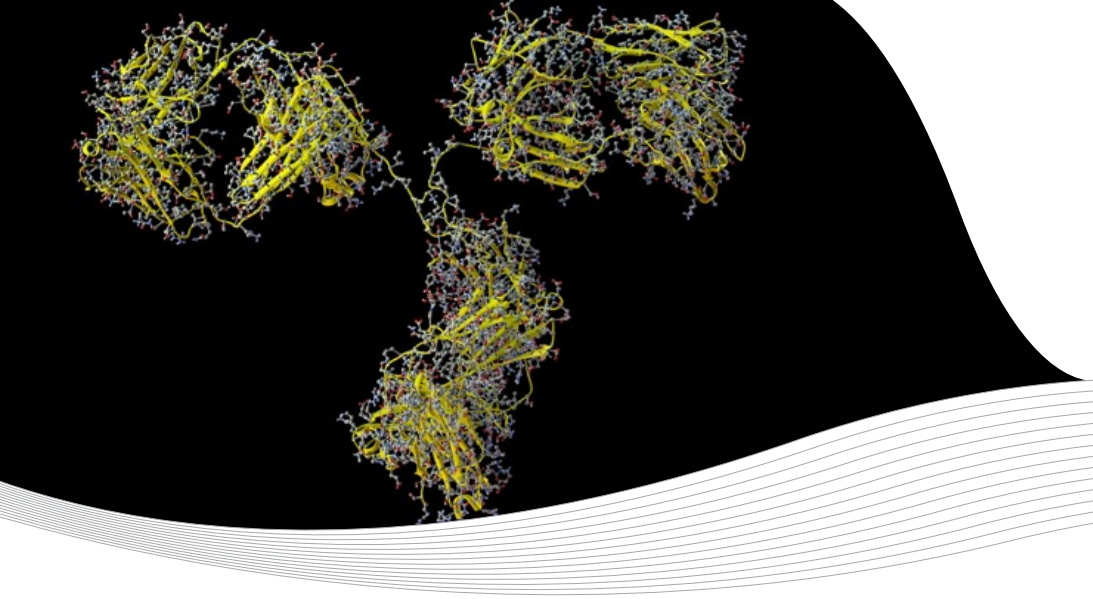

celerion
Translating Science to Medicine

Adalimumab:
Turn-key Biosimilar Development

Celerion's extensive bioanalytical and clinical pharmacology experience with adalimumab enables us to provide a complete program for clinical development and registration of adalimumab biosimilars:

Bioanalytical assays that meet rigorous regulatory validation requirements (Total development and validation ranges from $200K - $250K)*

- Assays that measure the concentration of the originator products in plasma for use in pharmacokinetic biosimilarity studies and to document exposure in patient studies
- Anti-drug antibody (ADA) assay to measure extent of immune response to the biosimilar
- Neutralizing-drug antibody assay to assess presence of this effect-nullifying immune response
- Validated and robust biomarker assays including TNFα

Pharmacokinetic study designed to demonstrate robust bioequivalence (Cost range for equivalent sized study is $3M - $3.5M total)*

- Single-blind parallel PK bioequivalence design to meet requirement that > 90% confidence exists in the geometric mean ratios for Cmax and AUC falling within the bioequivalence boundaries of 80 -125% against both the EU-sourced Humira and US-sourced Humira
- 100 -110 healthy subjects in each treatment group receive single 40mg subcutaneous injections
- Measure for presence of ADAs up to 3 months after each dose
- Measure time-related effect on TNFα serum levels over the study duration
- Compare standard measures of safety and tolerability

Background

Adalimumab is the leading selling drug in the world. It binds to tumor necrosis factor alpha (TNFα) that normally binds to the TNFα receptors leading to the anti-inflammatory response in autoimmune diseases. As such, it is valuable in treatment of rheumatoid arthritis (RA), axial spondyloarthritis, ankylosing spondylitis, plaque psoriasis, psoriatic arthritis, Crohn's disease, ulcerative colitis, polyarticular juvenile idiopathic arthritis, active enthesitis-related arthritis, hidradenitis suppurativa and non-infectious uveitis. Biosimilar legislation supports approval of a biosimilar for all indications if similarity with one indication can be shown.

The patent on the originating product, Humira, expired in 2016 in the US and the last quarter of 2018 in Europe. While biosimilar versions of adalimumab have already been approved by EMA, US and India, the size of the market and many indications leaves room for several additional competitors.

Efficient conduct of studies in patients to demonstrate clinical similarity in drug response (Cost range for equivalent sized study is $11M - $16M total)*

- Blinded, randomized, parallel group study in approximately 500 plaque psoriasis patients
- Three treatment groups: Humira 24 weeks (n=125) versus biosimilar 24 weeks (n=250) versus Humira 12 weeks then switch to biosimilar 12 weeks (n=125) 40 mg sc q2 weeks to demonstrate similarity at 12 and 24 weeks in:
  - ADA blood levels
  - % patients achieving at least 75% reduction in psoriasis area and severity index (PASI-75)
  - Safety and tolerability
  - Trough adalimumab and TNFα concentrations
- 36 - 40 sites (US/Europe/Asia depending on source of Humira) – recruitment and conduct 15 - 21 months

Regulatory submissions for IND/CTA and NDA/MA (Cost range of $30K - $250K depending on services required)*

Ask us about our experience with your biosimilar.
Contact us at info@celerion.com

*Costs include CRO, site and specialty vendor costs but do not include the cost of acquiring drug supply of the innovator biologic. These represent direct costs only for a typical study. Your actual study design and costs may vary.