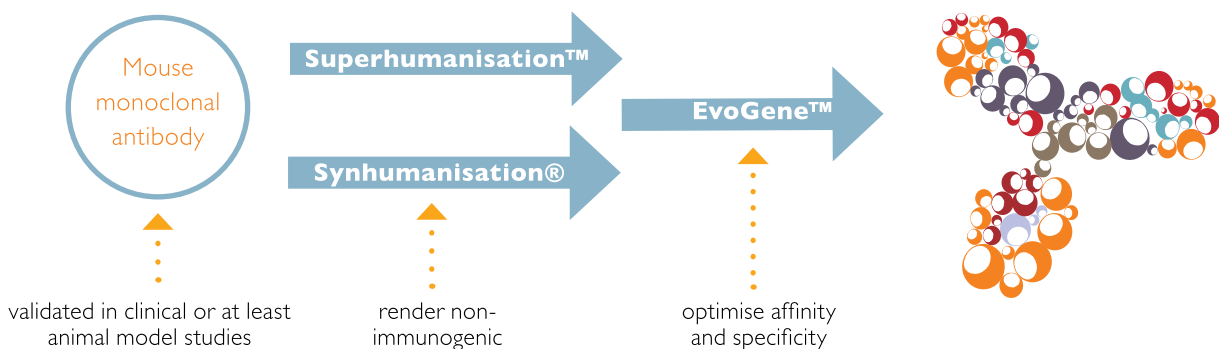
- Use of a minimal mutagenesis approach that introduces the fewest mutations necessary to gain the required improvement
- Use of a sequential process that characterises the mutants throughout the process to gain optimal performance with minimal alteration

The process has been validated extensively in-house and for the products under development by third parties, including GSK and CSL.

The technology is not specific for antibodies, but can be applied to any protein to increase its value as a therapeutic due to greater:

- Activity and potency (that reduces the required dose)
- Specificity (that reduces side effects)
- Stability and/or reduced production costs.

## integrated humanisation and optimisation



## Contact

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