**OBJECTIVE AND PRODUCT DESCRIPTIONS**

Evaluation of the potentiation of TG1050 activity by combining with immunomodulators or direct acting antivirals

**IMMUNOTHERAPEUTIC**

**TG1050** (Transgene SA) is based on a recombinant non-replicative adenovirus 5 vector encoding for truncated Core, an almost full-length polymerase and domains of Envelope.

It is in clinical development (PhI). In preclinical models TG1050 demonstrated the induction of functional HBV-specific T cells and an antiviral effect by decreasing both HBV viremia and circulating HBsAg.

**IMMUNOMODULATORS**

CpG-28 (Oligovax) is a class B CpG ODN. TLR9 agonists are well described as adjuvant of vaccination and have been shown to favor intrahepatic T cell proliferation.

Sildenafil is a PDE5 inhibitor, interfering with the inhibitory functions of MDSC. MDSCs have been detected in the liver of CHB patients in high frequency.

**DIRECT ACTING ANTIVIRALS**

siRNA-HBV (Abylnym Pharmaceuticals, licensed to Vir Biotechnology) is a GalNAc conjugated siRNA targeting one highly conserved sequence (silencing all viral products).

HEC73045 (HEC Pharma) is a 2nd generation capsid inhibitor (CpAM). CpAM treatment inhibits HBV encapsidation and decreases HBV viremia and HBV-RNA secretion.

Entecavir (ETV) is a standard care HBV polymerase inhibitor.

**HBV PERSISTENT MODEL**

AAV-HBV\(^{10}\) L.V. 5\(^{10}\) vg

Liver

HBV replication intermediates

HBcAg

Blood

HBV virions

HBsAg

HBV RNA

AAV-HBV: 5\(^{10}\) vg

CpG-28

siRNA-HBV

HEC73045

ABSENCE OF DETECTED HBV

HBsAg

HBV RNA

HBV replication

HBcAg

**CONCLUSION**

- Combination of TG1050 with 3 different types of drugs led to encouraging improvements of antiviral effects:
  - TLR9 agonist, MDSC inhibitor, siRNA
  - To be further evaluated in clinical trials

**ACKNOWLEDGEMENTS**

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9. AAV = Adeno-associated virus
10. GalNAc = N-acetylgalactosamine
11. LLOQ = Lower limit of quantification
12. MDSC = Myeloid-derived suppressor cell
13. ODN = Oligodeoxynucleotide
14. PEG – Polyethylene glycol 5
15. TLR – Toll-like receptor