Updated follow-up analysis in the REP 401 protocol: Treatment of HBsAg negative chronic HBV infection with REP 2139-Mg or REP 2165-Mg, tenofovir disoproxil fumarate and pegylated interferon alfa-2a

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INTRODUCTION
HBV subviral particles (SVPs) contribute more than 99.9% of circulating HBsAg and act to block immune control of HBV infection. The nucleoside polymer (NAP) REP 2139 blocks the assembly and release of SVP derived from cccDNA and integrated HBV DNA, allowing the efficient treatment of chronic HBV. This trial followed the treatment of patients with HBV genotype B and C with tenofovir disoproxil fumarate (TDF). The study compared the assembly and release of SVP derived from cccDNA and integrated HBV DNA, allowing the efficient treatment of chronic HBV. This trial followed the treatment of patients with HBV genotype B and C with tenofovir disoproxil fumarate (TDF) and pegylated interferon (PEG). The REP 2139 protocol (MCT-0050) is a randomized controlled trial assessing the safety and efficacy of the lead NAP compound (REP 2139) and a derivative with enhanced tissue clearance (REP 2165) in combination with tenofovir disoproxil fumarate (TDF) and pegylated interferon alfa-2a (PEG) in patients with chronic HBV negative HBV infection.

METHODS
Twenty-four weeks of treatment (TDF 300mg PO qd) was followed by rechallenge (TDF 300mg PO qd + interferon 1.5 mu/twice weekly for 24 weeks). Treatment response was assessed after 24, 48, 72, and 96 weeks of treatment, and patients with a 2-log drop in HBsAg after 24 weeks were eligible to receive Peg-IFN (figure below). Patients are monitored at the Abbott Architect and Baseline platforms.

RESULTS
HBV subviral particles (SVPs) contribute more than 99.9% of circulating HBsAg and act to block immune control of HBV infection. The nucleoside polymer (NAP) REP 2139 blocks the assembly and release of SVP derived from cccDNA and integrated HBV DNA, allowing the efficient treatment of chronic HBV. This trial followed the treatment of patients with HBV genotype B and C with tenofovir disoproxil fumarate (TDF). The study compared the assembly and release of SVP derived from cccDNA and integrated HBV DNA, allowing the efficient treatment of chronic HBV. This trial followed the treatment of patients with HBV genotype B and C with tenofovir disoproxil fumarate (TDF) and pegylated interferon (PEG). The REP 2139 protocol (MCT-0050) is a randomized controlled trial assessing the safety and efficacy of the lead NAP compound (REP 2139) and a derivative with enhanced tissue clearance (REP 2165) in combination with tenofovir disoproxil fumarate (TDF) and pegylated interferon alfa-2a (PEG) in patients with chronic HBV negative HBV infection.

CONCLUSIONS
• 48 weeks of REP 2139-Mg and REP 2165-Mg used in combination with TDF and pegIFN is safe and well tolerated in patients with HBsAg negative chronic HBV infection and uniquely achieve reduction or loss of HBsAg and HBsAb seroconversion in a high proportion of patients.
• In patients receiving the lead clinical therapy (upfront combination with REP 2139-Mg, pegIFN and TDF, response rates for achieving functional remission (HBV DNA < LLOQ) and functional repression (HBV DNA < 1000 IU/mL) were 60% and 80% respectively.
• Despite the use of suboptimal regimens where NAPs were added following 24 weeks of TDF + pegIFN or using the more stable REP 2165-Mg, rates of functional remission and functional repression were still 65% and 75% respectively (in patients completing treatment and 12 weeks of follow-up).
• Functional remission is highly correlated with HBsAg reduction ≥ 2 log from baseline during therapy.
• In seven patients, control of HBV DNA (< LLOQ) is currently maintained in the absence of antiviral therapy when anti-HBsAg is < 10 mIU/mL, suggesting the establishment of control of cccDNA in these patients.
• Introduction of other immunotherapies in place of pegIFN (thymosin alpha 1, TLR agonists or therapeutic vaccines) may further improve response rates.

REFERENCES

DISCLOSURES
MB and AV are employees and shareholders in Replicor Inc.