ABSTRACT FINAL ID: LB-7

TITLE: Preliminary safety and efficacy of REP 2139-Mg or REP 2165-Mg used in combination with tenofovir disoproxil fumarate and pegylated interferon alpha 2a in treatment naive Caucasian patients with chronic HBeAg negative HBV infection

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ABSTRACT BODY:

Abstract Body: Nucleic acid polymers (NAPs) block HBsAg release from HBV infected hepatocytes. The NAP REP 2139 clears serum HBsAg in chronic HBV infection, improving the efficacy of immunotherapy and facilitating establishment of functional control off treatment. The REP 401 protocol (NCT02565719) is a randomized, controlled trial assessing the safety and efficacy of REP 2139 and a REP 2139 derivative with improved clearance (REP 2165) in combination with tenofovir disoproxil fumarate (TDF) and pegylated interferon alpha 2a (peg-IFN) in treatment naïve patients with chronic HBeAg negative HBV infection.

Forty patients will receive 26 weeks of lead-in TDF (300mg PO qD) followed by randomization (1:1) into experimental and control groups. The experimental group will receive 48 weeks of TDF, peg-IFN (180ug SC qW) and REP 2139-Mg or REP 2165-Mg (1:1, 250 mg IV infusion qW). Patients in the control group will receive 48 weeks of TDF + peg-IFN but will crossover to 48 weeks of experimental therapy in the absence of a 3 log drop in HBsAg after 24 weeks of peg-IFN. Serum viremia is being monitored offsite at the Institute for Virology, University Hospital at the University Duisburg-Essen, Essen, Germany.

Enrolment is complete and 22 patients have received ≥ 12 weeks of treatment in control and experimental groups. After TDF lead-in, most patients have serum HBV DNA ≤ 10 IU / ml prior to peg-IFN exposure. Triple combination therapy is well tolerated in all patients and no infusion reactions have been observed with either NAP. Serum HBsAg reductions, increases in serum anti-HBs or serum ALT / AST / GGT flares were negligible or absent in all patients during TDF lead-in and in the control group to date. In patients having completed 12 weeks of NAP exposure, 4 / 5 receiving REP 2139-Mg and 4 / 6 patients receiving REP 2165-Mg have experienced multilog reductions in serum HBsAg and increases in serum anti-HBs. Two patients in the REP 2139-Mg group experienced multilog drops after only 4 weeks. An additional REP 2165-Mg patient (a 5th responder in this group) has also experienced a multilog HBsAg drop after 4 weeks of exposure. NAP-mediated HBsAg reductions are accompanied by otherwise asymptomatic ALT / AST / GGT flares substantially greater than those in the control group.

These preliminary data demonstrate the tolerability and efficacy of REP 2139 and REP 2165 when used in combination with peg-IFN and TDF in patients with HBeAg negative chronic HBV infection. Early clearance in serum HBsAg mediated by NAPs is correlated with the onset of an intense transaminase flare and suggests NAP-mediated HBsAg clearance improves the efficacy of peg-IFN in this patient population.

(No Image Selected)

Financial Conflict of Interest: Michel Bazinet: Yes conflict of interest; Replicor Inc.: Employment; Replicor Inc.: Board Membership; Replicor Inc.: Management Position; Replicor Inc.: Stock Shareholder; Replicor Inc.: Patent Held/Filed | Victor Pantea: No conflict of interest | Gheorghe Placinta: No conflict of interest | Iurie Moscalu: No conflict of interest | Valentin Cebotarescu: No conflict of interest | Liviu Iarovoi: No conflict of interest | Valentina Smesnoi: No conflict of interest | Tatiana Musteata: No conflict of interest | Alina Jucov: No conflict of interest | Adalbert Krawczyk: No conflict of interest | Andrew Vaillant: Yes conflict of interest; Replicor: Stock Shareholder; Replicor: Employment