āshibio Andecaliximab: A Promising Therapeutic Direction for FOP

Āshibio is a focussed, clinical-stage biotechnology company dedicated exclusively to developing necessary treatments for bone and connective-tissue disorders, notably Fibrodysplasia Ossificans Progressiva (FOP) and related forms of heterotopic ossification (HO). Founded in 2022, the company made its public debut in 2024, supported by substantial investment to responsibly advance its crucial research pipeline.

Andecaliximab stands as Āshibio's lead programme. This therapy is a humanised monoclonal antibody specifically designed to selectively inhibit the enzyme Matrix Metalloproteinase-9 (MMP-9). This enzyme has been identified by researchers as a key potential factor driving the abnormal bone formation characteristic of FOP.

Originally developed by Gilead Sciences, Andecaliximab is now being progressed by Āshibio in a global Phase 2/3 clinical trial.

The Scientific Rationale: Targeting MMP-9 in FOP

Scientific findings suggest that MMP-9 plays a pivotal role in the biological cascade that links an FOP flare-up to the eventual formation of extra bone.

The "Resilient Patient Project" highlighted a specific case: an adult with the classic FOP mutation (ACVR1 R206H) who nonetheless exhibited very limited HO. Genetic analysis revealed this individual carried additional mutations in MMP-9, suggesting that a natural reduction in MMP-9 activity may offer a protective effect against this abnormal bone growth.

This premise is further supported by animal and cell-based research, which has shown that either genetically removing (knockout) or pharmaceutically inhibiting MMP-9 significantly lessens trauma-induced HO. These collective findings establish a clear and plausible biological pathway for targeting MMP-9, positioning it as a highly promising candidate for therapeutic intervention in FOP.

Clinical Development and Regulatory Milestones for FOP

Regulatory Designations

- The European Medicines Agency (EMA) granted Orphan Drug Designation to andecaliximab in February 2024.
- The U.S. Food & Drug Administration (FDA) granted both Orphan Drug Designation and Rare Paediatric Disease Designation (RPDD) in March 2024.

Clinical Trial Status

A registered clinical trial (NCT06508021) is currently enrolling both paediatric and adult participants with FOP. Āshibio announced the dosing of the first participant in the Phase 2/3 "ANDECAL" study in January 2025.

The trial is structured into two main parts:

- Part 1: This initial phase is limited to sites in the US, focussing on ensuring safety, determining the drug's behaviour in the body (pharmacokinetics/pharmacodynamics or PK/PD), and identifying early signals of efficacy. Confirmed US sites include Mayo Clinic (Rochester, Minnesota), UCSF (San Francisco, California), and University of Pennsylvania (Philadelphia, Pennsylvania).

- Part 2: This will be a larger, definitive, randomised, double-blind, placebo-controlled study intended for regulatory registration. For our community in the UK and Europe, Part 2 is planned to include sites here, pending local regulatory and operational setup, though specific UK institutions have not yet been confirmed.

For further information:

Company and Drug Background

- Āshibio official website: https://ashibio.com
- Global Genes: https://globalgenes.org/raredaily/ashibio-raises-40-million-to-advance-therapies-for-bone-and-connective-tissue-disorders

MMP-9 and Biological Rationale

- Resilient Patient Project, *Journal of Bone & Mineral Research*: https://academic.oup.com/jbmr/article-abstract/39/4/382/7609505
- Penn Medicine: *A mutation hiding in one unique patient could save others from forming a 'second skeleton'.*

  An interview with Professor Fred Kaplan and Andrew Davis, about the Resilient Patient Project:

  https://www.pennmedicine.org/news/one-patients-gene-mutation-could-save-others-from-2nd-skeleton

Regulatory Designations

- FDA Orphan Drug and Rare Paediatric Disease Designation: https://www.accessdata.fda.gov/scripts/opdlisting/oopd/detailedIndex.cfm?cfgridkey=994223
- EMA Orphan Drug Designation: https://www.ifopa.org/andecaliximab_granted_orphan_drug_designation

Clinical Trials

- Āshibio trial information: https://ashibio.com/patients
- ClinicalTrials.gov NCT0650802: https://clinicaltrials.gov/study/NCT06508021
- IFOPA – ANDECAL trial sites and updates: https://www.ifopa.org/andecaliximab