Viral superinfection: clinically proven host-directed treatment platform for acute and persistent HBV (DNA) and HCV (RNA) infections
Emergency remedy to emerging viral diseases

FACTS SHEET AT A GLANCE

- Targeting host cell functions by an apathogenic double stranded RNA virus potent activator of antiviral gene responses
- Proof-of-principle clinical trials in unrelated DNA and RNA viral diseases
  - Safe and effective in 20 acute HBV and 22 acute HCV patients
  - Safe and effective in decompensated (CTP C) hepatitis (2 HBV and 2 HCV)
  - Does not require life-long treatment in HBV patients
- Revenue potential >€7 billion
- Extensive intellectual property

PROJECT OBJECTIVES

Hundreds of viruses are known to cause human disease, but antiviral therapies are approved only for a few. We focus on finding a cure for viral diseases with unmet needs, which is unlikely to be met solely by the prevailing “one drug, one bug” drug-development approaches. The company is developing a clinically tested innovative therapy: hepatitis patients are superinfected by the apathogenic dsRNA avian infectious bursal disease virus (IBDV). IBDV superinfection is a host-directed approach (1) because it stimulates the native immune system of the host by activating its interferon-dependent antiviral gene program. Since interferon is active against most vertebrate-infecting viruses, superinfection therapy (SIT) could be developed into the first technological platform, which will be registered for the “one drug, multiple bugs” treatment approach of viral diseases (2). A conventionally produced virus has been effective against a DNA virus (HBV) and an RNA virus (HCV). Our primary goal is to conduct a First-in-human (FIH) safety and dose finding clinical trial because our new drug candidate (R903/78) is now produced by reverse genetics complying with FDA and EMA requirements for constancy. SIT rapidly diminish viral loads in HBV (DNA) and HCV (RNA) infections and does not require life-long treatment in HBV patients. The SIT platform technology could alleviate the logistic hurdles of surge capacity in vaccine production and thus contribute to global health protection and national security preparedness against several acute and chronic viral infections like Ebola, Dengue, Yellow fever etc. Therefore, we will propose its fast track development within the PRIME program of EMA for the post-infection treatment of HBV/HCV infections.

TECHNOLOGY

Manufacture of IBDV is probably one of the simplest and most cost effective for a biological drug requiring only filtration technology. Regulatory requirements are further simplified as it is an oral biological. Costs can be further substantially reduced as the same drug can be used against several acute and chronic virus infections including important pandemic targets.

CLINICAL STUDIES

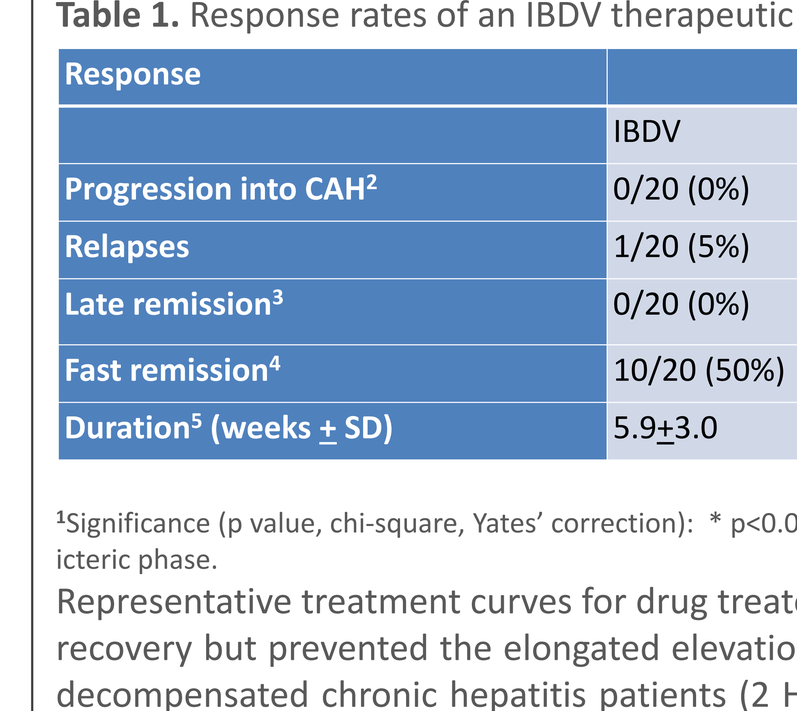
The safety and efficacy of SIT was reported in 42 acute hepatitis patients (20 HBV and 22 HCV) in a preliminary clinical trial using a conventionally produced IBDV drug substance (3) (Table 1).

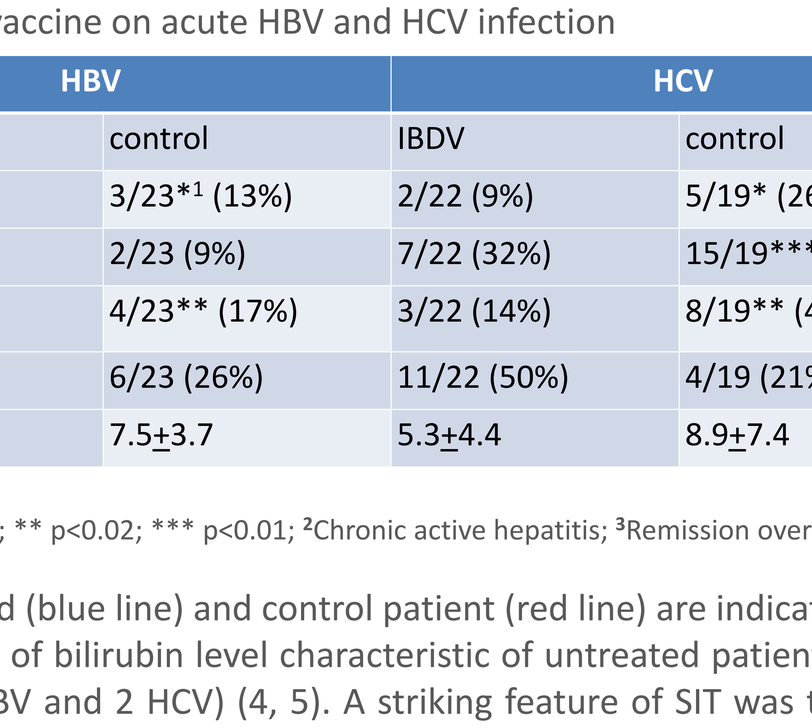
Table 1. Response rates of an IBDV therapeutic vaccine on acute HBV and HCV infection

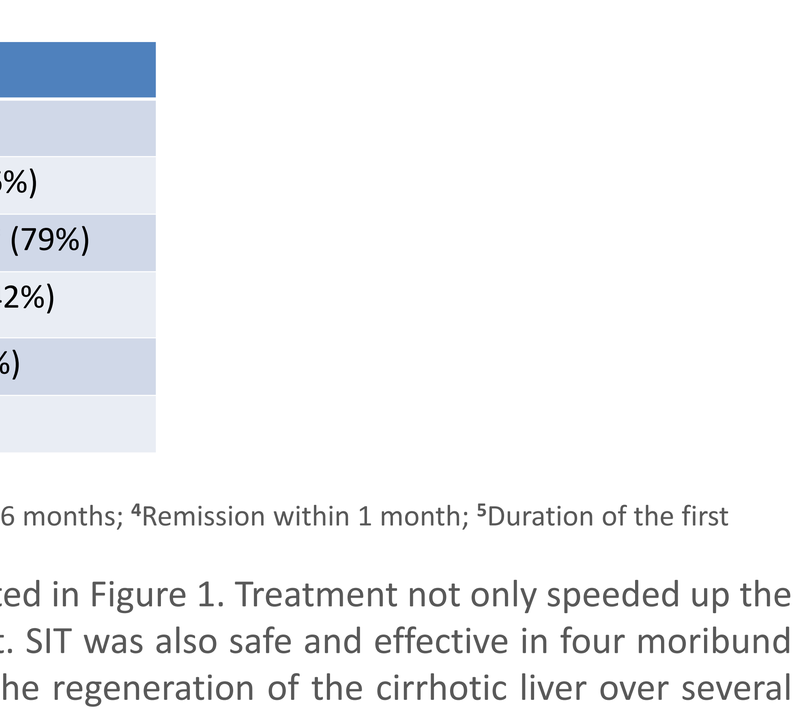
Response	HBV		HCV	
	IBDV	control	IBDV	control
Progression into CAH[2]	0/20 (0%)	3/23*[1] (13%)	2/22 (9%)	5/19* (26%)
Relapses	1/20 (5%)	2/23 (9%)	7/22 (32%)	15/19*** (79%)
Late remission[3]	0/20 (0%)	4/23** (17%)	3/22 (14%)	8/19** (42%)
Fast remission[4]	10/20 (50%)	6/23 (26%)	11/22 (50%)	4/19 (21%)
Duration[5] (weeks ± SD)	5.9±3.0	7.5±3.7	5.3±4.4	8.9±7.4

[1]Significance (p value, chi-square, Yates’ correction): * p<0.05; ** p<0.02; *** p<0.01; [2]Chronic active hepatitis; [3]Remission over 6 months; [4]Remission within 1 month; [5]Duration of the first icteric phase.

Representative treatment curves for drug treated (blue line) and control patient (red line) are indicated in Figure 1. Treatment not only speeded up the recovery but prevented the elongated elevation of bilirubin level characteristic of untreated patient. SIT was also safe and effective in four moribund decompensated chronic hepatitis patients (2 HBV and 2 HCV) (4, 5). A striking feature of SIT was the regeneration of the cirrhotic liver over several years of follow up (Figure 2). No significant therapy associated toxicity was reported. Expression levels of several interferon-related genes increased in the liver tissue of mice following intravenous IBDV injection. IRF7 gene expression can be seen in Figure 3.







The Company believes that its lead drug candidate R903/78, which is now homogeneously produced by reverse genetics (6), will be the first drug to receive regulatory approval employing the novel SIT concept because of its superior delivery characteristics, its safety profile and its efficacy for clinical applications with unmet medical need (7). HepC currently is focusing on two key niche populations making use of its IBDV technology: (a) treatment of decompensated HBV/HCV patients on the liver transplant waiting lists (Lead product HC001); (b) treatment of chronic HBV within a finite course (Lead product HC001). Since the same drug candidate is targeting two different patient populations and disease indications, respectively, separate clinical trials will be needed.

MARKET OPPORTUNITY

The estimated market sizes for our leading drug HC001 in two different niche populations:

1. **Advanced HBV/HCV patients**: approx. 34 million in the EU, USA, Japan and Russia, who cannot be safely treated by conventional therapy. Using only around 10% of this market segment, HepC aims to initially treat the 3,400 million patients who are the total potential users of IBDV therapy in EU, USA + Japan + Russia (Lead Drug, HBV, HCV).
2. **Chronic HBV patients**: 35 million HBV patients are expected to die of HCC over the coming 15 years (until 2030) (8); to prevent these HCC deaths, HepC will aim to treat approx. 3% of this market, thus 1 million HBV patients who live in the US and in the EU only.

Applying an estimated reasonable pharmaceutical royalty revenue share of 10% on HepC's lead (HC001) candidate on a Gross Profit basis, **will generate a revenue potential of well over €7 billion over the expected life of the drug candidate of 25 years.**

SIT will be able to:

- **delist advanced decompensated HBV/HCV patients from liver transplantation waiting lists**
- **provide cure in chronic HBV patients without life-long treatment**
- **prevent HCC mortality by eliminating the carcinogenic cccDNA of HBV**
- **treat HCV patients, who had reached the "point of no return"**
- **treat HCV in HBV/HCV co-infected patients without reactivation of HBV**
- **improve fragile liver function in HBV or HCV positive advanced HCC patients**
- **reduce morbidity and mortality of arbovirus infected patients**

VALUE PROPOSITION

According to a standard financial cash flow forecast model, HepC's management believes the Company has a current Enterprise Value of approximately EUR 14.8 million. However, having completed the planned FIH safety and dose finding clinical trial, the indication of SIT will be extended to less severe chronic HBV infection such that the future Enterprise Value may increase up to approximately EUR 41 million. This value was derived by projecting expected cash flows out 13 years (with no Terminal Value), using an estimated large pharmaceutical royalty revenue share agreement on HepC's lead drug candidate (HC001; Hepatitis) in years 8-13 on a Gross Profit basis (using projected estimated Cost of Production analyses). Expected R&D and G&A expenses were also projected. Consistent with the Venture Capital method of valuing private early stage enterprises, future expected cash flows were discounted with a 50% discount rate.

Venture Financing

HepC is seeking a Staged Venture Financing from potential VC Partner Investors as follows:

1st Round Venture Financing in 2018 (€ 2 to € 4 million)

2nd Round Venture Financing in 2019/2020 (€ 5 to € 10 million)

Use of Proceeds

Our strategy is to complete a Phase I/II chronic hepatitis clinical trial in the shortest possible timeframe and conclude a corporate partnership on this product candidate. On the longer timeframe we will seek approval for liver cancer product while pursuing other applications.

Exit Strategy

Sale the lead drug to a large pharmaceutical company or sale of majority equity stake in HepC Inc.

Proprietary Position

HepC has issued US patent (No. 8,398,969) and issued patent in EU (No. EP2101797) for composition and methods on the IBDV technology. There are claims related to treatment of viral hepatitis, but the invention also provides claims to treat other viral infections not related to viral hepatitis. HepC has collaborated with a German CMO, Vibalogics (www.vibalogics.com) to develop proprietary manufacturing and assay process and also has a corporate partnership in the USA for research and development.

FORE MORE INFORMATION

Hungary Business Office:
Tamás Bakács, MBA
Chief Executive Officer
Miko u. 3. II. em. 11. ,1012 Budapest, HU
Tel: +36-30-688-1121
Email: tabakacs@hepcinc.com

USA Business Office:
Imre Kovesdi, Ph.D.
COO & Partner
7713 Warbler, Rockville, MD, 20855, USA
Tel: +1-301-963-1641
Fax: +1-240-238-2741
Email: ikovesdi@hepcinc.com

Company overview (www.hepcinc.com)

HepC, Inc. is a privately-held biotechnology firm which is based in Budapest, Hungary, and Rockville, MD in the USA. The company was founded as an Ltd in 2005 and converted to incorporation in 2014. HepC is focused on the development and commercialization of antiviral biologic products for the treatment of advanced chronic HBV/HCV infections with unmet needs and for the adjuvant therapy of HBV/HCV positive HCC with fragile liver function

References

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