

THE BIOSIMILARS ALLIANCE®

celerion 



The Biosimilars Alliance – leverage 20 years of biologics drug development experience to enable early assessment viability of biosimilars, and bridge the gap between newly sourced products and patient studies.

Developing a biosimilar carries more risk, labor and expense than a traditional generic drug, and requires in-depth knowledge of biopharmaceutical drug development.

The first critical step is to manufacture or source the large molecule drug and ensure it has similar or better properties than the innovator product. The drug product is then assessed for safety, PK and immunogenicity to ensure it behaves in a manner that is comparable to the reference compound. Finally efficacy and safety must be demonstrated in patient studies, to meet regulatory requirements for market approval.

Celerion has partnered with Ricerca Biosciences to form “The Biosimilars Alliance” and bring together the specific expertise required to guide clients through the complex development process. This includes:

- Early safety and PK assessment of biologic drug candidates in animals and humans
- Extensive experience in assays of human insulins, interleukins, interferons, pegylated interferons, erythropoietins, monoclonal antibodies and fusion proteins
- Immunotoxicology expertise within Europe’s largest Non Human Primate (NHP) research facility
- Extensive expertise in the monitoring and quantification of antigenicity (anti-drug antibodies) in animal and human samples from clinical studies
- PK/PD assessment of biological products in patients and healthy volunteers
- Regulatory expertise to guide full biosimilar development programs
- Full program development leadership and/or *ad hoc* consulting services spanning preclinical to pivotal clinical studies

Early Safety Assessment

- Off-target adverse event assays and on-target therapeutic models extend *in vitro* results or detect potentially important primary and/or secondary pharmacodynamic activities
- Assay portfolio provides screening for unexpected effects before advancing to formal toxicology
- All major organ systems and therapeutic categories offered with particular expertise in pain, inflammation, cardiovascular and metabolic disease

Immunotoxicology

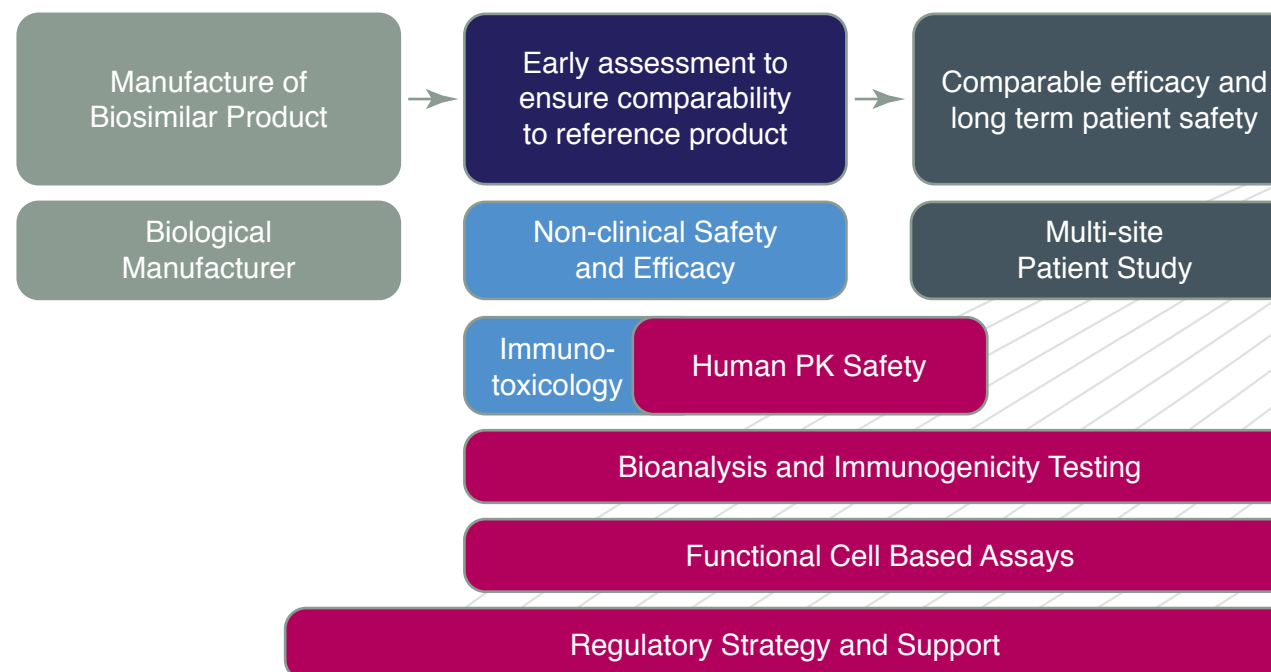
- Extensive experience and expertise in immune system evaluation enabling sponsors to rapidly assess the impact of possible immunological adverse effects in a variety of different species
- Full range of assays is validated on many different species, including models for immunosuppression, allergy and autoimmunity
- Fully GLP-compliant assays are performed in compliance with international regulatory requirements (ICH S8) either as part of ongoing toxicological evaluations or as stand-alone studies

Bioanalytical and immunogenicity assay development (preclinical and clinical)

- Bioanalytical scientists who have over 20 years experience working with all classes of biopharmaceuticals and biosimilars
- Bioanalytical laboratories use state-of-the-art immunogenicity technology to detect if antibodies are generated to biosimilars, and determine if the antibodies are neutralizing
- Experience in working within a regulatory environment that includes EMA and FDA amongst others



The bridge between manufacturing and clinical efficacy



Developing preclinical and clinical study designs

- Experience in developing both preclinical and early phase comparative studies to maximize the potential of similarity in clinical phase including employing modeling and simulation techniques
- The experience to design comparability studies to assess the similarity between biosimilars and the marketed reference compounds
- Expert knowledge of pharmacodynamic (PD) markers that can serve as surrogate endpoints for biosimilar clinical trials

Monitoring and quantification of antigenicity

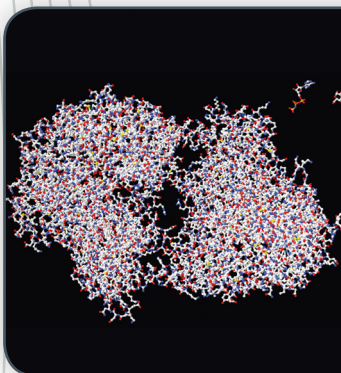
- Multiple technologies used to screen the appearance of antibodies
- Ability to analyze 15,000 samples per month - speed
- GLP-certified by Swissmedic for preclinical and clinical sample analysis, and also accepted by all regulatory bodies throughout the OECD

Regulatory guidance and preparation of clinical programs

- Experienced regulatory team helps companies execute efficient regulatory strategies and tactical support to ensure timely communication and quality submissions
- Key members of the Celerion organization have navigated through the scientific and regulatory process of bringing biologics to the marketplace

Program Management

- Integrated services offering a one stop shop solution with efficient timelines
- Certified project managers to track each stage of a biosimilar program to ensure they meet clients' timelines



Benefits of leveraging The Biosimilars Alliance:

- The Biosimilars Alliance team members include experienced:
 - Pharmacologists/Toxicologists
 - Bioanalytical scientists
 - Certified project managers
 - Clinical pharmacologists and therapeutic area experts
 - Former regulatory agency reviewers
- Two global laboratories located in Europe (Zurich, Switzerland) and the USA (Lincoln, NE)
 - Small and large molecule assays, biomarkers and immunogenicity tests
 - Only CRO with global harmonized electronic laboratory notebook
 - Technologies include: ELISA, RIA, ECLA, Luminex, LC-MS/MS
- Global, GLP compliant pre-clinical laboratory in Lyon, France with more than 40 years of experience in Drug Safety Assessment
 - Conducts more than 40% of business with biologics
 - State of the art technologies for study performance and on-time reporting. Specialization in parenteral routes of administration
- Four global clinical Phase 0, I and IIa facilities located in Europe (Belfast, Northern Ireland, UK) and the USA (Lincoln, NE; Neptune, NJ; Phoenix, AZ)
 - Over 730 beds (including 24 in-hospital) and conduct over 200 complete studies annually
 - Conducted over 6,000 Phase I studies across our global clinical sites

