Hepion Pharmaceuticals Announces Clinical Collaboration with HepQuant in Phase 2b NASH Trial

– HepQuant Evaluation Offers Sensitive Measurement of Hepatic Function and Correlation with Clinical Outcomes –

– Dedicated Phase 2b Trial Supports Overarching NASH Program for Rencofilstat –

– Four-Month, Three Arm Trial will Inform on Numerous NASH Functional Biomarkers –

EDISON, N.J., May 03, 2022 — Hepion Pharmaceuticals, Inc. (NASDAQ:HEPA), a clinical stage biopharmaceutical company focused on Artificial Intelligence ("AI")-driven therapeutic drug development for the treatment of non-alcoholic steatohepatitis ("NASH"), Hepatocellular Carcinoma ("HCC"), and other chronic liver diseases, today announced that it has entered into a clinical collaboration with HepQuant, a Denver-based, privately held company with novel, proprietary investigational technology for evaluating liver function and health in patients with chronic liver diseases. Hepion will incorporate the HepQuant 'SHUNT' test into a dedicated Phase 2b clinical trial in presumed NASH F3 subjects, initiating in Q3 of this year.

Hepion will evaluate three doses of rencofilstat (CRV431) in 60 presumed NASH F3 subjects using the HepQuant SHUNT test along with numerous NASH biomarkers collected over four months of once daily oral dosing. HepQuant's SHUNT test may provide a sensitive measurement of hepatic function and is designed to provide detailed information on the role rencofilstat plays in improving the liver health in NASH subjects with advanced fibrosis.

This trial will supplement the Company's larger 12-month Phase 2b NASH clinical trial in biopsy-proven F2/F3 NASH subjects ('ASCEND-NASH'), which will begin in Q3 of this year; and will run concurrently with Hepion's ongoing Phase 2a clinical trial for hepatocellular carcinoma ("HCC").

"Challenges in conducting liver biopsies in NASH clinical programs are well recognized, so we are impressed with the SHUNT test's potential to indicate changes in liver health over short periods of time, and even potentially replace the need for biopsy in NASH trials," commented Todd Hobbs, MD, Hepion's Chief Medical Officer. "The HepQuant SHUNT test will allow us to collect significant data on rencofilstat's impact on hepatic function after a four-month dosing period, much longer than that of our Phase 2a AMBITION trial that was completed last year. We are looking forward to

gaining added confidence in rencofilstat's ability to improve fibrosis in NASH patients as we begin our larger Phase 2b biopsy trial in parallel."

HepQuant's CEO and Chief Medical Officer, Greg Everson, MD commented, "The noninvasive, blood-based HepQuant SHUNT test of liver function and physiology addresses the unmet need for an endpoint that directly quantifies liver health in liver therapeutic trials. In many ways, HepQuant SHUNT is to the liver as creatinine clearance is to the kidney – as HepQuant SHUNT worsens, the likelihood of clinical complications or clinical outcomes of liver disease increases. We have used the test in studies of HCV, HCC, NASH, PSC, cirrhosis; and in interventional trials in HCV, NASH, and HCC. Our research suggests that HepQuant SHUNT could be a useful tool for detecting early treatment effects, dose response, target engagement, and time of onset of action of drugs or treatments."

Robert Foster, PharmD, PhD, Hepion's CEO, commented, "Our mandate at Hepion is to provide answers to transformative questions as quickly as possible. We recognize that our Phase 2b ASCEND-NASH trial will take time to generate results, as we need to account for subject recruitment and subsequent dosing of rencofilstat for 12 months before the final study read-out. In the meantime, however, we believe HepQuant's technology will enable us to determine the impact of rencofilstat on liver function in an expeditious manner, with accelerated clinical read-outs compared with the Phase 2b ASCEND-NASH study. As biopsy studies are a requirement of regulators, Hepion will conduct both the paired biopsy ASCEND-NASH trial and the HepQuant trial simultaneously; the latter providing important answers in a shorter timeframe.

About Hepion Pharmaceuticals

The Company's lead drug candidate, rencofilstat, is a potent inhibitor of cyclophilins, which are involved in many disease processes. Rencofilstat is currently in clinical-phase development for the treatment of NASH, with the potential to play an important role in the overall treatment of liver disease – from triggering events through to end-stage disease. Rencofilstat has been shown to reduce liver fibrosis and hepatocellular carcinoma tumor burden in experimental models of NASH, and has demonstrated antiviral activities towards HBV, HCV, and HDV through several mechanisms, in nonclinical studies. In November 2021, the U.S. Food and Drug Administration ("FDA") granted Fast Track designation for rencofilstat for the treatment of NASH. That was soon followed in December 2021 by the FDA's acceptance of Hepion's investigational new drug (IND) application for rencofilstat for the treatment of hepatocellular carcinoma (HCC).

Hepion has created a proprietary AI platform, called AI-POWR™, which stands for Artificial Intelligence – Precision Medicine; Omics (including genomics, proteomics, metabolomics, transcriptomics, and lipidomics); World database access; and Response and clinical outcomes. Hepion intends to use AI-POWR™ to help identify which NASH patients will best respond to rencofilstat, potentially shortening development timelines and increasing the delta between placebo and treatment groups. In addition to using AI-POWR™ to drive its ongoing NASH clinical development program, Hepion intends to use the platform to identify additional potential indications for rencofilstat to expand the company's footprint in the cyclophilin inhibition therapeutic space.

About HepQuant

Headquartered in Denver, Colorado, HepQuant, LLC, is a privately-held diagnostics company. HepQuant's products are investigational combination drug and in-vitro diagnostic devices and have not yet been evaluated or reviewed by the US Food and Drug Administration (FDA) for commercial sale. They are currently available for investigational use via the FDA guidelines for investigational device exemptions (IDEs). For additional information, visit www.hepquant.com

Forward Looking Statements

Certain statements in this press release are forward-looking within the meaning of the Private Securities Litigation Reform Act of 1995. These statements may be identified by the use of forward-looking words such as "anticipate," "believe," "forecast," "estimated," and "intend," among others. These forward-looking statements are based on Hepion Pharmaceuticals' current expectations and actual results could differ materially. There are a number of factors that could cause actual events to differ materially from those indicated by such forward-looking statements. These factors include, but are not limited to, substantial competition; our ability to continue as a going concern; our need for additional financing; uncertainties of patent protection and litigation; risks associated with delays, increased costs and funding shortages caused by the COVID-19 pandemic; uncertainties with respect to lengthy and expensive clinical trials, that results of earlier studies and trials may not be predictive of future trial results; uncertainties of government or third party payer reimbursement; limited sales and marketing efforts and dependence upon third parties; and risks related to failure to obtain FDA clearances or approvals and noncompliance with FDA regulations. As with any drug candidates under development, there are significant risks in the development, regulatory approval, and commercialization of new products. There are no guarantees that future clinical trials discussed in this press release will be completed or successful, or that any product will receive regulatory approval for any indication or prove to be commercially

successful. Hepion Pharmaceuticals does not undertake an obligation to update or revise any forward-looking statement. Investors should read the risk factors set forth in Hepion Pharmaceuticals' Form 10-K for the year ended December 31, 2021, and other periodic reports filed with the Securities and Exchange Commission.

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