ENYO Pharma Announces 16 Weeks Vonafexor (EYP001) Top-Line Interim Results from Two on-going Phase 2a Studies in Chronic Hepatitis B Patients

– Vonafexor is the first oral treatment to reduce HBsAg an average of -1.0 log_{10} after 16 weeks when administered in combination with peg-IFN in viremic, HBeAg negative, CHB patients –

– Vonafexor was safe and well tolerated –

Lyon, France., July 30, 2021 - ENYO Pharma (ENYO), a private clinical stage biotechnology company developing innovative drug candidates, today announced positive proof of concept data from Study EYP001-203 of Vonafexor in combination with pegylated-Interferon (peg-IFN) in viremic patients with chronic hepatitis B (CHB). Vonafexor met the primary endpoint of lowering HBsAg by an average of ≥ 1 log_{10}, a key biomarker of viral activity in the liver, after 16 weeks of treatment. These results in CHB patients are further positive news for Vonafexor, after the recent disclosure of strong positive clinical results in Non-Alcoholic Steato-Hepatitis (NASH) patients on July 28, 2021.

In the EYP001-203 Phase 2a trial, 20 subjects with CHB were randomized 1:1 to receive oral, once-daily Vonafexor at 200 mg in combination with 180 µg peg-IFN subcutaneous injection weekly and also with or without oral once-daily 0.5 mg Entecavir for 16 weeks. The subjects were thereafter maintained for the next 24 weeks on oral, once-daily 0.5 mg Entecavir only.

The study results clearly discriminated between those subjects who were HBeAg negative (n=13) and who significantly responded to Vonafexor plus peg-IFN treatment and those who were HBeAg positive (n=7) who did not respond. Established data on CHB patients confirm that more and more patients are HBeAg negative (>80% currently) as a consequence of the chronic evolution of their disease.

Subjects negative for HBeAg (n=13) had a mean HBV-DNA baseline level of 4.6 log_{10} IU/mL and a mean HBsAg baseline level of 3.1 log_{10} IU/mL compared to HBV-DNA level of 7.8 log_{10} IU/mL and HBsAg level of 4.2 log_{10} IU/mL for subjects positive for HBeAg (n=7).

In HBeAg negative subjects, HBsAg was reduced by -1 log_{10} IU/mL compared to baseline after 16 weeks of dual regimen Vonafexor/peg-IFN, while the reduction was only -0.6 log_{10} IU/mL compared to baseline after triple regimen Vonafexor/peg-IFN/Entecavir. Three out of 13 subjects had a reduction of HBsAg greater than -1 log_{10} IU/mL after 16 weeks of either dual or triple regimens with 2 out of 13 subjects achieving levels of HBsAg lower than 100 IU/mL.
At week 20 (1 month after stopping the Vonafexor/peg-IFN treatment), 5 out of 12 subjects had a reduction of HBsAg greater than -1 log_{10} IU/mL with all of these patients achieving levels of HBsAg lower than 100 IU/mL..

In addition, the viremia measured by HBV-DNA decreased rapidly in HBeAg negative subjects to reach levels close to or below the Lower Limit Of Quantification (LLOQ of 20 IU/mL) for both dual and triple regimens.

Vonafexor was safe and well tolerated. Some good Alanine Aminotransferase (ALT) / Aspartate Aminotransferase (AST) flares were observed concomitantly with the decrease of HBV-DNA and HBsAg in 4 out of 10 subjects for the dual regimen combination Vonafexor/peg-IFN and in 8 out of 10 subjects for the triple regimen combination Vonafexor/peg-IFN/Entecavir but these were not associated with an increase of any other liver biomarkers. Mild, transient grade 1 and localized pruritus was observed in some subjects but did not result in discontinuation or withdrawal from the study.

"We were very pleased to obtain these exciting results of Vonafexor in combination with the immune modulator Interferon, in previously untreated and viremic HBeAg negative patients. The results are very encouraging for two reasons: first, the decline seen in HBsAg, reaching an average of -1 log_{10} is 2 to 3 times greater than what is reported historically with interferon alone, especially in the patients studied who had significant high HBsAg plasma levels at the start of treatment ranging from 340 to 7,050 IU/mL and were therefore a difficult to treat population; And secondly, all subjects had complete viral suppression in less than half of the time needed by usual mono treatment regimens of peg-IFN and/or Nucleot(-s)ides" **explained Pietro Scalfaro, MD, ENYO's Chief Medical Officer.**

"In CHB HBeAg negative subjects, Vonafexor combined with peg-IFN induced a rapid, early and significant HBV-DNA decline which translated to its suppression in all 12 subjects after only a few weeks of treatment and 100% of subjects had HBV-DNA levels below LLOQ between weeks 16 and 20. In addition the -1.0 log_{10} HBsAg reduction seen at week 16 supports further assessment of Vonafexor for its potential to improve functional cure rates with longer treatment duration" **commented Prof. Chao-Wei Hsu, MD, Investigator of the trial and Director of Hepatology at Chang Gung Memorial Hospital in Taiwan.**

Part of these results were already presented at the recent EASL meeting but more detailed results of this study will be submitted for presentation at a scientific conference in Fall this year.

In the second Phase 2a study reported today (EYP001-201) 26 virally suppressed patients with CHB already receiving chronic daily Nucleot(-s)ides treatment were randomized 2:1 to receive oral, once-daily Vonafexor at 200 mg or Placebo for 16 weeks. The subjects were then maintained for an extra 24 weeks on oral once-daily 0.5 mg Entecavir.

A recent interim analysis conducted by the DSMC (Drug Safety Monitoring Committee) for this study concluded that Vonafexor was well tolerated and safe (no ALT/AST flares were observed) but there was no apparent efficacy benefit of Vonafexor with Entecavir in these virally suppressed CHB patients. Therefore, no additional subjects are being recruited in this trial. These data are somehow consistent with the EYP001-203 study where the triple regimen including Entecavir was apparently less efficacious than the dual regimen without Entecavir.

"These results help us further define the CHB patient population for whom Vonafexor can produce the greatest benefit, namely viremic CHB patients when combined with an immune-modulator as seen in Study 203. We have pre-clinical data to support the synergy of Vonafexor with peg-IFN which suggest that Vonafexor is enabling the innate immune response necessary to help HBeAg negative patients move towards a functional cure" **said Pietro Scalfaro, MD, ENYO's Chief Medical Officer.**

"The results of the 203 trial for Vonafexor in combination with Interferon are very encouraging as HBeAg negative patients represent more than 80 % of the CHB patient population. They fully support the continued development of Vonafexor in this population in combination with peg-IFN and we are working on the design of pivotal regulatory studies, including potential combination studies of Vonafexor with therapeutics having other mechanisms of action to maximize the benefit of such treatments for CHB patients." **added Jacky Vonderscher, PhD, co-founder and Chief Executive Officer of ENYO.**

About Chronic Hepatitis B (CHB)

According to the WHO, more than 350 million people are chronically infected with the hepatitis B virus worldwide, half of them in Asia. Despite advances in mass vaccination, an estimated 300 million people will still be chronically infected by 2030, putting them at high risk of developing cirrhosis and liver cancer. The therapies currently approved for the treatment of Hepatitis B (peg-Interferon and Nucleot(-s)ides like Tenofovir or Entecavir) effectively suppress the presence of the virus in the blood, but rarely cure patients, as the virus continues its deleterious course in the liver cells of these patients into which it has integrated its cccDNA.

About Vonafexor (EYP001)

Vonafexor is a synthetic non-steroidal, non-Bile Acid, highly selective FXR agonist orally bioavailable with preferential liver distribution and sustained target engagement that is currently in Phase II clinical development for the treatment of Chronic Hepatitis B (CHB) and of Non-Alcoholic Steato-Hepatitis (NASH).

The ENYO founding team discovered that FXR agonists interfere with interactions between FXR and HBx, a hepatitis B viral protein essential for virus replication. Current treatments are lifelong and control viral replication, which does not allow total cure of the disease. Vonafexor targets cccDNA, the reservoir for the virus, and works synergistically with peg-IFN to boost the innate immune system and has the potential to deliver functional cure for the disease compared to existing treatments.

FXR agonists have gained attention as potential therapeutic agents in hepatobiliary and metabolic diseases. FXR activation has a favorable effect on liver growth and regeneration and has been shown to prevent and resolve liver fibrosis and steatosis in rodents and humans. FXR has multiple activities and regulates several metabolic pathways. In particular, it controls the homeostasis of bile acids in the liver and intestine, it influences the insulin sensitivity of tissues where it is highly expressed and impacts upon lipid metabolism.

About ENYO Pharma

ENYO Pharma is a privately held, clinical stage biopharmaceutical company incorporated in January 2014 and headquartered in Lyon, France. The Company's most advanced compound, Vonafexor (EYP001), is a small molecule (non-Bile Acid FXR agonist) therapeutic in Phase II clinical development for the treatment of Chronic Hepatitis B and NASH. EYP001 and the Company's discovery programs are based on a proprietary technology platform that uses a virus bio-mimetic approach to enable the rapid discovery of first-in-class drug candidates with good safety profiles. ENYO's founders are a mix of virus-host protein interactions experts from the French Infectiology Research Center in Lyon and pharmaceutical industry executives with an impressive track record in drug development. For more information on ENYO and EYP001, please visit http://www.enyopharma.com/.

# # # #

Contacts:
Investor Relations:
Tel: +33 (0)4 37 70 02 27
communication@enyopharma.com

Media Relations:
Annie-Florence Loyer, NewCap Media
+33 (0)1 44 71 00 12/ +33 (0)6 88 20 35 59
afloyer@newcap.fr