Moving the Needle (literally) in Drug Development

November 30, 2022
Safe Harbor and “Forward-looking Statements”

These materials include “forward-looking statements” within the meaning of the safe harbor provisions of the United States Private Securities Litigation Reform Act of 1995. These statements are based upon the current beliefs and expectations of HepQuant’s management and are subject to significant risks and uncertainties. If underlying assumptions prove inaccurate or risks or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements. HepQuant’s products are not FDA approved and are for investigational use only under an Investigational Device Exemption. These products are not offered for sale to physicians or patients. None of the descriptions of potential uses of the products should be interpreted as a statement that the products are safe or effective for the possible uses discussed.

Risks and uncertainties include but are not limited to, general industry conditions and competition; general economic factors, including interest rate and currency exchange rate fluctuations; the impact of pharmaceutical industry regulation and health care legislation in the United States and internationally; global trends toward health care cost containment; technological advances, new products and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approval; HepQuant’s ability to accurately predict future market conditions; manufacturing difficulties or delays; financial instability of international economies and sovereign risk; dependence on the effectiveness of HepQuant’s patents and other protections for innovative products; and the exposure to litigation, including patent litigation, and/or regulatory actions. HepQuant undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise.
# The Problem of Chronic Liver Disease

## Substantial Need for Better Liver Testing

### STAT
- **Risk Assessment Market**
  - 50 - 130 million Patients
- **Disease Management Market**
  - >15 million Patients

### SHUNT
- **At-Risk for Chronic Liver Disease**
- **Chronic Liver Disease**
- **Non-Cirrhotic Fibrosis**
- **Compensated Cirrhosis**
- ** Decompensated Cirrhosis**

### Sources:
See Appendix.

---

Proprietary & Confidential. HepQuant’s products are not FDA-approved and are for investigational use only in clinical trials under FDA IDE guidelines.
The Dual Cholate Test in a Patient with Liver Disease

Blood Samples at 0, 5, 20, 45, 60, 90 min

DSI 28.7
SHUNT 52.1%

IV 13C-CA, Systemic Hepatic Filtration Rate (Systemic HFR)

PO d4-CA, Portal HFR

Serum Concentration (μM)

Time (minutes)

IV Curve
Oral Curve
Endogenous
Key Discussion Points

• Recent Experience in Clinical Trials
• Update on Regulatory Pathways
• New research and development
Recent Experience in Clinical Trials
Hepion Pharmaceuticals Announces Initiation of Dosing in Phase 2 'ALTITUDE-NASH' Liver Function Trial

ALTITUDE-NASH is a Phase 2, randomized, multi-center, open-label study to evaluate the safety and efficacy of rencofilstat in 60 adult subjects. Subjects included in the trial will be presumed F3, based on either historical biopsy or by using the AGILE 3+ criteria as defined by a screening Fibroscan score alongside common clinical and laboratory parameters. Subjects will be randomized to receive a once daily, oral dose of 75, 150, or 225 mg rencofilstat soft gelatin capsules (20 subjects in each dosing cohort) over a period of four months. The HepQuant ‘SHUNT’ test, a measure of hepatic function, will be performed at baseline, and changes in Disease Severity Index (‘DSI’) relative to baseline measurements will be determined at days 60 and 120. Other NASH biomarkers will be collected throughout the study duration.

“When evaluating hepatic drug efficacy, clinicians and regulatory agencies rely on the assessment of many parameters, including liver fat content, inflammation, ballooning, and fibrosis, which require an invasive liver biopsy,” stated Greg Everson, MD, CEO and Chief Medical Officer of HepQuant. “Although biopsy is the gold standard, it measures only surrogates to liver function and does not truly determine the extent of hepatic impairment or improvement with clinical interventions. HepQuant’s non-invasive, blood-based technology determines a DSI score that relies on liver-specific uptake of cholate to measure hepatic and portal blood flow; and portal-systemic shunt in patients with chronic liver disease, providing a direct assessment of liver function and physiology. To date, HepQuant’s procedure has been successfully utilized in 26 studies with over 1,100 subjects.”
BI 685509 improves first-pass hepatic extraction of cholate in a dose-dependent manner within 27 days: A randomized controlled trial with 6 subjects per arm

Detecting early signal
Small Sample Size

Hepatology 2021
Presented at AASLD 2021
BI 685509 selectively enhanced hepatic uptake of cholate from the portal circulation

Hitting the drug target

Hepatology 2021
Presented at AASLD 2021
Hepatology 2022; Presented at ACP and AASLD Meetings in 2022.
HepQuant Test Parameters are more predictive of Drug AUC than Child-Pugh Score

<table>
<thead>
<tr>
<th>Multivariable Regression</th>
<th>Port HFR</th>
<th>STAT</th>
<th>DSI</th>
<th>SHUNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>HQ Variable</td>
<td>0.06</td>
<td>0.0101</td>
<td>0.0143</td>
<td>0.0024</td>
</tr>
<tr>
<td>CP Score</td>
<td>0.09</td>
<td>0.89</td>
<td>0.31</td>
<td>0.40</td>
</tr>
<tr>
<td>Age</td>
<td>0.14</td>
<td>0.89</td>
<td>0.36</td>
<td>0.73</td>
</tr>
<tr>
<td>Gender</td>
<td>0.34</td>
<td>0.15</td>
<td>0.30</td>
<td>0.16</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>0.57</td>
<td>0.30</td>
<td>0.59</td>
<td>0.49</td>
</tr>
<tr>
<td>BMI</td>
<td>0.43</td>
<td>0.44</td>
<td>0.32</td>
<td>0.95</td>
</tr>
<tr>
<td>Coeff of Determination, $r^2$</td>
<td><strong>0.8187</strong></td>
<td><strong>0.8591</strong></td>
<td><strong>0.8519</strong></td>
<td><strong>0.8851</strong></td>
</tr>
</tbody>
</table>

Hepatology 2022; Presented at ACP and AASLD Meetings in 2022.
Unique Attributes of Our PIVOTAL Study
(Representative of the current population in the United Stages undergoing EGD Screening for Varices)

• US only – 27 clinical study sites throughout the US
• The etiology of liver disease was nonalcoholic fatty liver disease in 50% of the cases (total n=306)
• Average BMI 35 kg/m²
• Average age 62 years

• PIVOTAL Study – older, heavier US population with NAFLD

• Literature – younger, leaner Europeans/Asians with viral hepatitis

HepQuant’s products are not FDA-approved and are for investigational use only in clinical trials under FDA IDE guidelines. The information provided in this slide deck is proprietary and confidential.
**SHUNT-V Pivotal Study: STATIN / Metformin Treatment Effect**

In Multivariable Analysis the Use of STATINs or METFORMIN were Independently Associated with Lower SHUNT% and Lower DSI

<table>
<thead>
<tr>
<th></th>
<th>Impact on SHUNT%</th>
<th>Impact on DSI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Decline in SHUNT%</td>
<td>p</td>
</tr>
<tr>
<td>Statin</td>
<td>-6.3%</td>
<td>0.0132</td>
</tr>
<tr>
<td>Metformin</td>
<td>-5.9%</td>
<td>0.0475</td>
</tr>
<tr>
<td>Diabetes Diagnosis</td>
<td>-1.4%</td>
<td>0.64</td>
</tr>
<tr>
<td>NASH Diagnosis</td>
<td>-1.3%</td>
<td>0.61</td>
</tr>
</tbody>
</table>

The combined effect of the use of STATINs plus METFORMIN was 20% less portal-systemic shunting (lower SHUNT%) and 20% better function (lower DSI).
Update on Regulatory Pathways
STAT and SHUNT Timelines*

* Contingent upon FDA review and decisions.
New Research and Development
Next Generation Tests: Reducing Samples and Testing Time

SHUNT
- 90 minutes
- 5 BLOOD SAMPLES

STAT
- 1 BLOOD SAMPLE

Next Gen
- 60 minutes
- 1 BLOOD SAMPLE
- Enhanced test parameters

Compartmental Model
Artificial Intelligence
Machine Learning
Appendix: Sources for TAM Estimates


