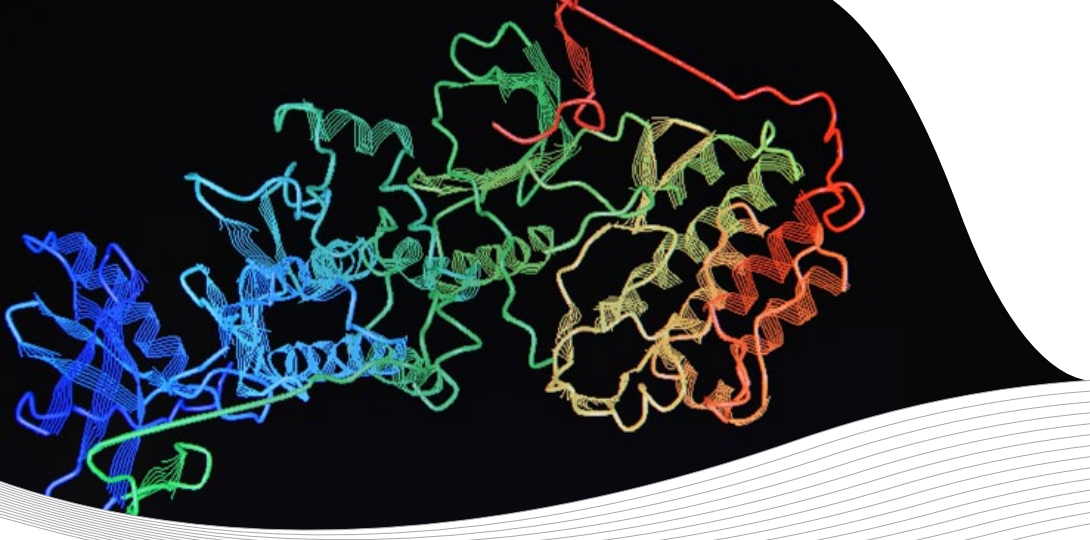

celerion
Translating Science to Medicine

Biosimilar Clinical Development

Ranibizumab:
Turn-key Biosimilar Development

Celerion's bioanalytical laboratories have developed plasma assays to measure ranibizumab concentration as well as anti-drug antibodies that may be generated after administration of this protein product. All three of Celerion's confined clinical sites are equipped with modern technology to measure eye function. Finally, Celerion's multi-site clinical study management infrastructure is perfectly aligned to execute studies in patients with with age-related macular degeneration (AMD) and diabetic macular edema. Based on these capabilities, we can offer you a complete clinical development solution to bring a ranibizumab biosimilar to registration.

Background

Ranibizumab is a monoclonal antibody fragment that inhibits angiogenesis by inhibiting vascular endothelial growth factor A (VEGF-A). It treats age-related macular degeneration (AMD), a common source of vision loss with aging. It is also effective in diabetic macular edema.

The patent on the originating product, Lucentis, will expire in June 2020 in the US and 2022 in Europe. Interest is building from several biosimilar manufacturers.

Ranibizumab is administered via intravitreal injection directly into the eye; however, a significant amount of the injected dose moves out of the eye and into the systemic circulation. Drug systemic exposure and immunogenicity remain important criteria upon which to base similarity assessments.

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 VEGF and PlGf

Phase I/II safety comparison of biosimilar candidate with Lucentis in patients with neovascular AMD (Total development and validation ranges from $800K - $1200K)*

- Three intravitreal injections on Day 1, Day 28 and Day 56
- Safety assessment visits made on Day 2, 7, 14 and 80 and at 6 and 12 months
- Double blind, randomized, parallel group study in 12 patients receiving Lucentis and 12 patients receiving the biosimilar candidate
- Eye examinations include: reading chart, intraocular pressure measurement, measurement of retinal thickness (photo) and examination of eyes blood vessels (photo following dye injection)
- Blood collection during safety visits to measure concentrations of ranibizumab and ADA

Efficient conduct of Phase III study in patients with wet AMD to demonstrate clinical similarity in drug response (Cost range for equivalent sized study is $13M - $20M total)*

- Blinded, randomized, parallel group study in approximately 650 AMD patients (20 - 30 sites)
- Two treatment groups: Lucentis (n=325) versus biosimilar (n=325); 0.5 mg q28 days
- Compare change from baseline in retinal thickness at 1, 6 and 12 months, change from baseline in visual acuity at 2, 6 and 12 months, AEs/SAEs, percentage of patients with measureable ADA
- 20 - 30 sites (US/Europe/Asia depending on source of Lucentis) – 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.