EDISON

Hepion Pharmaceuticals

Clinical update

First data on liver enzymes encouraging

Pharma & biotech

Hepion has announced interim results from its ongoing Phase IIa study of CRV431 in non-alcoholic steatohepatitis (NASH). The preliminary results are from the low-dose arm of the study (75mg, n=12) and showed a 18.4% decline in alanine aminotransferase (ALT) and a 12.1% decline in aspartate aminotransferase (AST) liver biomarkers after 28 days. Although these data were underpowered for significance, this is the first indication of meaningful clinical activity in this patient group. This is the first look at the potential for this drug and, although small, it is very encouraging.

Year end	Revenue ($m)	PBT* ($m)	EPS* ($)	DPS ($)	P/E (x)	Yield (%)
12/18	0.0	(9.8)	(50.18)	0.0	N/A	N/A
12/19	0.0	(7.9)	(3.26)	0.0	N/A	N/A
12/20e	0.0	(17.5)	(1.65)	0.0	N/A	N/A
12/21e	0.0	(18.5)	(0.58)	0.0	N/A	N/A

Note: *PBT and EPS are normalised, excluding amortisation of acquired intangibles, exceptional items and share-based payments.

Study designed to provide rapid feedback on activity

The Phase IIa AMBITION study is exploratory, biomarker driven and designed to identify whether CRV431 has the potential to provide a clinical benefit in NASH patients. The course of the study is relatively short (28 days) because it is not designed to observe the clinical resolution of NASH, but rather early indications of clinical activity, such as the ALT and AST biomarkers presented in these data. We expect these data to be analysed with the company's AI-driven biomarker platform, AI-POWR, after completing dosing in the high-dose (225mg) cohort in Q121.

Data very preliminary but in the right direction

These data are very preliminary because they lack details such as baseline characteristics or a statistical analysis, but they are consistent with what one would expect from a drug that is active in this patient group. Little change was seen in the placebo group by comparison (0.65% reduction in ALT and a 2.52% increase in AST at 28 days). Moreover, these data appear to be consistent with observations in other drugs that are being advanced for the treatment of NASH such as obeticholic acid (OCA) and resmetirom.

Valuation: Increased to $102.4m from $52.5m

We have increased our valuation to $102.4m from $52.5m, although it is lower on a per share basis: $3.20 per basic share versus $5.82 previously. The company underwent a $34.5m offering ($31.7m net) in November 2020, which we believe will be sufficient to finance clinical development until approximately 2023. Additionally, we have increased the probability of success for CRV431 to 15% from 10% following the initial data from the Phase IIa study.

13 January 2021

Price	**US$2.21**
Market cap	**US$71m**

Net cash ($m) at Q320 + offering	45.2
Shares in issue	32.0m
Free float	99.8%
Code	HEPA
Primary exchange	NASDAQ
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	27.0	(31.6)	(59.1)
Rel (local)	22.4	(36.4)	(64.9)

52-week high/low	US$5.74	US$1.15

Business description

Hepion Pharmaceuticals is a clinical-stage biopharmaceutical company focused on developing therapeutics for chronic liver disease. The company's lead asset is CRV431, a cyclophilin inhibitor being developed for the treatment of non-alcoholic steatohepatitis.

Next events

Phase IIa high-dose cohort complete	Q121

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Edison profile page

Improvement in liver enzymes is first indication that CRV431 might be active

The primary endpoints of the Phase IIa AMBITION study are to determine the safety, tolerability and pharmacokinetic profile of CRV431 in NASH patients. However, we expect the study to provide useful early insight into the efficacy of the compound. The gold standard for evaluating NASH drugs is improvement in liver fibrosis, but this a very difficult endpoint to assess under the best conditions and would require an extended clinical study to allow patients sufficient time to develop a meaningful and measurable difference in fibrosis. Instead, Hepion opted to carry out a short biomarker study to serve as a 'first look' at the activity of the product before moving to more cumbersome studies. The AMBITION study is collecting a range of biomarker data (in addition to the ALT and AST levels presented in these initial data) that the company anticipates will provide a picture of the drug's clinical activity without having to wait for improvement in fibrosis. Hepion intends to analyse these data with its proprietary AI-POWR platform, although what insight this can provide remains to be seen.

ALT and AST are enzymes that are released from the liver when it is under stress and are widely used biomarkers for liver function. At 28 days after dosing, patients in the 75mg arm (n=12) showed an 18.4% decline in ALT and a 12.1% decline in AST, compared to a 0.65% reduction and a 2.52% increase respectively in the placebo arm (n=6). These data were not statistically significant in this small patient group, but are consistent with what one might expect if the drug were active. These improvements are roughly consistent with what was seen at early timepoints with OCA in its pivotal Phase III study (although detailed data have not been provided apart from graphs). OCA is the NASH treatment advanced by Intercept Pharmaceuticals, which recently received a complete response letter and a request for more data from the FDA. Data from the Phase II study of Madrigal's resmetirom showed similar reductions in these enzymes (similarly, early data are not broken out). It is worth noting the earliest timepoint for the Madrigal data is after dosing for 12 weeks, three times longer than the data presented for CRV431.

The data from Hepion's release are very limited, but this is the first window that we have into the activity of this drug in this patient population and these data are consistent with an active drug profile. Caution should be taken when drawing conclusions from such early data, especially for data that do not reach statistical significance, but any information on activity at this stage is helpful. The data presented here are consistent with a drug that would be having an active impact on liver health, but more data will be needed to draw more definitive conclusions. The high-dose (225mg) cohort of the study is planned to complete dosing in Q121 and we expect the complete analysis of the study sometime after that. Additionally, the Phase Ib multiple ascending dose study has been completed and we await a complete analysis of the data (although it was noted previously that no serious adverse events were observed for the primary endpoint of safety). This study examined doses of CRV431 up to 375mg in healthy volunteers.

Valuation

We have increased our valuation to $102.4m from $52.5m, although it is lower on a per share basis at $3.20 per basic share from $5.82. This is driven in large part by the offering completed in Q420 (23m shares issued at $1.50 each), increasing net cash to $45.2m (Q320 pro-forma plus offering) from $17.4m (as of Q220) in our last report. We have also increased the probability of success for CRV431 from 10% to 15% to reflect these newly reported data. We acknowledge these data are very preliminary, but they are incrementally improving our confidence in the program. Our initial

assessment of risk was very conservative in the absence of efficacy data in NASH patients and, when complete data from the Phase IIa study are released, we may adjust our valuation further. In addition to the above changes, we have rolled forward our NPVs and adjusted our near term R&D spending as described below.

Exhibit 1: Valuation of Hepion

Program	Market	Prob. of success	Launch Year	Peak Revenue ($m)	Valuation ($m)
CRV431	US	15%	2026	370.8	37.76
	Europe	15%	2027	373.0	30.95
	R&D & Milestones				(11.51)
Total					57.20
Net cash and equivalents pro-forma (Q320 + offering)					45.23
Total firm value ($m)					102.44
Total basic shares (m)					32.03
Value per basic share ($)					3.20
Convertible preferred stock					0.02
Dilutive options and warrants (m)					0.60
Total diluted shares					32.65
Value per diluted share ($)					3.17

Source: Hepion reports, Edison Investment Research.

Financials

We have adjusted our R&D spending forecasts to align with the current timeline, which includes the delay of a $3m milestone payable to former Ciclofilin shareholders (payable on the completion of a Phase II study) to 2021. This is partially offset in the 2020 forecast by increased R&D and S&A expenses reported in the third quarter ($3.8m and $2.4m respectively, compared to $3.0 and $1.8m in Q220). These effects are carried forward and the net effect on our 2021 forecasts is to increase the expected net loss to $20.9m from $11.5m previously. We assume that some of these expenses are associated with Hepion's exploratory COVID-19 program.

Hepion underwent a major recapitalization in November 2020, with the offering of 23m in new stock at $1.50 ($34.5m total, $31.7m net). This should provide sufficient capital for the company to fund operations into 2023, including initiating the next stage of its clinical development, which we expect to be a longer-term Phase IIb study focusing on fibrosis. We have reduced our expected financing requirement for the company to $100m ($55m in 2023, and $45m in 2025) from $115m previously.

Exhibit 2: Financial summary

$'000	2018	2019	2020e	2021e
31-December	IFRS	IFRS	IFRS	IFRS
INCOME STATEMENT				
Revenue	0.0	0.0	0.0	0.0
Cost of Sales	0.0	0.0	0.0	0.0
Gross Profit	0.0	0.0	0.0	0.0
R&D	(7,593.7)	(3,184.1)	(12,495.6)	(13,537.3)
SG&A	(7,000.4)	(4,586.0)	(7,154.8)	(7,369.4)
EBITDA	(14,340.9)	(7,677.2)	(17,238.0)	(18,522.5)
Normalised operating profit	(14,359.6)	(7,703.9)	(17,266.2)	(18,522.5)
Amortisation of acquired intangibles	0.0	0.0	0.0	0.0
Exceptionals	0.0	0.0	0.0	0.0
Share-based payments	(234.5)	(66.2)	(2,384.2)	(2,384.2)
Reported operating profit	(14,594.2)	(7,770.1)	(19,650.4)	(20,906.7)
Net Interest and financial income	4,608.9	(175.9)	(234.0)	0.0
Joint ventures & associates (post tax)	0.0	0.0	0.0	0.0
Exceptionals	0.0	0.0	0.0	0.0
Profit Before Tax (norm)	(9,750.8)	(7,879.8)	(17,500.1)	(18,522.5)
Profit Before Tax (reported)	(9,985.3)	(7,946.0)	(19,884.3)	(20,906.7)
Reported tax	536.0	1,227.3	(33.5)	(35.3)
Profit After Tax (norm)	(9,227.4)	(6,662.7)	(17,529.6)	(18,553.7)
Profit After Tax (reported)	(9,449.3)	(6,718.7)	(19,917.9)	(20,941.9)
Minority interests	0.0	0.0	0.0	0.0
Deemed Dividend	(8,451.9)	(5,442.9)	(5.3)	0.0
Discontinued operations	0.0	0.0	0.0	0.0
Net income (normalised)	(9,227.4)	(6,662.7)	(17,529.6)	(18,553.7)
Net income (reported)	(17,901.1)	(12,161.6)	(19,923.1)	(20,941.9)
Basic average number of shares outstanding (m)	184	2,043	10,598	32,025
EPS - normalised (c)	(5,018.18)	(326.09)	(165.41)	(57.93)
EPS - diluted normalised ($)	(50.18)	(3.26)	(1.65)	(0.58)
EPS - basic reported ($)	(97.35)	(5.95)	(1.88)	(0.65)
Dividend ($)	0.00	0.00	0.00	0.00
BALANCE SHEET				
Fixed Assets	5,221.2	6,043.9	6,004.0	5,840.0
Intangible Assets	1,870.9	1,870.9	1,870.9	1,870.9
Tangible Assets	32.4	57.2	38.3	38.3
Investments & other	3,317.8	4,115.9	4,094.8	3,930.8
Current Assets	2,968.0	14,388.7	43,432.2	23,033.9
Stocks	0.0	0.0	0.0	0.0
Debtors	0.0	0.0	0.0	0.0
Cash & cash equivalents	2,832.4	13,923.0	42,791.0	22,392.7
Other	135.6	465.7	641.2	641.2
Current Liabilities	(2,849.9)	(1,251.9)	(4,857.4)	(2,852.8)
Creditors	(748.4)	(491.6)	(2,198.0)	(2,577.5)
Tax and social security	0.0	0.0	0.0	0.0
Short term borrowings	(1,440.0)	0.0	0.0	0.0
Other	(661.4)	(760.3)	(2,659.4)	(275.3)
Long Term Liabilities	(3,364.3)	(2,995.1)	(3,534.9)	(3,534.9)
Long term borrowings	0.0	0.0	(176.6)	(176.6)
Other long term liabilities	(3,364.3)	(2,995.1)	(3,358.3)	(3,358.3)
Net Assets	1,975.1	16,185.6	41,043.9	22,486.1
Minority interests	0.0	0.0	0.0	0.0
Shareholders' equity	1,975.1	16,185.6	41,043.9	22,486.1
CASH FLOW				
Op Cash Flow before WC and tax	(14,340.9)	(7,677.2)	(17,238.0)	(18,522.5)
Working capital	(970.5)	(754.6)	3,090.2	(2,004.6)
Exceptional & other	(870.7)	(360.6)	(78.8)	164.0
Tax	536.0	1,227.3	(33.5)	(35.3)
Net operating cash flow	(15,646.0)	(7,565.1)	(14,260.1)	(20,398.3)
Capex	0.0	(51.5)	(11.4)	0.0
Acquisitions/disposals	0.9	0.0	2.2	0.0
Net interest	0.0	0.0	0.0	0.0
Equity financing	12,192.5	19,826.5	42,960.8	0.0
Dividends	0.0	0.0	0.0	0.0
Other	(1,000.0)	(1,119.4)	0.0	0.0
Net Cash Flow	(4,452.6)	11,090.5	28,691.5	(20,398.3)
Opening net debt/(cash)	(5,954.0)	(1,392.4)	(13,922.9)	(42,614.5)
FX	0.0	0.0	0.0	0.0
Other non-cash movements	(109.0)	1,440.0	0.0	0.0
Closing net debt/(cash)	(1,392.4)	(13,922.9)	(42,614.5)	(22,216.1)

Source: Hepion reports, Edison Investment Research.

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