ENYO Pharma Announces Positive Vonafexor (EYP001) Results for the LIVIFY Phase 2a Study in F2-F3 NASH Patients over 12 weeks

– Key primary and secondary endpoints were met demonstrating a robust impact on NASH –

– Vonafexor was safe and well tolerated –

– Vonafexor is the first FXR agonist showing improvement of renal function over 12w treatment –

Lyon, France., July 28, 2021 - ENYO Pharma (ENYO), a private clinical stage biotechnology company developing innovative drug candidates, today announced that Vonafexor met the primary and several secondary endpoints in the LIVIFY clinical study conducted in F2-F3 Non Alcoholic Steato-Hepatitis (NASH) patients.

In this Phase 2a trial, 96 patients with NASH were randomized 1:1:1 to receive oral, once-daily Vonafexor at 200 mg or 100 mg, or placebo. The results show that Vonafexor met its primary endpoint of lowering liver fat content as measured by MRI-PDFF (Magnetic Resonance Imaging – Proton Density Fat Fraction), with absolute reductions of 6.3 % in the 100 mg cohort and 5.4 % in the 200 mg cohort, compared with 2.3 % in the placebo cohort ($p<0.001$); this led to mean relative reductions of 30.5 % in the 100 mg cohort and 25.3 % in the 200 mg cohort, compared with 10.6 % in the placebo cohort ($p<0.001$). There were no significant differences in efficacy endpoints between the 100 mg and the 200 mg Vonafexor treatment groups.

<u>The following notable results were observed for the 100 mg treatment group at week 12:</u>

- Vonafexor treatment achieved a 5 % or greater, absolute liver fat reduction in 58 % of patients compared with 22 % in the placebo cohort ($p<0.001$), and a 30 % or greater relative liver fat reduction in 50 % of patients compared with 13 % in the placebo cohort ($p<0.05$), a threshold which has been associated with higher odds of histologic response and NASH resolution (Stine JG, Clin. Gastro. and Hepatology, 2020).
- Vonafexor treatment achieved a mean absolute reduction of cT1 (Liver Multiscan® Fibro-Inflammation Marker iron corrected T1) of 79 msec compared to 10 msec in the placebo arm ($p<0.001$); 36 % of Vonafexor treated patients had a reduction greater than 88 msec, a difference which has been reported to correlate with 2-point lower NAS score (Dennis A, Front. Endocrinol., 2021).
- Vonafexor treatment achieved a 42 % mean reduction in GGT (Gamma Glutamyl-Transferase, a biomarker of liver injury) vs 8 % for placebo ($p<0.001$). This reduction was achieved very quickly and was kept during the entire treatment period.
- Vonafexor treatment achieved a 20 % mean reduction in ALT (Alanine Amino-Transferase) vs 12 % for placebo. 52 % of Vonafexor treated patients reached an ALT reduction of > 17 IU/L compared to 25 % for placebo ($p<0.05$). This cut-off is often considered as a strong predictor of histological NAS score improvement of 2 points (Loomba R., Gastroenterology, 2019).

- Vonafexor treatment achieved a significant mean improvement in eGFR (estimated Glomerular Filtration Rate) of +5.6 mL/min/1.73 m2 compared to baseline while patients receiving placebo had a decrease in eGFR of -2.8 mL/min/1.73 m2. 76 % of the patients receiving Vonafexor had improved kidney function as measured by eGFR over 12 weeks while 66 % of patients receiving placebo had deterioration of kidney function over the 12 week study period[1)].
- Vonafexor treatment has also shown a significant effect on several other parameters which are usually described as providing metabolic and cardio-vascular morbidity benefits (e.g. reductions in body weight, waist circumference, waist to height ratio, …)
- LDL cholesterol increase was comparable to that seen with other FXR agonists and when deemed clinically appropriate, this was easily managed by the addition of statins.
- Pruritus was observed as for other FXR agonists and was generally mild, transient and localized. Less than 10 % of patients dropped out of the trial due to pruritus.

"The positive results seen on several key non-invasive tests at 12 weeks of dosing are highly encouraging and support advancement of this compound forward in NASH. The additional positive impact on renal function is very interesting and is a potential differentiator in this class of drugs to treat NASH" **commented Prof. Stephen A. Harrison, Principal Investigator for the LIVIFY study and Medical Director of Pinnacle Clinical Research.**

"We were very pleased to obtain these promising results with Vonafexor, which indicate the potential of the product to offer rapid improvements in liver function and liver fat for NASH patients for whom there is no approved therapy. Besides the remarkable effects seen on liver parameters, the improvement in the kidney function of the patients treated with Vonafexor may be highly beneficial for those NASH patients who are often impacted by co-morbidities like diabetes which have significant impact on kidney function" **declared Pietro Scalfaro, MD, ENYO's Chief Medical Officer.**

More results from this study will be submitted for presentation at a scientific conference in fall this year.

"These excellent results fully support the continued development of Vonafexor for NASH 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 NASH patients." **added Jacky Vonderscher, PhD, co-founder and Chief Executive Officer of ENYO.**

1) Data provided by LabCorp have indicated that 64% of NASH patients in USA have a reduced kidney function (eGFR < 90 mL/min/1.73 m2)

About Non-Alcoholic Steato-Hepatitis (NASH)

NASH is a liver disease characterized by excess liver fat, ballooning, inflammation and fibrosis. Millions of people are subjects to this disease which remains silent until signs of liver degradation are noticed. It may progress to liver failure, a life-threatening disease necessitating a liver transplant, and possibly to liver cancer. There is currently no approved therapies for NASH.

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 (cHBV) and of Non-Alcoholic Steato-Hepatitis (NASH).

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, is a small molecule (non-Bile Acid FXR agonist) therapeutic in Phase II clinical development for the treatment of Chronic Hepatitis B and NASH. Vonafexor 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 Vonafexor, please visit http://www.enyopharma.com/.

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