EDISON

Hepion Pharmaceuticals

Clinical update

AMBITION trial shows positive biomarker data

Pharma & biotech

Recently, Hepion released top-line data from its AMBITION Phase IIa trial with CRV431, a cyclophilins inhibitor, in non-alcoholic steatohepatitis (NASH) patients. All primary safety, tolerability and pharmacokinetics were met and support once-a-day dosing. The company plans to conduct a Phase IIb (ASCEND-NASH) trial this year in NASH patients with fibrosis levels 2 or 3 (F2 or F3). The ASCEND-NASH trial will be significantly larger with 300 patients enrolled. The primary endpoint will be a 1-point reduction in fibrosis score in liver biopsies.

Year end	Revenue ($m)	PBT* ($m)	EPS* ($)	DPS ($)	P/E (x)	Yield (%)
12/19	0.0	(7.9)	(3.42)	0.0	N/A	N/A
12/20	0.0	(17.9)	(1.86)	0.0	N/A	N/A
12/21e	0.0	(27.0)	(0.35)	0.0	N/A	N/A
12/22e	0.0	(28.5)	(0.36)	0.0	N/A	N/A

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

Final AMBITION NASH trial results with high dose

Hepion reported that the high dose (225mg) demonstrated a statistically significant 21.1% reduction in alanine transaminases (ALT) levels versus baseline after 28 days. The company has already reported the 75mg dose showed a reduction in liver enzymes of 18.4%. Specifically, CRV431 was safe and well tolerated with pharmacokinetics that support once-a-day dosing, given the half-life is approximately 30 hours.

The ASCEND-NASH Phase IIb trial to begin in Q421

The objective of the study is to determine the efficacy of once daily (QD) oral dosing of CRV431 in biopsy proven NASH F2 and F3 patients compared to placebo. The trial is looking for a 1-point reduction in fibrosis score in liver biopsies (pathologist and AI read). The AI-POWR system is intended to identify biomarkers of CRV431 response from several data sources to identify the NASH patients that could be the best responders in a Phase III trial.

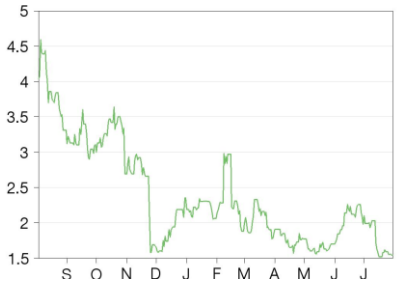
Valuation: Increased to $197.9m from $182.9m

We have adjusted our net present value (NPV) to reflect the positive results from the AMBITION trial. Our probability of success was increased from 15% to 20%. The equity value is now $197.9m, or $2.59 per diluted share, up from $2.40 per share previously. The company has net cash of $115.3m, which we believe should fund operations for the next three years. Despite the positive results, the shares were under pressure. This quarter, Hepion was added to the Russell Microcap Index.

3 August 2021

Price	**$1.54**
Market cap	**US$117m**
Net cash ($m) at end Q121	115.3
Shares in issue	76.2m
Free float	88.7%
Code	HEPA
Primary exchange	Nasdaq
Secondary exchange	N/A

Share price performance



%	1m	3m	12m
Abs	(22.2)	(11.0)	(63.4)
Rel (local)	(24.0)	(15.3)	(73.0)
52-week high/low	US$4.59		US$1.52

Business description

Hepion Pharmaceuticals is a clinical-stage biopharmaceutical company focused on developing therapeutics for chronic liver disease. The lead product candidate is CRV431, a cyclophilin inhibitor being developed to treat NASH.

Next events

Additional data from the AMBISTION NASH trial	2021H221
Start of the Phase 2b ASCEND-NASH	2021Q421

Analyst

Carol Werther +1 646 653 7026

healthcare@edisongroup.com

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AMBITION NASH Phase IIa trial details

This CRV431 trial enrolled patients with NASH and F2 or F3. At day 28 there was a demonstrated reduction in ALT for both the 75mg and 225mg doses, an early efficacy sign in F2 and F3 subjects. The company has reported that its clinical pharmacology group has already developed a population pharmacokinetic-pharmacodynamic, or PK-PD, model which predicts CRV431 blood concentration effect on ALT reductions, which it indicates is not usually possible at this early stage in drug development.

Most of the adverse events were mild and deemed unrelated. Body aches were possibly related. Probably related were constipation and a sensation of the heart beating strongly. There were no serious adverse events. Hepion uses its artificial intelligence platform (AI-POWR), which revealed significant interactions between the drug with collagen-regulating genes. As the AMBITION trial is evaluated further, we expect the company to release additional details of the data.

Exhibit 1: AMBITION biomarker results

Test	Placebo	CRV431 75mg	CRV431 225mg
	n = 14	n = 12	n = 15
ALT (%)	-6.1% (±) 13.3 (mean ± SD)	-18.4 +/- 25.8 (mean ± SD)*	-21.1 ± 21.1 (mean ± SD)*
	-5.2 (median)	-15.9 (median)	-20.0 (median)
Area under the ALT curve AUC (IU*D/L)	1465.1 ± 810.9	1190.5 ± 712.1	859.9 ± 387.0**

Source: Hepion. Note: *Pooled 75mg and 225mg statistically significant versus placebo P<0.05, unpaired t-test. **Statistically significant versus placebo, p<0.05, ANOVA w/ Bonferroni Post-Hoc statistical analysis.

Design of the potential ASCEND-NASH Phase IIb trial

The company plans on beginning a Phase IIb ASCEND-NASH trial in Q421. This trial is expected to enrol 300 biopsy proven NASH subjects with advanced fibrosis (F2/F3). This a multi-centre, triple-blind, placebo-controlled (2:1) study. The current plan is to use the same two doses, 75mg and 225mg, for six months, followed by six months of CRV431 or placebo. There is a three-month observation period at the end of the 12 months. Additional data that will be obtained includes liver biopsies, MRI scans, Fibroscan, ALT, AST, Pro-C3, ELF-Score, fibrosis biomarkers, lipidomics, genomics and proteomics.

Exhibit 2: ASCEND-NASH trial design

F2/F3 NASH Patients (n=300)

Cohort*	Fibrosis Stage	N	6-12 Months	3 Month
A	F2/F3	100	CRV431 low dose	Observation/Follow-up
B		50	Placebo	
C	F2/F3	100	CRV431 high dose	
D		50	Placebo	

*randomized assignment; 2:1 – CRV431:placebo

**final protocol in preparation, subject to change

Source: Hepion

Valuation

We have adjusted our NPV to reflect the positive results from the AMBITION trial. We changed our valuation by increasing the probability of success from 15% to 20%. The new equity valuation is

$197.9m, up from $182.9m previously. Our valuation is now $2.59 per diluted share, up from $2.40 per share previously.

Exhibit 3: Valuation of Hepion

Program	Market	Prob. of success	Launch year	Peak revenue ($m)	Valuation ($m)
CRV431	US	20%	2026	370.8	51.87
	Europe	20%	2027	373.0	42.53
	R&D & milestones				(11.86)
Total					82.55
Net cash and equivalents (Q121)					115.32
Total firm value ($m)					197.87
Total basic shares (m)					76.23
Value per basic share ($)					2.60
Convertible preferred stock					0.02
Dilutive options and warrants (m)					0.69
Total diluted shares (m)					76.94
Value per diluted share ($)					2.59

Source: Hepion reports, Edison Investment Research

Financials

Hepion ended Q121 with $115.3m in net cash ($115.5m gross cash offset by $0.2m debt). On 16 February 2021, Hepion, conducted a public offering of 44,200,000 shares of Hepion common stock at a price of $2.00 per share. This resulted in net proceeds of approximately $82.1m, after deducting underwriting discount, commissions and offering expenses. We expect this to be enough cash to complete the ASCEND-NASH Phase IIb trial and sustain the company for the next three years. Hepion's approximate burn rate is $5–7m quarterly; this is likely to increase as the ASCEND-NASH trial is underway. We estimate the company may need additional financing of $25m (in 2025).

This quarter, Hepion was included in the Russell Microcap Index.

Exhibit 4: Financial summary

$'000	2019	2020	2021e	2022e
31-December	IFRS	IFRS	IFRS	IFRS
INCOME STATEMENT				
Revenue	0.0	0.0	0.0	0.0
Cost of Sales	0.0	0.0	0.0	0.0
Gross Profit	0.0	0.0	0.0	0.0
R&D	(3,184.1)	(11,997.3)	(21,000.0)	(22,250.0)
SG&A	(4,586.0)	(8,148.8)	(8,393.3)	(8,645.1)
EBITDA	(7,677.2)	(17,732.2)	(27,013.9)	(28,515.7)
Normalised operating profit	(7,703.9)	(17,766.7)	(27,013.9)	(28,515.7)
Amortisation of acquired intangibles	0.0	0.0	0.0	0.0
Exceptionals	0.0	0.0	0.0	0.0
Share-based payments	(66.2)	(2,379.4)	(2,379.4)	(2,379.4)
Reported operating profit	(7,770.1)	(20,146.1)	(29,393.3)	(30,895.1)
Net Interest and financial income	(175.9)	(177.3)	0.0	0.0
Joint ventures & associates (post tax)	0.0	0.0	0.0	0.0
Exceptionals	0.0	0.0	0.0	0.0
Profit Before Tax (norm)	(7,879.8)	(17,944.0)	(27,013.9)	(28,515.7)
Profit Before Tax (reported)	(7,946.0)	(20,323.4)	(29,393.3)	(30,895.1)
Reported tax	908.7	(30.6)	(44.2)	(46.5)
Profit After Tax (norm)	(6,978.7)	(17,971.0)	(27,054.6)	(28,558.6)
Profit After Tax (reported)	(7,037.3)	(20,353.9)	(29,437.5)	(30,941.6)
Minority interests	0.0	0.0	0.0	0.0
Deemed Dividend	(5,442.9)	(5.3)	0.0	0.0
Discontinued operations	0.0	0.0	0.0	0.0
Net income (normalised)	(6,978.7)	(17,971.0)	(27,054.6)	(28,558.6)
Net income (reported)	(12,480.3)	(20,359.2)	(29,437.5)	(30,941.6)
Basic average number of shares outstanding (m)	2.0	9.7	76.2	80.0
EPS - normalised (c)	(341.55)	(185.69)	(35.49)	(35.68)
EPS - diluted normalised ($)	(3.42)	(1.86)	(0.35)	(0.36)
EPS - basic reported ($)	(6.11)	(2.10)	(0.39)	(0.39)
Dividend ($)	0.00	0.00	0.00	0.00
BALANCE SHEET				
Fixed Assets	6,222.9	6,011.0	5,847.0	5,683.0
Intangible Assets	1,870.9	1,870.9	1,870.9	1,870.9
Tangible Assets	57.2	108.4	108.4	108.4
Investments & other	4,294.8	4,031.6	3,867.6	3,703.6
Current Assets	14,388.7	42,634.3	97,765.2	69,552.1
Stocks	0.0	0.0	0.0	0.0
Debtors	0.0	0.0	0.0	0.0
Cash & cash equivalents	13,923.0	40,726.8	95,857.7	67,644.7
Other	465.7	1,907.5	1,907.5	1,907.5
Current Liabilities	(1,609.5)	(4,661.8)	(4,563.2)	(4,748.4)
Creditors	(491.6)	(3,722.4)	(3,623.8)	(3,809.0)
Tax and social security	0.0	0.0	0.0	0.0
Short term borrowings	0.0	0.0	0.0	0.0
Other	(1,117.9)	(939.4)	(939.4)	(939.4)
Long Term Liabilities	(3,385.4)	(3,463.0)	(3,463.0)	(3,463.0)
Long term borrowings	0.0	(176.6)	(176.6)	(176.6)
Other long term liabilities	(3,385.4)	(3,286.5)	(3,286.5)	(3,286.5)
Net Assets	15,616.7	40,520.4	95,585.9	67,023.7
Minority interests	0.0	0.0	0.0	0.0
Shareholders' equity	15,616.7	40,520.4	95,585.9	67,023.7
CASH FLOW				
Op Cash Flow before WC and tax	(7,677.2)	(17,732.2)	(27,013.9)	(28,515.7)
Working capital	(826.2)	1,628.8	(98.6)	185.2
Exceptional & other	29.7	(31.2)	164.0	164.0
Tax	908.7	(30.6)	(44.2)	(46.5)
Net operating cash flow	(7,565.1)	(16,165.2)	(26,992.7)	(28,213.0)
Capex	(51.5)	(88.0)	0.0	0.0
Acquisitions/disposals	0.0	2.2	0.0	0.0
Net interest	0.0	0.0	0.0	0.0
Equity financing	19,826.5	42,878.3	82,123.6	0.0
Dividends	0.0	0.0	0.0	0.0
Other	(1,119.4)	0.0	0.0	0.0
Net Cash Flow	11,090.5	26,627.3	55,130.9	(28,213.0)
Opening net debt/(cash)	(1,392.4)	(13,922.9)	(40,550.3)	(95,681.1)
FX	0.0	0.0	0.0	0.0
Other non-cash movements	1,440.0	0.0	0.0	0.0
Closing net debt/(cash)	(13,922.9)	(40,550.3)	(95,681.1)	(67,468.1)

Source: Company reports, Edison Investment Research

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Frankfurt +49 (0)69 78 8076 960
Schumannstrasse 34b
60325 Frankfurt
Germany

London +44 (0)20 3077 5700
280 High Holbom
London, WC1V 7EE
United Kingdom

New York +1 646 653 7026
1185 Avenue of the Americas
3rd Floor, New York, NY 10036
United States of America

Sydney +61 (0)2 8249 8342
Level 4, Office 1205
95 Pitt Street, Sydney
NSW 2000, Australia