BACKGROUND
VM1500A is a novel, potent NNRTI with unique clinical PK profile and broad-spectrum activity across HIV-1 variants. An oral dosage form of elvitegravir (Elpida®), a pro-drug of VM1500A, has been approved in 2017 in Russia for treatment of HIV-infected patients in combination with standard ART. A long-acting injectable (LAI) form of VM1500A has been developed to expand the dosing options of VM1500A.

METHODS
This was a Phase 1 first-in-human open-label, single-center study to evaluate safety, tolerability and pharmacokinetics of single and multiple ascending intramuscular doses of the LAI formulation of VM1500A (VM1500A-LAI) in HIV-uninfected volunteers. The study has been conducted in Russia.

RESULTS
27 HIV-uninfected male volunteers (5 Asians, 22 Caucasians) with a mean age of 26 years and mean BMI of 23.9 kg/m² were enrolled and received single ascending doses (SAD) of VM1500A of 150 mg, 300 mg, 600 mg, and 1200 mg once a month during 96 weeks treatment in the study. Median (range) plasma concentrations of VM1500A were 62 (35, 92), 69 (51, 106) ng/ml for the 28 days after the 1st and 28 days after the 2nd IM injections with 600 mg (300 mg x 2) gm respectively. These results show that being split into 2 simultaneous injection the dose of 600 mg/ml supports the required therapeutic Ctrough level.

CONCLUSIONS
Pharmacokinetic parameters demonstrated dose-proportionality over the range of four doses tested in this study.

• Single monthly injection with 600 mg of VM1500A-LAI achieved median plasma Ctrough above target level for at least 3 weeks.
• Single monthly injection with 1200 mg achieved median plasma Ctrough for 35 days.
• Two consecutive monthly injections of 600mg split into 2 x 300 mg achieved target level for 4 weeks after 1st and 5 weeks after 2nd injections also showing drug accumulation in plasma.

In summary, VM1500A LAI was well tolerated and had an acceptable PK profile in healthy volunteers following single and multiple IM dosing. These data support further development of VM1500A-LAI as a novel, long-acting antiretroviral agent for the treatment of HIV-1 infection.