

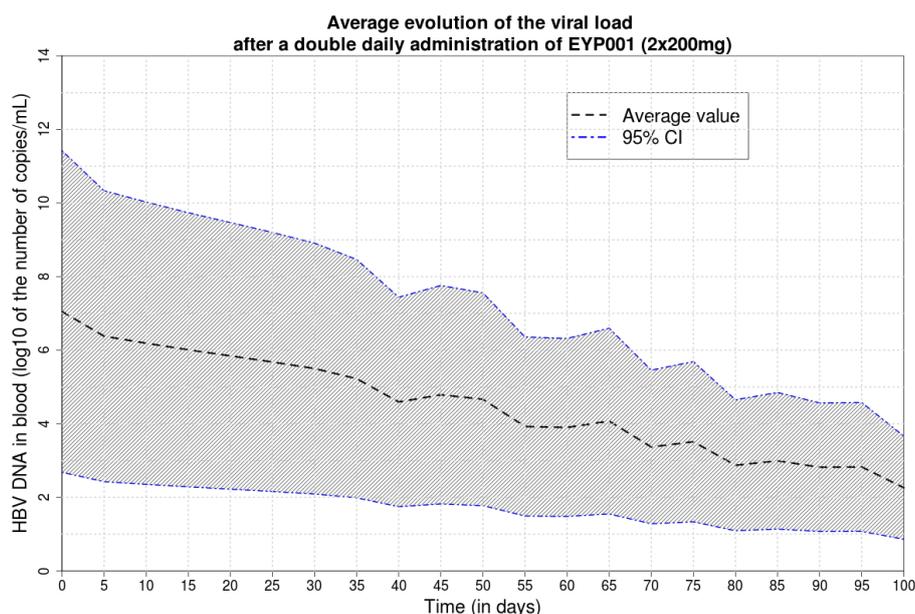
PAGE 2018 MEETING: AN *IN SILICO* MODEL OF HEPATITIS B VIRUS PREDICTS PATIENTS RESPONSE TO ENYO PHARMA'S DRUG CANDIDATE EYP001

- **NOVADISCOVERY presents first results from the *in silico* component of the exploratory clinical program initiated by ENYO Pharma on EYP001, a non-bile acid FXR receptor agonist currently in phase 1b trial for the treatment of chronic Hepatitis B.**
- **Applying NOVADISCOVERY's WISE® technology platform, the *in silico* model successfully reproduces the pharmacokinetics & pharmacodynamics of EYP001.**
 - **The study further anticipates the best dose for optimum antiviral response.**
- **These first results will be presented at the PAGE 2018 in Montreux, Switzerland.**

Lyon, May 16th, 2018 - NOVADISCOVERY, a pioneer in *in silico* medicine, today announces that its *in silico* model and first analysis of the effect of EYP001 treatment on Hepatitis B virus (HBV) infected patients will be presented at the Population Approach Group in Europe (PAGE) Meeting, May 29th – June 1st, 2018, Montreux, Switzerland.

EYP001 is a synthetic non-bile acid Farnesoid X-receptor (FXR) agonist currently under clinical development by ENYO Pharma for chronic HBV infection. Following on a collaboration agreement signed with ENYO Pharma, NOVADISCOVERY has built a mathematical disease model to simulate the effect of the compound on HBV-infected virtual patients. NOVADISCOVERY has applied its proprietary **WISE®** technology platform (**Whitebox In Silico Engine**), an open ecosystem that combines the company's expertise in modeling and simulation. The two-step process has involved building a model using the literature-based, community-driven knowledge management platform **GitHealth** (<https://githealth.io>) by integrating bile acids physiology, cholesterol metabolism, HBV replication and EYP001 mode of action (MoA), the latter based on non-clinical data. The **SimWork®** simulation platform was then used to implement and calibrate the model, before testing by a team blinded to clinical EYP001 data on a large cohort (10,000 HBV infected virtual patients).

The resulting model successfully reproduced the pharmacokinetic (plasma concentration and time profiles) and pharmacodynamic (viral particles in the blood and FXR engagement as evidenced by FGF19 - Fibroblast Growth Factor 19 - and C4 - 7αhydroxy-4-cholesten-3-one - dynamics) profiles of EYP001. In addition, the model anticipates that prolonged, but not short-term treatment with the compound results in viral replication inhibition, and establishes the dose regimen of 200mg EYP001 twice daily for optimal response.



*“Our approach relies on the use of two complementary platforms. GitHealth allows curated extraction of knowledge from white and grey scientific literature to build a complete mechanistic model that includes physiological and pathological knowledge as well as non-clinical data on the mode of action of the drug candidate. SimWork® then calibrates the model using virtual populations whose characteristics are within the constraints dictated by biology, before simulating the effect of the compound on these virtual patients”, explains **Dr. Claudio MONTEIRO-SOUSA, bio-modeler at NOVADISCOVERY and project manager leading this work.** “In HBV, we were not only capable of replicating in silico the clinical profile of EYP001 using our WISE® platform, but we also predict the optimal dose regimen and length of treatment to achieve maximum antiviral response”.*

*“These are extremely encouraging results in the framework of our exploratory clinical program in HBV: we now have solid proof that the in silico approach developed by NOVADISCOVERY can predict clinical data, strengthening the value of our ongoing collaboration”, says **Dr. Jacky VONDERSCHER, CEO of ENYO Pharma.** “Now we can build on their new findings to better design our clinical studies. For instance, we can use their model to identify best responders in the population and assist on the future design of a phase II clinical trial. Given the complexity of such trials, the financial and human challenges and the inherent limits of our knowledge, in silico modelling and simulation will most certainly become mandatory as a directing line in clinical studies”.*

*“Our partnership with ENYO Pharma started less than a year ago, and yet we have already managed to produce a robust model for the use of EYP001 in HBV. This testifies on the power of our in silico methodology and our technology platform, which allies raw performance, interpretability and resistance to overfitting, key machine learning features here at the service of medicine. These very positive results will open the way to many more to come in the context of several other ongoing collaborations”, concludes **François-Henri BOISSEL, CEO and co-founder of NOVADISCOVERY.***

The accepted abstract for the PAGE 2018 Meeting is available at:
<https://www.page-meeting.org/default.asp?abstract=8471>

About NOVADISCOVERY

Pioneer of *in silico* medicine, NOVADISCOVERY improves R&D productivity and maximizes patients' chances by predicting new drugs clinical benefits by computer simulation long before human trials.

NOVADISCOVERY's innovative approach combines mathematical models of diseases and treatments with virtual patients in an open and scalable technological ecosystem called WISE® (Whitebox In Silico Engine), which brings together all the modeling and simulation expertise of the company.

Headquartered in Lyon, France, NOVADISCOVERY relies on the Effect Model, a novel methodology discovered by Pr. Jean-Pierre BOISSEL, one of the founding fathers of systems medicine. The company has a team of scientists, engineers & clinicians who work at the interface of systems biology, pharmacology, meta-analysis, mathematics & computer sciences.

More information at www.novadiscovery.com and @novadiscovery

About ENYO Pharma

ENYO Pharma is a clinical stage biotechnology company headquartered in Lyon (France). Its innovative drug discovery engine is inspired by the strategy used by viruses to hijack the intracellular machinery of the infected host. ENYO Pharma's approach focuses on the understanding of virus-host protein interactions to subsequently derive small molecules mimicking how such viral proteins modulate human targets. The company is currently specialized in infectious and metabolic diseases with a focus on Hepatitis B and NASH.

More information at www.enyopharma.com

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