Hypophosphatasia is a genetic disease characterized by the deficiency in tissue non-specific alkaline phosphatase activity. The causal treatment of this disease is of course enzyme replacement therapy where a bone affinity tag of the recombinant product developed causes enrichment in the bone microenvironment and substitutes for the membrane anchorage of this enzyme. The very variable skeletal manifestations of hypophosphatasia comprise alterations in bone development, insufficiency and fragility fractures besides inflammatory problems due to crystallopathy. In adult patients suffering from mild HPP osteoporosis and insufficiency and fragility fractures may mimic primary osteoporosis which is probably mistreated when using standard bisphosphonate treatment. In HPP both bone mass and quality are severely altered and questions arise if these patients may get benefit from anabolic treatment modalities which should at least enhance bone mass (if not quality) and fracture resistance. Intermittent parathyroid hormone treatment has been reported to be successful in some cases, but also negative reports can be found in the literature. Upcoming anabolic treatment modalities are e.g. anti-sclerostin antibodies, anti DKK1 antibodies and activin antagonists, the cathepsin K antagonist Odanacatib is being developed as an „osteoclast-friendly“ antiresorptive. A phase two clinical trial is already ongoing using an antiscleerostin antibody in mildly affected adult HPP patients, which will demonstrate to what extend this principle is capable of stimulating bone formation in HPP. Other future developments of supportive treatment modalities in mild HPP could target TNSALP homing at the membrane, which is regulated by phospholipase activity. Although phospholipase inhibitors are being developed as anti-tumor agents so far no attempts have been made to set up studies in HPP patients. Such approaches might also have some potential for the extraskelatal effects of alkaline phosphatase e.g. in the central nervous system and in muscle. Given the comparably low numbers of affected patients interdisciplinary and international cooperations are needed.