



ENPP1 Inhibitor

REC-102

May 2026

REC-102: ENPP1 Inhibitor

A preliminarily non-immunogenic, potent, highly selective ENPP1 inhibitor for hypophosphatasia (HPP)

Unmet need¹

- **~7,800 diagnosed** HPP patients, mostly with limited ERT access
- Opportunity to **significantly reduce costs**

Mechanism of Action

- **Potent, highly selective ENPP1** inhibitor

Thesis & Differentiation

- **First oral disease-modifying therapy**
- **ENPP1** inhibition a **genetically validated** target in HPP models
- **Non-immunogenic** small molecule, potentially safer than ERT
- **More tolerable and affordable** vs ERTs

Recursion Approach

- **Precision designed for both high potency, chronic dosing**
- **Maintained selectivity** for candidate with **high oral bioavailability** in clinic

Program Status

- **IND-enabling studies ongoing**
- Data driven go/no-go decision on **Phase 1 initiation in 2H26**

Platform insight: Precision designed for both high potency and a lifetime of chronic dosing using Recursion OS

Biology

Novel insights

- **ENPP1 inhibition** helps correct phenotypes caused by **LOF mutations in ALPL gene**
- **Oral drug** reduces cost and improves convenience and access over ERT



Generative Approach



ML models



Selection Coverage Score

Design

Novel scaffolds

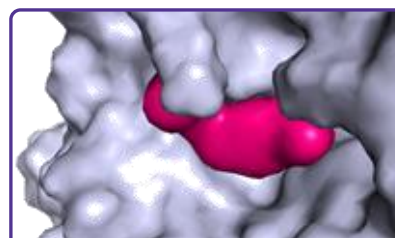
- Structurally distinct molecules to prevent selectivity issues

High bar for safety

- Optimized pharmacophore against closely-related metalloenzymes through structural enablement and 3D / ML model platform

Low (predicted) human oral dose

- Highly optimized ADME using robust 2D ML methods

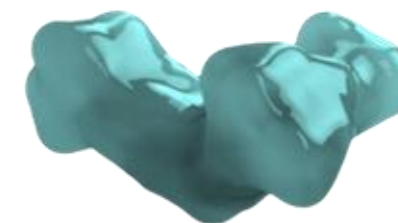


3D interaction filters

Prioritize

Efficient unbiased testing

- Modern use of information theory to select fewest compounds for testing but with maximal information gain

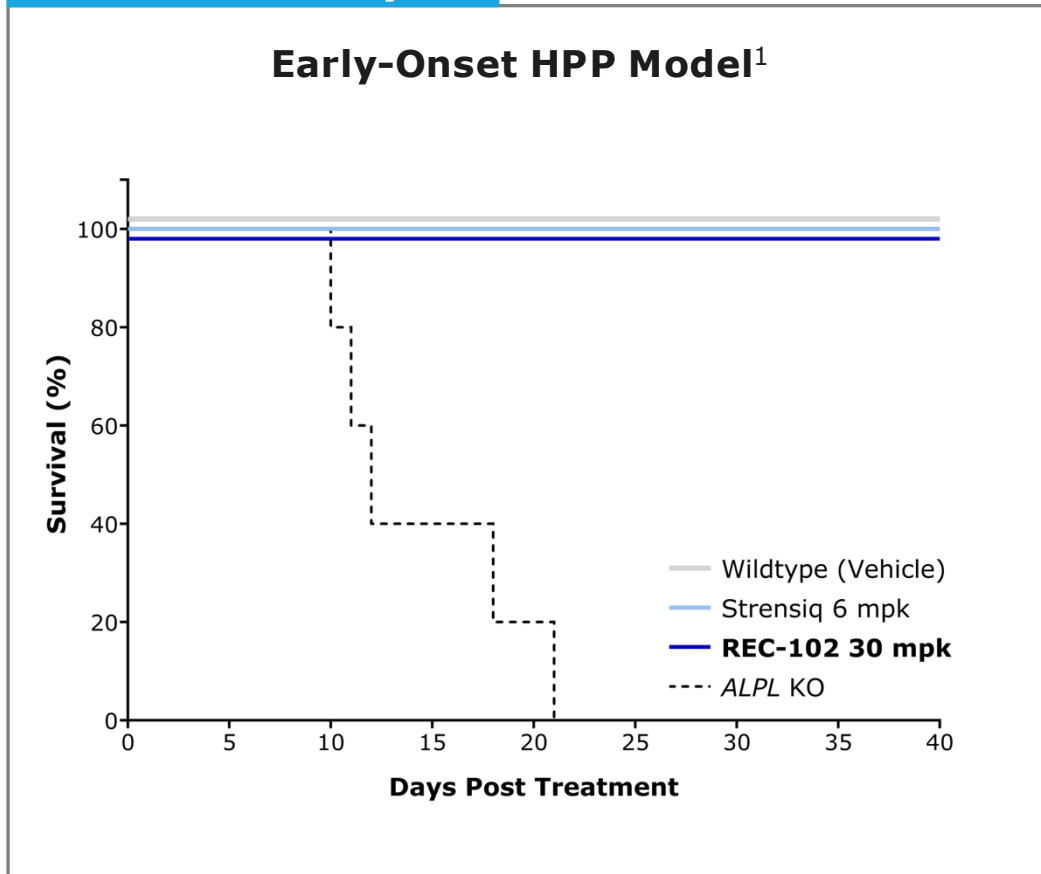


Recursion OS Platform:

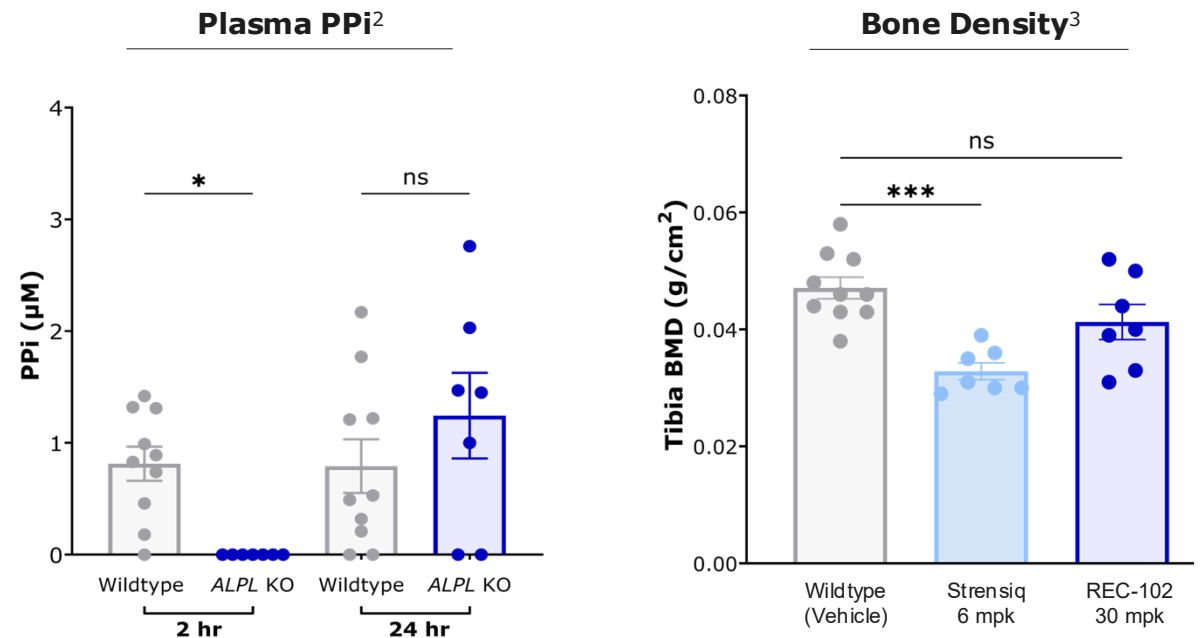
A highly potent, selective, orally bioavailable compound developed through our multi-parameter optimization engine

Preclinical: REC-102 restores bone health and survival in an unpublished *ALPL* early-onset knockout mouse model of HPP

In Vivo Efficacy



- REC-102 **extends survival** in an early-onset *ALPL* KO mice model
- REC-102 **transiently reduces PPI levels** to enhance mineralization
- **Tibia BMD is restored, close to wildtype** levels in treated mice

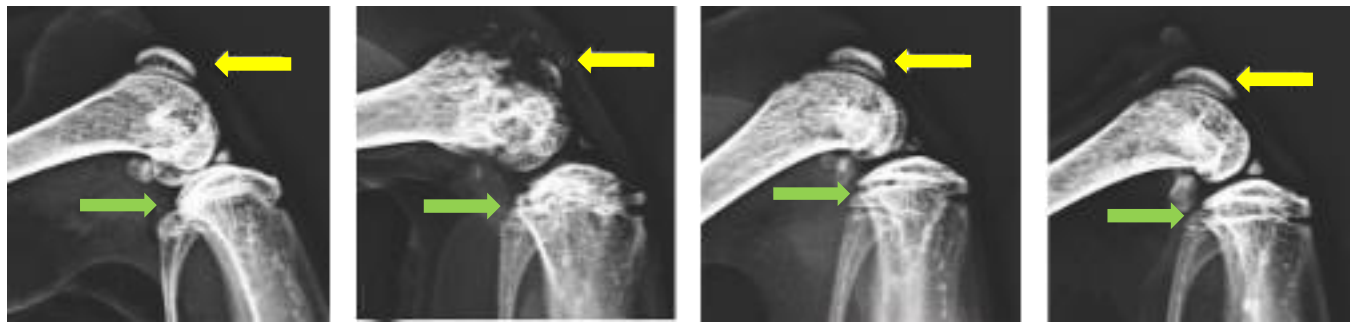


1. N=10 mice in wildtype group, N=5 mice in ALPL KO group, N=7 in Strensiq and REC-102 groups. REC-102 and Strensiq administered QD SC. Vehicle treated ALPL KO mice stopped growing at day 7-10 and all died at day 22
2. PPI concentrations at 2h or 24h after the last dose of 30 mg/kg REC-102. <LLOQ data points are shown on the graph as 0 values.
3. ALPL KO group not shown given all mice die around weaning age

Preclinical: Chronic dosing of REC-102 improves bone phenotype in a late-onset knockout mouse model of HPP

In Vivo Efficacy¹

Late-Onset HPP Model²



Wildtype

Control KO

REC-102 30mpk

REC-102 100mpk

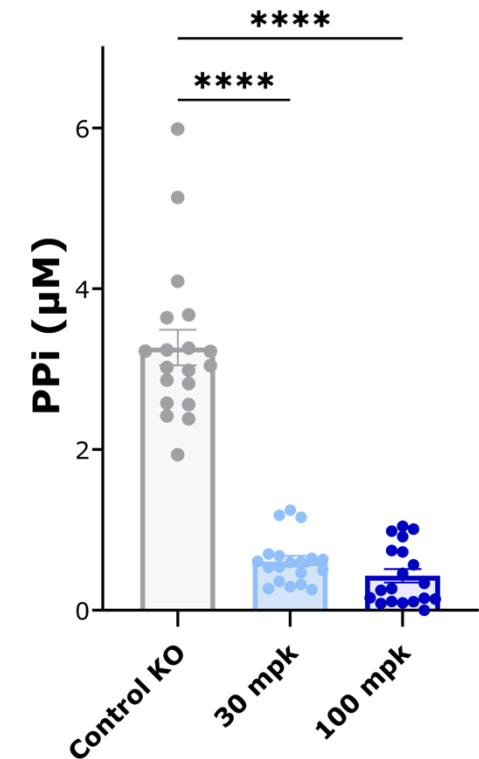
Patella (yellow arrow)

Growth plate (green arrow)

- Untreated mice present **underdeveloped patellofemoral** joints
- REC-102 treatment corrects bone defect and **improves patella structure**
- REC-102 treatment **significantly reduces plasma PPI concentrations**



Plasma PPI

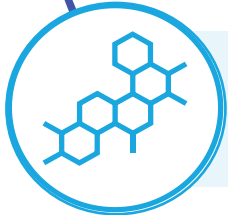


REC-102: ENPP1 – Summary & next steps



Biological Insight

Reduction of PPI production via controlled ENPP1 inhibition to restore bone hypomineralization



Design

AI-driven generative design via **fragment screening** to enhance **metalloenzyme selectivity**



In Vivo Data

Significant survival benefit in HPP mice through transient PPI reduction validates mechanistic rationale



Clinical

Opportunity to address significant unmet needs in **juvenile** and **adult-onset HPP patients**

REC-102 Target Profile

- Potential **first-in-class** ENPP1 inhibitor
- **High oral bioavailability** supports QD or BID dosing
- **No kinases** inhibited >70% at 10 μM
- No significant in vitro safety liabilities identified

What's Next

- IND-enabling studies **ongoing**
- Data driven go/no-go decision on **Phase 1 initiation in 2H26**