

## Orphan Drug Development Guidebook

### Milestone: Nonclinical PoP milestone

PoP: Proof of Principle

Pre-clinical research is a preliminary phase that involves testing the drug in lab models (in-vitro) and on animals, including basic testing for safety flags. Before testing a drug in humans, researchers must find out whether it has the potential to cause serious harm, also called toxicity. The two types of preclinical research are:

- In vitro (i.e. by chemical testing, in cells, in organoids or in isolated tissues or organs)
- In vivo (i.e. in animals)

PoP is achieved when a sufficient evidence of biological activity in vitro and in vivo is demonstrated, an adequate understanding of the pharmaco-kinetics and pharmaco-dynamics of the drug is gathered, and some initial toxicology and safety information is generated. With these data, researchers can plan the following phase of extensive testing of toxicology and biodistribution, which is required to move into clinical studies.