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LAI Prodrugs are designed to obtain compounds with low solubility, high melting point, and stable crystalline form. After IM or SC administration, the drug forms a depot in vivo, slowly releases in blood stream then rapidly transformed to the parent drug.

The marketed drug paliperidone palmitate (once every 6 months) and aripiprazole lauroxil (once every 2 months) and others have validated LAI based prodrug technology.

## HNC

B **PD** 





## LAI



Pharmacokinetic (PK) and pharmacodynamic (PD) studies were conducted following single ascending doses (SAD) of HNC364 in healthy volunteers. Platelet MAO-B activity was utilized as a PD biomarker\*. Additionally, a cohort of subjects received multiple oral doses of the marketed drug rasagiline (AZILECT®) as a positive control (Figure 1). \*Research indicates that inhibiting MAO-B activity by over 80% in the central nervous system influences central dopamine levels[1]. Furthermore, a strong positive correlation exists between MAO-B inhibition rates in the brain and platelets following the administration of an MAO-B inhibitor[2].

Using the population PK /PD model, various HNC364 doses administered via intramuscular injection once every month were simulated (Figure 2).

## K F

- The prodrug HNC364 was not detected in plasma.
- intramuscularly every 4 weeks, maintained MAO-B activity inhibition above 90%.

Regensburger M, Ip CW, Kohl Z, Schrader C, Urban PP, Kassubek J, Jost WH (2023) Clinical benefit of MAO-B and COMT inhibition in Parkinson's disease: practical considerations. Journal of Neural Transmission 130, 847-861. Kettler R, Cesura AM, Dingemanse J, Prada M (1990) MAO-B inhibition in rabbit tissues and in human platelets by Ro 19-63



- Single doses of 60 or 80 mg of HNC 364 achieved >90% inhibition of MAO-B activity at 4 weeks post-dose. - Simulation results from the population PK /PD model indicate that repeated 60 mg doses of HNC 364, administered