SCE 0902 Public Evidence Appendix

Preclinical evidence

Literature review date: September 13, 2026

Controlling principle. Preclinical evidence can establish plausibility, characterize product activity, refine dose and route, and identify safety concerns. It does not by itself establish clinical efficacy. Interpretation remains specific to the exact product, manufacturing process, experimental model, endpoint, and translational question.

Point-by-point framework

Controlling Point	Primary value	Key limitation
In-vitro models	Controlled study of mechanism, potency, dose-response, target engagement, and toxicity.	Simplified systems lack many whole-organism interactions and cannot prove patient benefit.
Organoids	Three-dimensional modeling of selected tissue architecture and cell-cell interactions.	They remain incomplete models and often lack mature vasculature, systemic immunity, metabolism, and long-term disease evolution.
Small-animal models	Whole-organism study of biodistribution, persistence, dose, route, efficacy, and safety.	Species biology and artificial disease models can limit prediction of human outcomes.
Large-animal models	Human-relevant anatomy, scale, physiology, procedures, imaging, or biomechanics in selected applications.	Cost, small samples, and imperfect disease models remain important limitations.
Disease-model validity	Determines how well a model represents the human biological or clinical question.	A model may reproduce only selected disease features and can exaggerate apparent treatment effects.
Reproducibility	Tests whether findings persist across repetitions, investigators, materials, and analytical choices.	Poor reporting, product heterogeneity, bias, and selective publication can undermine reproducibility.
Translation failures	Identify where promising preclinical assumptions fail in clinical development.	Failure may reflect model validity, product changes, dose/route, patient heterogeneity, endpoint mismatch, or insufficient mechanism.

Evidence-handling rules

Positive, negative, mixed, null, and inconclusive findings are retained according to model validity, experimental design, product identity, manufacturing consistency, bias control, reproducibility, endpoint relevance, and directness to the intended clinical question.

Mechanistic activity, preclinical efficacy, toxicology, clinical efficacy, clinical safety, development stage, regulatory status, and manufacturing quality remain separate analytical dimensions.

Principal references

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