Molybdenum is an essential trace element needed for the survival of apr. 60% of organisms from all kingdoms of life. In order to gain biological activity, molybdenum is chelated into cofactors, of which nearly all (except nitrogenase) form a pterin-based structure that binds molybdenum via one or two dithiolates forming the so-called molybdenum cofactor (Moco). Moco is synthesized by a complex and highly conserved biosynthetic pathway involving four steps, with cyclic pyranopterin monophosphate (cPMP), molybdopterin (MPT) and adenylated MPT as known intermediates. We have characterized this pathway in detail and investigated its deficiency in humans as well. A defect in the synthesis of Moco leads to a loss of all Mo-enzyme activities. In patients with Moco deficiency (MoCD), the accumulation of toxic metabolites, especially sulfite (derived from the loss of sulfite oxidase activity), resulting in severe neurological damage and early childhood death. An animal model is presented, that resembles the phenotype of human patients and has been used to develop a first causal therapy to treat MoCD. We isolated and characterized the first intermediate of the pathway, cPMP, and used this molecule to treat Moco-deficient mice. Recently, we reported the first human exposure of cPMP, which is now used to treat additional patients in an experimental therapy. All patients show normalization of metabolic markers, disappearance of seizures as well as significant clinical improvement.